# LIBRA JOURNAL CLUB
# 25-SEP-1-OCT-2023

**Our legal office confirmed that articles NOT OPEN ACCESS cannot be distributed to the members of the list. Thus, we will transmit only the titles of articles.**
**ABSTRACTS of almost all these articles are available from PubMed, and full papers can be obtained through your institutions' library.**
**OPEN ACCESS articles are available by accessing the articles from PubMed using just the PMID for the search (eg PMID: 35514131 without . at the end)**

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

1

Respir Res

- 
- 
- 

. 2023 Sep 29;24(1):239.

doi: 10.1186/s12931-023-02545-9.

# Comparative cardiovascular safety of LABA/LAMA FDC versus LABA/ICS FDC in patients with chronic obstructive pulmonary disease: a population-based cohort study with a target trial emulation framework

Chun-Yu Chen[1,2], Sheng-Wei Pan[3,4], Chia-Chen Hsu[2,5], Jason J Liu[1], Hiraku Kumamaru[6], Yaa-Hui Dong[7,8,9]

Affiliations expand

- PMID: 37775734

- DOI: 10.1186/s12931-023-02545-9

**Abstract**

**Background:** Use of combinations of long-acting $\beta_2$ agonists/long-acting muscarinic antagonists (LABA/LAMA) in patients with chronic obstructive pulmonary disease (COPD) is increasing. Nevertheless, existing evidence on cardiovascular risk associated with LABA/LAMA versus another dual combination, LABA/inhaled corticosteroids (ICS), was limited and discrepant.

**Aim:** The present cohort study aimed to examine comparative cardiovascular safety of LABA/LAMA and LABA/ICS with a target trial emulation framework, focusing on dual fixed-dose combination (FDC) therapies.

**Methods:** We identified patients with COPD who initiated LABA/LAMA FDC or LABA/ICS FDC from a nationwide Taiwanese database during 2017-2020. The outcome of interest was a hospitalized composite cardiovascular events of acute myocardial infarction, unstable angina, heart failure, cardiac dysrhythmia, and ischemic stroke. Cox regression models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for composite and individual cardiovascular events after matching up to five LABA/LAMA FDC initiators to one LABA/ICS FDC initiator using propensity scores (PS).

**Results:** Among 75,926 PS-matched patients, use of LABA/LAMA FDC did not show a higher cardiovascular risk compared to use of LABA/ICS FDC, with a HR of 0.89 (95% CI, 0.78-1.01) for the composite events, 0.80 (95% CI, 0.61-1.05) for acute myocardial infarction, 1.48 (95% CI, 0.68-3.25) for unstable angina, 1.00 (95% CI, 0.80-1.24) for congestive heart failure, 0.62 (95% CI, 0.37-1.05) for cardiac dysrhythmia, and 0.82 (95% CI, 0.66-1.02) for ischemic stroke. The results did not vary substantially in several pre-specified sensitivity and subgroup analyses.

**Conclusion:** Our findings provide important reassurance about comparative cardiovascular safety of LABA/LAMA FDC treatment among patients with COPD.

**Keywords:** Cardiovascular events; Chronic obstructive pulmonary disease; Cohort study; Fixed-dose combinations (FDC); Long-acting β2 agonists/inhaled corticosteroids (LABA/ICS); Long-acting β2 agonists/long-acting muscarinic antagonists (LABA/LAMA); Target trial emulation framework.



- 54 references

supplementary info

Grants and fundingexpand

2

BMJ Open

. 2023 Sep 29;13(9):e074336.

doi: 10.1136/bmjopen-2023-074336.

# Implementing a package of essential non-communicable diseases interventions in low- and middle-income countries: a realist review protocol

Anju Vaidya[1], Padam Simkhada[2], Andrew Lee[3], Susan Jones[4], Ferdinand C Mukumbang[5]

Affiliations expand

- PMID: 37775288

- DOI: 10.1136/bmjopen-2023-074336

**Abstract**

**Introduction:** The burden of non-communicable diseases (NCDs) is increasing rapidly, particularly in low- and middle-income countries (LMIC), accounting for 85% of premature deaths in the region. LMICs have been facing an increasing trend of a double burden of disease (infectious diseases and NCDs) that has led to multiple challenges in prioritising strategies for NCDs control amidst limited resources. Evidence indicates that measures such as the WHO's package of essential non-communicable (PEN) diseases interventions can prevent and control NCDs. However, because of the complexity of such health

interventions, there is limited evidence that explains how the intervention works, for whom and in what context. We aim to unpack the causal mechanisms explaining how, why, for whom and in what context PEN prevents and controls NCDs.

**Methods and analysis:** We propose a realist review to understand how, why, for whom and under what circumstances PEN works or does not work. The review process includes five steps applied iteratively throughout the study: clarification of review scope, searching for evidence, appraising and extracting data, synthesising evidence and drawing conclusions, and disseminating the findings. Programme theories will be developed using the realist logic for theory formulation-Retroductive Theorising. The context-mechanism-outcome (CMO) heuristic tool will be used to develop the programme theories. Portions of the reviewed documents describing constructs of context, mechanism and outcomes will be coded inductively and extracted. These extracted constructs will then be linked abductively to formulate CMO configurations.

**Ethics and dissemination:** Formal ethical approval is not required for this review. Study findings will be disseminated through publications in peer-reviewed journals, conference presentations and formal and informal reports.

**Keywords:** coronary heart disease; health policy; organisation of health services; primary health care; public health; pulmonary disease, chronic obstructive.



# Conflict of interest statement

Competing interests: None declared.

. 2023 Sep 29.

doi: 10.1513/AnnalsATS.202211-975OC. Online ahead of print.

# Predictors of Patient-Reported and Pharmacy Refill Measures of Maintenance Inhaler Adherence in Veterans with COPD

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

Affiliations expand

- PMID: 37774091

- DOI: 10.1513/AnnalsATS.202211-975OC

**Abstract**

**Rationale:** Suboptimal adherence to inhaled medications in patients with chronic obstructive pulmonary disease (COPD) remains a challenge.

**Objectives:** Examine the sociodemographic, clinical characteristics, and medication beliefs associated with adherence measured by self-report and pharmacy data.

**Methods:** A cross-sectional analysis of data from a prospective observational cohort study of patients with COPD was completed. Participants underwent spirometry and completed questionnaires regarding sociodemographic data, inhaler use, dyspnea, social support, psychological and medical comorbidities, and medication beliefs (Beliefs about Medicines Questionnaire, BMQ). Self-reported adherence with inhaled medications was measured with the Adherence to Refills and Medications Scale (ARMS) and pharmacy-based adherence was calculated from administrative data using the ReComp score. Multivariable linear regression was used to examine the sociodemographic, clinical, and medication belief factors associated with both adherence measures.

**Results:** Among 269 participants with both ARMS and ReComp data, adherence was the same for each measure (38.3%), however only 18% of participants were adherent by both measures. In multivariable adjusted analysis, a 10-year increase in age (β 0.54, 0.14-0.94 95% confidence interval) and number of maintenance inhalers (β 0.53, 0.04-1.02) were associated with increased adherence by self-report. Improved ReComp adherence was associated with chronic prednisone use (β 0.18, 0.04-0.31) and number of maintenance inhalers (β 0.11, 0.05-0.17). In adjusted analyses examining patient beliefs on medications, an increase in the BMQ general Harm score (β -0.15, -0.26 to -0.04) and COPD-specific

Concerns score (-0.12, -0.20 to -0.05) was associated with reduced self-reported adherence. No significant associations between ReComp adherence and BMQ were found in adjusted analyses.

**Conclusions:** Adherence to COPD inhaled medications was poor as measured by either self-report or pharmacy refill data. There were notable differences in factors associated with adherence based on the method of adherence measurement. Older age, chronic prednisone use, number of prescribed maintenance inhalers, and patient beliefs about medication safety were associated with adherence. Overall, fewer variables were associated with adherence by pharmacy refill. Pharmacy refill and self-report adherence may measure distinct aspects of adherence and be affected by different factors. These results also underscore the importance of addressing patient beliefs when developing interventions to improve medication adherence.



4

Am J Respir Crit Care Med

. 2023 Sep 29.

doi: 10.1164/rccm.202309-1630ED. Online ahead of print.

# Who Drives the COPD Bus? Protease-rich EVs in Cigarette Smoke Associated Alveolar Damage

Vaughn D Craddock[1], Navneet K Dhillon[2]

Affiliations expand

- PMID: 37774012

- DOI: 10.1164/rccm.202309-1630ED

***No abstract available***

full text links

Proceed to details

Cite

Share

5

**Editorial**

Ann Am Thorac Soc

. 2023 Oct;20(10):1402-1403.

doi: 10.1513/AnnalsATS.202307-618ED.

# The Autonomous Nervous System: A Novel and Potentially Modifiable Risk Factor for Chronic Obstructive Pulmonary Disease in the Population?

Viktor Hamrefors[1,2]

Affiliations expand

- PMID: 37772941

- DOI: 10.1513/AnnalsATS.202307-618ED

***No abstract available***

## Comment on

- Cardiovascular Autonomic Function and Incident Chronic Obstructive Pulmonary Disease Hospitalizations in Atherosclerosis Risk in Communities.
MacDonald DM, Ji Y, Adabag S, Alonso A, Chen LY, Henkle BE, Juraschek SP, Norby FL, Lutsey PL, Kunisaki KM.Ann Am Thorac Soc. 2023 Oct;20(10):1435-1444. doi: 10.1513/AnnalsATS.202211-964OC.PMID: 37364277



**Editorial**

Eur J Heart Fail

. 2023 Sep 28.

doi: 10.1002/ejhf.3041. Online ahead of print.

# Sodium-glucose co-transporter 2 inhibitors in heart failure with preserved ejection fraction and chronic obstructive pulmonary disease - no heterogeneity

Camilla Hage[1,2], Lars H Lund[1,2]

Affiliations expand

- PMID: 37771264

- DOI: 10.1002/ejhf.3041

***No abstract available***

supplementary info

Publication typesexpand

full text links

Proceed to details

Cite

Share

7

Sr Care Pharm

- 
- 
- 

. 2023 Oct 1;38(10):404-415.

doi: 10.4140/TCP.n.2023.404.

# Chronic Obstructive Pulmonary Disease, Part 5: Clinical Pearls for Comorbid COPD

Kalin M Clifford[1], Mary S Klein[1], Lindsay A Courtney[1], Alaina Van Dyke[1], Meredith Sigler[1], Rachel L Basinger[1]

Affiliations expand

- PMID: 37771052

- DOI: 10.4140/TCP.n.2023.404

**Abstract**

Chronic obstructive pulmonary disease (COPD) is often diagnosed with other comorbid conditions. This can complicate therapy overall by contributing to adverse events leading to poor outcomes to not only COPD, but other comorbid conditions. This manuscript will discuss common comorbid conditions often seen with COPD, update vaccination recommendations for COPD patients, and provide information regarding smoking cessation in COPD. The senior care pharmacist has an important role where they can recommend medication adjustments to potentially avoid these adverse events, immunize their patients appropriately, and provide assistance with smoking cessation to improve not only COPD outcomes but outcomes associated with other comorbid conditions.



J Clin Psychol Med Settings

. 2023 Sep 28.

doi: 10.1007/s10880-023-09976-y. Online ahead of print.

# Psychometric Properties of the Short Scale Anxiety Sensitivity Index Among Adults with Chronic Respiratory Disease

Heather L Clark[1], Laura J Dixon[1], Sujith Ramachandran[2], Patric J Leukel[2], Aaron A Lee[3]

Affiliations expand

- PMID: 37770802

- DOI: 10.1007/s10880-023-09976-y

**Abstract**

Approximately one-third of adults with chronic respiratory disease (CRD) have comorbid depressive and anxiety disorders; yet these disorders are often unrecognized in this patient population. Transdiagnostic processes such as anxiety sensitivity (AS) are useful for identifying mechanisms underlying psychological and heath conditions. The Short-Scale AS Index (SSASI) is a brief self-report measure of AS which has potential clinical utility among CRD populations to evaluate psychological distress and inform comprehensive care. The present study investigated the psychometric properties of the SSASI among adults with CRDs. Participants were recruited from a web-based panel of adults with CRDs (n = 768; 49.3% female; 57.8% White) including adults with asthma only (n = 230), COPD only (n = 321), or co-occurring asthma and COPD (n = 217). Participants completed a battery of self-report questionnaires assessing psychological and medical symptoms. Analyses were conducted to examine the factor structure and measurement invariance across CRD groups. Convergent validity and criterion validity of the SSASI were assessed within each group. Results supported partial measurement invariance across CRD groups. The SSASI demonstrated high reliability, convergent validity, and criterion validity with each CRD group. Findings from this study and existing work indicate that the SSASI is an effective and economical assessment tool for identifying patients CRD who may benefit from psychological interventions to reduce AS.

**Keywords:** Anxiety sensitivity; Asthma; Chronic obstructive pulmonary disease; Respiratory disease.

. 2023 Sep 28;62(3):2301470.

doi: 10.1183/13993003.01470-2023. Print 2023 Sep.

# All roads lead to COPD… or not?

Alvar Agusti[1 2 3 4], Rosa Faner[5 3 4 6]

Affiliations expand

- PMID: 37770089

- DOI: 10.1183/13993003.01470-2023

***No abstract available***

## Conflict of interest statement

Conflict of interest: A. Agusti reports grants (paid to institution) from GSK and AstraZeneca, consulting fees from GSK, AstraZeneca, Chiesi, Menarini and Sanofi, payment or honoraria for lectures, presentations, manuscript writing or educational events from GSK, AstraZeneca, Chiesi, Menarini and Zambon, and is the chair of the board of directors of GOLD (unpaid). R. Faner reports grants from GSK, Menarini, AstraZeneca and Chiesi, consulting fees from AstraZeneca, and payment or honoraria for lectures, presentations, manuscript writing or educational events from AstraZeneca, Chiesi and Menarini.

## Comment on

- From pre-COPD to COPD: a Simple, Low cost and easy to IMplement (SLIM) risk calculator.
  Divo MJ, Liu C, Polverino F, Castaldi PJ, Celli BR, Tesfaigzi Y.Eur Respir J. 2023 Sep 28;62(3):2300806. doi: 10.1183/13993003.00806-2023. Print 2023 Sep.PMID: 37678951 **Free PMC article.**

10

Ann Am Thorac Soc

- 
- 
- 

. 2023 Sep 28.

doi: 10.1513/AnnalsATS.202305-458OC. Online ahead of print.

# Lifestyle Intervention and Excess Weight in COPD: INSIGHT COPD Randomized Clinical Trial

David H Au[1,2], Emily Gleason[3], Rachel Hunter-Merrill[4], Anna E Barón[5], Margaret Collins[6], Corina Ronneberg[7], Nan Lv[8], Peter Rise[4], Travis Hee Wai[9], Robert Plumley[10], Stephen R Wisniewski[11], Frank Sciurba[12], Dong-Yun Kim[13], Paul Simonelli[14], Jerry A Krishnan[15], Christine H Wendt[16], Laura C Feemster[17,18], Gerard J Criner[19], Veeranna Maddipati[20], Arjun Mohan[20,21], Jun Ma[8,22]; Pulmonary Trials Cooperative

Affiliations expand

- PMID: 37769182

- DOI: 10.1513/AnnalsATS.202305-458OC

**Abstract**

Rationale Being overweight or obese is common among patients with chronic obstructive pulmonary disease (COPD), but whether interventions targeted at weight loss improve functional impairments is unknown. Objectives INSIGHT tested whether a pragmatic low-intensity lifestyle intervention would lead to better physical functional status among participants with overweight or obesity and COPD. Methods The trial was a 12-month, multicentered, patient-level pragmatic clinical trial. Participants were recruited from April 2017 to August 2019 from 38 sites across the U.S. and randomized to either usual care or usual care plus lifestyle intervention. The intervention was a self-directed video program delivering the Diabetes Prevention Program's Group Lifestyle Balance curriculum. Results The primary outcome was six-minute walk test (6MWT) distance at 12 months. Priority secondary outcomes were post-walk modified Borg dyspnea at 12 months and weight at

12 months. Participants (N=684; mean 67.0 [SD 8.0] years, 41.2% female) on average were obese (BMI, 33.0 [SD 4.6] kg/m2) with moderate COPD (FEV1% predicted, 58.1% [SD 15.7%]). At 12 months, participants randomized to the intervention walked farther (adjusted difference, 42.3 ft [95%CI: 7.9, 76.7]; P=0.02), had less dyspnea at end of the 6MWT (adjusted difference, -0.36 [95%CI: -0.63, -0.09]; P=0.008) and greater weight loss (adjusted difference, -1.34 kg [95%CI: -2.33, -0.34]; P=0.008) than controls. The intervention did not improve the odds of achieving clinically meaningful thresholds of walk distance (98.4 ft) or dyspnea (1 unit) but did achieve meaningful thresholds of weight loss (3 and 5% weight loss). Conclusions Among participants with COPD who were overweight or obese, a self-guided low intensity video-based lifestyle intervention led to modest weight loss but did not lead to clinically important improvements in physical functional status and dyspnea. Clinical Trial Registration ClinicalTrials.gov; Registration number NCT02634268 Primary Source of Funding Supported by 1U01HL128868 (NIH/NHBLI) and the Network Management Core for the Pulmonary Trials Cooperative (NIH/NHLBI U01HL128954).




11

Am J Respir Crit Care Med

- 
- 
- 

. 2023 Sep 28.

doi: 10.1164/rccm.202307-1303LE. Online ahead of print.


# Recognising and Managing the Burdens of *Chronic Breathlessness* Alongside the Burdens of COPD

David C Currow[1], Rajam Iyer[2], Joseph Clark[3], Sujeet K Rajan[4]

Affiliations expand

- PMID: 37769150

- DOI: 10.1164/rccm.202307-1303LE

***No abstract available***

full text links

Proceed to details

Cite

Share

12

**Review**

Eur Respir Rev

- 
- 
- 

. 2023 Sep 27;32(169):230103.

doi: 10.1183/16000617.0103-2023. Print 2023 Sep 30.

# Methods to assess COPD medications adherence in healthcare databases: a systematic review

Delphine Vauterin[1], Frauke Van Vaerenbergh[1], Anna Vanoverschelde[1,2], Jennifer K Quint[3], Katia Verhamme[1,4], Lies Lahousse[5,2]

Affiliations expand

- PMID: 37758274

- PMCID: PMC10523153

- DOI: 10.1183/16000617.0103-2023

**Free PMC article**

**Abstract**

**Background:** The Global Initiative for Chronic Obstructive Lung Disease 2023 report recommends medication adherence assessment in COPD as an action item. Healthcare databases provide opportunities for objective assessments; however, multiple methods exist. We aimed to systematically review the literature to describe existing methods to assess adherence in COPD in healthcare databases and to evaluate the reporting of influencing variables.

**Method:** We searched MEDLINE, Web of Science and Embase for peer-reviewed articles evaluating adherence to COPD medication in electronic databases, written in English, published up to 11 October 2022 (PROSPERO identifier CRD42022363449). Two reviewers independently conducted screening for inclusion and performed data extraction. Methods to assess initiation (dispensing of medication after prescribing), implementation (extent of use over a specific time period) and/or persistence (time from initiation to discontinuation) were listed descriptively. Each included study was evaluated for reporting variables with an impact on adherence assessment: inpatient stays, drug substitution, dose switching and early refills.

**Results:** 160 studies were included, of which four assessed initiation, 135 implementation and 45 persistence. Overall, one method was used to measure initiation, 43 methods for implementation and seven methods for persistence. Most of the included implementation studies reported medication possession ratio, proportion of days covered and/or an alteration of these methods. Only 11% of the included studies mentioned the potential impact of the evaluated variables.

**Conclusion:** Variations in adherence assessment methods are common. Attention to transparency, reporting of variables with an impact on adherence assessment and rationale for choosing an adherence cut-off or treatment gap is recommended.



# Conflict of interest statement

Conflict of interest: Outside this manuscript, J.K. Quint received grants paid to her institution from the Medical Research Council, Health Data Research UK, GlaxoSmithKline, Boehringer Ingelheim, Asthma + Lung UK and AstraZeneca, and consulting fees from

GlaxoSmithKline, Evidera, AstraZeneca and Insmed. None of which are related to the content of this work. Outside this manuscript, K. Verhamme received unconditional research grants paid to her institution from Chiesi, Amgen, Union Chimique Belge (UCB), Johnson & Johnson (J&J) and the European Medicines Agency (EMA). None of which are related to the content of this work. Outside this manuscript, L. Lahousse received a consulting fee paid to her institution from AstraZeneca and honoraria for lectures paid to her institution from Chiesi and IPSA vzw, a non-profit organisation facilitating lifelong learning for healthcare providers. L. Lahousse is an unpaid member of European Respiratory Society and Belgian Respiratory Society, member of Faculty board of Ghent University – Faculty of Pharmaceutical Sciences and faculty committees. None of which are related to the content of this work. All other authors declare no competing interests.

- 200 references
- 1 figure

supplementary info

Publication typesexpand

full text links

Proceed to details

Cite

Share

13

PLoS One

- 
- 
- 

. 2023 Sep 28;18(9):e0292388.

doi: 10.1371/journal.pone.0292388. eCollection 2023.

# The impact of wearing facemask on COPD patients: A protocol of a systematic review and meta-analysis

Xuwen Chen[1], Ibrahim Sani[1], Xiaoli Xia[2], Yi Li[3], Caiyun Li[1], Feiyan Yue[1], Xinhua Wang[1], Shisan Bao[1], Jingchun Fan[1]

Affiliations expand

- PMID: 37768979
- PMCID: PMC10538665
- DOI: 10.1371/journal.pone.0292388

**Free PMC article**

## Abstract

**Introduction:** Chronic obstructive pulmonary disease (COPD) is a common, irreversible but preventable disease characterized by persistent respiratory symptoms. The mortality rate of COPD is predicted to reach 5.4 million by the year 2060. Despite its heavy burden on healthcare expenditure worldwide, only 15% of cases are medically identified. The potential benefits of facemask-wearing for COPD patients remain a topic of debate.

**Methods:** We will conduct a systematic review of all randomized trials and non-randomized controlled trials to evaluate the impact of facemasks on COPD patients. Our review will be based on literature obtained through a comprehensive search strategy across multiple electronic databases, including the Cochrane Library, Embase, PubMed, Web of Science, the Chinese Biomedical Database (SinoMed), and China National Knowledge Infrastructure (CNKI), with no restrictions on language or date of publication. Two independent researchers will extract and assess all relevant data using pre-designed data extraction forms. The included studies will be assessed using the Cochrane RoB2 tool and the suggested risk of bias criteria proposed by the Effective Practice and Organization of Care reviews group of the Cochrane collaboration. The quality of evidence will be assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. We will use Review Manager 5.4 software for statistical analysis.

**Discussion:** In the context of COVID-19, it is important for COPD patients to wear facemasks. This study aims to conduct a comprehensive and systematic assessment of the impact of facemasks on the physiology and activity of COPD patients.

**Trial registration:** PROSPERO registration number CRD42022326265.

## Conflict of interest statement

The authors have no conflicts of interest to declare.

- 34 references

supplementary info

Grants and fundingexpand

full text links

Proceed to details

Cite

Share

14

Nurs Res

- 
- 
- 

. 2023 Sep 26.

doi: 10.1097/NNR.0000000000000694. Online ahead of print.

# Systematic Review and Meta-Analysis of Psychological Distress and Acute Exacerbation of Chronic Obstructive Pulmonary Disease and Consequences

Prasert Kham-Ai[1], Karen Heaton, Chunhong Xiao, Pariya Wheeler

Affiliations expand

- PMID: 37768970

- DOI: 10.1097/NNR.0000000000000694

**Abstract**

**Background:** People with chronic obstructive pulmonary disease (COPD) occasionally develop acute exacerbation of COPD-a potentially fatal condition. Psychological distress was associated with acute exacerbation of COPD. However, the evidence on the effect of psychological distress on acute exacerbation of COPD remains unclear.

**Objective:** To explore the influence of psychological distress on acute exacerbation of COPD and its consequences.

**Methods:** The current review was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines using three databases (PubMed, CINAHL, and PsyINFO) that were searched to identify relevant articles. Pooled risk ratios and 95% confidential interval were calculated from the included studies' data with random-effect methods to estimate the effect of psychological distress on acute exacerbation of COPD and its consequences.

**Results:** Nineteen articles were included in the review. Most revealed that psychological distress was significantly associated with increased risk of acute exacerbation of COPD and its consequences. The meta-analyses showed that psychological distress increased risk of acute exacerbation of COPD, COPD-related hospitalization, and death.

**Conclusion:** Psychological distress had negative effects on acute exacerbation of COPD and its consequences. The results of the meta-analyses show that persons with COPD and psychological distress had a greater risk of acute exacerbation of COPD, hospitalization, and death.



# Conflict of interest statement

The authors have no conflicts of interest to report.

Can J Hosp Pharm

. 2023 Sep 1;76(4):296-301.

doi: 10.4212/cjhp.3421. eCollection 2023 Fall.

# Effect of Pharmacist-Initiated Interventions on Duration of Antibiotic Therapy for Acute Exacerbation of Chronic Obstructive Pulmonary Disease and Community-Acquired Pneumonia

Giovanni Iovino[1], Lynn Nadeau[2]

Affiliations expand

- PMID: 37767382

- PMCID: PMC10522359 (available on 2024-03-01)

- DOI: 10.4212/cjhp.3421

**Abstract**

in English, French

**Background:** Current guidelines for the treatment of acute exacerbation of chronic obstructive pulmonary disease (AECOPD) and community-acquired pneumonia (CAP) recommend 5 days of antimicrobial therapy. Despite these recommendations, the duration of therapy exceeds 5 days for up to 70% of patients, with most superfluous prescribing occurring upon discharge from hospital. Shortening the duration of antibiotic therapy could decrease adverse events, resistance, and costs.

**Objective:** To determine whether a pharmacist-initiated modification to the duration of antibiotic therapy prescribed for the treatment of AECOPD or CAP reduced the duration of antibiotic prescriptions.

**Methods:** In this prospective, single-centre study of adult inpatients receiving antibiotics for the treatment of AECOPD or CAP between October 2020 and March 2021, pharmacists assigned a 5-day duration to antimicrobials prescribed for these indications. For patients discharged before completion of therapy, the antibiotic start date and intended duration were included on the discharge prescription. Study patients were matched 1:1 with historical controls to compare the total duration of antibiotic therapy with and without the intervention.

**Results:** A total of 100 patients (66 with CAP and 34 with AECOPD) met the inclusion criteria and had their antibiotic treatment duration modified to 5 days. Mean total duration of antibiotic therapy was 5.31 days in the intervention group and 7.11 days in the control group ($p < 0.001$). Outpatient antibiotic prescribing was 0.86 days in the intervention group and 3.2 days in the control group ($p < 0.001$). In both groups, the rates of readmission at 30 and 90 days were 19% and 31%, respectively.

**Conclusions:** Pharmacist-initiated modification of antimicrobial therapy resulted in shortening of the duration of therapy by almost 2 days. Including information about treatment duration on the discharge prescription reduced outpatient prescribing without affecting readmission rates.

**Keywords:** acute exacerbation of chronic obstructive pulmonary disease; antibiotic duration; antimicrobial stewardship; community-acquired pneumonia; pharmacist.



# Conflict of interest statement

Competing interests: None declared.

. 2023 Sep 21;26:100597.

doi: 10.1016/j.lana.2023.100597. eCollection 2023 Oct.

# Guideline-discordant inhaler regimens after COPD hospitalization: associations with rurality, drive time to care, and fragmented care - a United States cohort study

Arianne K Baldomero[1,2,3], Ken M Kunisaki[1,2], Chris H Wendt[1,2], Carrie Henning-Smith[4], Hildi J Hagedorn[3], Ann Bangerter[3], R Adams Dudley[1,2,3]

Affiliations expand

- PMID: 37766800

- PMCID: PMC10520452

- DOI: 10.1016/j.lana.2023.100597

**Abstract**

**Background:** Many patients receive guideline-discordant inhaler regimens after chronic obstructive pulmonary disease (COPD) hospitalization. Geography and fragmented care across multiple providers likely influence prescription of guideline-discordant inhaler regimens, but these have not been comprehensively studied. We assessed patient-level differences in guideline-discordant inhaler regimens by rurality, drive time to pulmonary specialty care, and fragmented care.

**Methods:** Retrospective cohort analysis using national Veterans Health Administration (VA) data among patients who received primary care and prescriptions from the VA. Patients hospitalized for COPD exacerbation between 2017 and 2020 were assessed for guideline-discordant inhaler regimens in the subsequent 3 months. Guideline-discordant inhaler regimens were defined as short-acting inhaler/s only, inhaled corticosteroid (ICS) monotherapy, long-acting beta-agonist (LABA) monotherapy, ICS + LABA, long-acting muscarinic antagonist (LAMA) monotherapy, or LAMA + ICS. Rural residence and drive time to the closest pulmonary specialty care were obtained from geocoded addresses.

Fragmented care was defined as hospitalization outside the VA. We used multivariable logistic regression models to assess associations between rurality, drive time, fragmentated care, and guideline-discordant inhaler regimens. Models were adjusted for age, sex, race/ethnicity, Charlson Comorbidity Index, Area Deprivation Index, and region.

**Findings:** Of 33,785 patients, 16,398 (48.6%) received guideline-discordant inhaler regimens 3 months after hospitalization. Rural residents had higher odds of guideline-discordant inhalers regimens compared to their urban counterparts (adjusted odds ratio [aOR] 1.18 [95% CI: 1.12-1.23]). The odds of receiving guideline-discordant inhaler regimens increased with longer drive time to pulmonary specialty care (aOR 1.38 [95% CI: 1.30-1.46] for drive time >90 min compared to <30 min). Fragmented care was also associated with higher odds of guideline-discordant inhaler regimens (aOR 1.56 [95% CI: 1.48-1.63]).

**Interpretation:** Rurality, long drive time to care, and fragmented care were associated with greater prescription of guideline-discordant inhaler regimens after COPD hospitalization. These findings highlight the need to understand challenges in delivering evidence-based care.

**Funding:** NIHNCATS grants KL2TR002492 and UL1TR002494.

**Keywords:** Access to care; Drive time to care; Health care disparity; Rural health; Veterans affairs.

# Conflict of interest statement

AKB reported grants from the National Institutes of Health. CHS reported grants from the Health Resources and Services Administration, Federal Office of Rural Health Policy, the National Institutes of Health and the CDC; payment or honoraria from Iowa Primary Care Association, Southern Gerontological Society, and the University of Michigan; and leadership or fiduciary role in the National Rural Health Association Board of Trustees. KMK reported personal fees from Nuvaira and Organicell (Data and Safety Monitoring Boards) outside of this work; consulting fees from Allergan/AbbVie and leadership or fiduciary role in the American Thoracic Society Proposal Review Committee, the American Thoracic Society Clinical Problems, and the Assembly Planning Committee.

- 57 references
- 2 figures

full text links

Proceed to details

17

Thorax

- 
- 
- 

. 2023 Sep 27;thorax-2023-220522.

doi: 10.1136/thorax-2023-220522. Online ahead of print.

# Core outcome set for pulmonary rehabilitation of patients with COPD: results of a modified Delphi survey

Sara Souto-Miranda[1,2,3,4], Isabel Saraiva[5], Martijn A Spruit[2,6], Alda Marques[7,3]

Affiliations expand

- PMID: 37758457

- DOI: 10.1136/thorax-2023-220522

**Abstract**

**Introduction:** There is high heterogeneity of outcomes and measures reported in pulmonary rehabilitation (PR) trials of people with chronic obstructive pulmonary disease (COPD). This hinders study comparability and benchmarking of PR. We have developed a core outcome set (COS) to overcome these challenges.

**Methods:** This study was informed by a systematic review and two qualitative studies and had patient involvement since its inception. A two-round Delphi survey was available in seven languages. Outcomes (n=63) scored 7-9 (crucial) by ≥70% of the participants and 1-3 (not that important) by ≤15% of participants from both groups in the Likert scale were automatically included in the COS, while outcomes that were considered crucial by only one of the groups were further discussed by the authors in a meeting.

**Results:** A total of 299 people (n=229 healthcare professionals/researchers/policy-makers; n=70 people with COPD and informal caregivers) participated in the survey (83% retention), which covered 29 countries/five continents. After the second round, six

outcomes were included and three were added in the meeting. The final COS contains dyspnoea, fatigue, functional exercise capacity, health-related quality of life, health behaviours/lifestyle, knowledge about the disease, lower limb muscle function, personal goals and problematic activities of daily living.

**Conclusion:** A COS for PR of people with COPD is now available and can be used by different stakeholders to improve consistency and comparability of studies, benchmark PR and improve the quality of care provided. Future research should establish the core measures and investigate the uptake of this COS.

**Keywords:** pulmonary rehabilitation; respiratory measurement.



## Conflict of interest statement

Competing interests: None declared.



18

Thorax

. 2023 Sep 27;thorax-2022-219696.

doi: 10.1136/thorax-2022-219696. Online ahead of print.

# Spirometric patterns in young and middle-aged adults: a 20-year European study

Anne-Elie Carsin[1 2 3 4], Judith Garcia-Aymerich[5 2 3], Simone Accordini[6], Shyamali Dharmage[7], Bénédicte Leynaert[8], Marti de Las Heras[5 2 3], Lidia Casas[9 10], Seraina Caviezel[11], Pascal Demoly[12 13], Bertil Forsberg[14], Thorarinn Gislason[15 16], Angelo Guido Corsico[17 18], Christer Janson[19], Rain Jogi[20], Jesús Martínez-Moratalla[21], Dennis Nowak[22], Leopoldo Palacios Gómez[23], Isabelle Pin[24 25], Nicole Probst-Hensch[11], Chantal Raherison-Semjen[26], Giulia Squillacioti[27], Cecilie Svanes[28 29], Kjell Torén[30 31], Isabel Urrutia[32], Ismael Huerta[33], Josep Maria Anto[5 2 3], Debbie Jarvis[34], Stefano Guerra[5 35]

Affiliations expand

- PMID: 37758456

- DOI: 10.1136/thorax-2022-219696

## Abstract

**Background:** Understanding the natural history of abnormal spirometric patterns at different stages of life is critical to identify and optimise preventive strategies. We aimed to describe characteristics and risk factors of restrictive and obstructive spirometric patterns occurring before 40 years (young onset) and between 40 and 61 years (mid-adult onset).

**Methods:** We used data from the population-based cohort of the European Community Respiratory Health Survey (ECRHS). Prebronchodilator forced expiratory volume in one second ($FEV_1$) and forced vital capacity (FVC) were assessed longitudinally at baseline (ECRHS1, 1993-1994) and again 20 years later (ECRHS3, 2010-2013). Spirometry patterns were defined as: restrictive if $FEV_1/FVC \geq LLN$ and FVC<10th percentile, obstructive if $FEV_1/FVC < LLN$ or normal otherwise. Five spirometry patterns were derived depending on whether participants never developed restrictive/obstructive (normal), developed restrictive/obstructive at baseline (young onset) or at last follow-up (mid-adult onset). The characteristics and risk factors associated with these patterns were described and assessed using multilevel multinomial logistic regression analysis adjusting for age, sex, sample (random or symptomatic) and centre.

**Results:** Among 3502 participants (mean age=30.4 (SD 5.4) at ECRHS1, 50.4 (SD 5.4) at ECRHS3), 2293 (65%) had a normal, 371 (11%) a young restrictive, 301 (9%) a young obstructive, 187 (5%) a mid-adult onset restrictive and 350 (10%) a mid-adult onset obstructive spirometric pattern. Being lean/underweight in childhood and young adult life was associated with the occurrence of the young spirometric restrictive pattern (relative risk ratio (RRR)=1.61 95% CI=1.21 to 2.14, and RRR=2.43 95% CI=1.80 to 3.29; respectively), so were respiratory infections before 5 years (RRR=1.48, 95% CI=1.05 to 2.08). The main determinants for young obstructive, mid-adult restrictive and mid-adult obstructive patterns were asthma, obesity and smoking, respectively.

**Conclusion:** Spirometric patterns with onset in young and mid-adult life were associated with distinct characteristics and risk factors.

**Keywords:** COPD epidemiology; Clinical Epidemiology.



## Conflict of interest statement

Competing interests: None declared.



19

Respir Physiol Neurobiol

- 
- 
- 

. 2023 Sep 25;104166.

doi: 10.1016/j.resp.2023.104166. Online ahead of print.

# Integrative Assessment of Cerebral Blood Regulation in COPD Patients

Daniel I Corrêa[1], Marcelo de-Lima-Oliveira[1], Ricardo C Nogueira[1], Regina M Carvalho-Pinto[2], Edson Bor-Seng-Shu[1], Ronney B Panerai[3], Celso R F Carvalho[4], Angela Sm Salinet[5]

Affiliations expand

- PMID: 37758031

- DOI: 10.1016/j.resp.2023.104166

**Abstract**

Cerebrovascular responses were compared between COPD and non-COPD participants. The association between COPD severity and cognitive function was also investigated. Cerebral blood velocity in the middle cerebral artery, blood pressure, and end-tidal $CO_2$ were recorded at rest, followed by a brain activation paradigm, and an inhaled gas mixture (5% $CO_2$) to assess cerebral autoregulation (CA), neurovascular coupling (NVC) and cerebrovascular reactivity to carbon dioxide ($CVR_{CO2}$), respectively. Pulmonary function, blood gas analysis (COPD) and cognitive function (MoCA test) were also performed. No difference in baseline (systemic and cerebral parameters) and CA was found between 20 severe COPD and 21 non-COPD. Reduced NVC and $CVR_{CO2}$ test were found in the COPD group. Lower pulmonary function was positively correlated with CA, NVC and $CVR_{CO2}$ in COPD patients. Cognitive impairment (MoCA<26) was associated with lower NVC responses (COPD and non-COPD) and lower pulmonary function (COPD). Both mechanisms, $CVR_{CO2}$ and NVC, were lower in COPD patients. Moreover, disease severity and cognitive impaired were associated with worse cerebrovascular regulation.

**Keywords:** cerebral autoregulation; cerebral blood flow; cerebrovascular reactivity; chronic obstructive pulmonary disease; cognitive impairment; neurovascular coupling.



20

Am J Respir Crit Care Med

. 2023 Sep 27.

doi: 10.1164/rccm.202305-0924OC. Online ahead of print.

# Activation of CD8+ T Cells in COPD Lung

Ana B Villaseñor-Altamirano[1,2], Dhawal Jain[3], Yunju Jeong[1,2], Jaivardhan A Menon[1], Mari Kamiya[1,2], Hibah Haider[1], Reshmi Manandhar[1], Muhammad Dawood Amir Sheikh[1], Humra Athar[1,3], Louis T Merriam[1], Min Hyung Ryu[4,2], Takanori Sasaki[2,5], Peter J Castaldi[4,2], Deepak A

Rao[5,2], Lynette M Sholl[6,2], Marina Vivero[6,2], Craig P Hersh[4,2], Xiaobo Zhou[4,2], Justus Veerkamp[7], Jeong H Yun[4,2], Edy Y Kim[1,8]; MGB-Bayer Pulmonary Drug Discovery Lab

Affiliations expand

- PMID: 37756440

- DOI: 10.1164/rccm.202305-0924OC

**Abstract**

**Rationale:** Despite the importance of inflammation in chronic obstructive pulmonary disease (COPD), the immune cell landscape in the lung tissue of patients with mild-moderate disease has not been well characterized at the single-cell and molecular level.

**Objective:** To define the immune cell landscape in lung tissue from patients with mild-moderate COPD at single-cell resolution.

**Methods:** We performed single-cell transcriptomic (RNA-seq), proteomic (CITE-seq), and T cell receptor repertoire analysis on lung tissue from patients with mild-moderate COPD (n=5, GOLD I or II), emphysema without airflow obstruction (n=5), end-stage COPD (n=2), control (n=6), or donors (n=4). We validated in an independent patient cohort (N=929) and integrated with the *Hhip*(+/-) murine model of COPD.

**Measurements and main results:** Mild-moderate COPD lungs have increased abundance of two CD8+ T cell subpopulations: cytotoxic KLRG1+TIGIT+CX3CR1+T effector memory CD45RA+(TEMRA) cells; and DNAM-1+CCR5+T resident memory ($T_{RM}$) cells. These CD8+ T cells interact with myeloid and alveolar type II cells via *IFNG* and have hyperexpanded TCR clonotypes. In an independent cohort, the CD8+KLRG1+TEMRA gene signature is increased in mild-moderate COPD lung compared to control or end-stage COPD lung. Human CD8+KLRG1+TEMRA cells are similar to CD8+ T cells driving inflammation in an aging-related, murine model of COPD.

**Conclusions:** CD8+ TEMRA cells are increased in mild-moderate COPD lung and may contribute to inflammation that precedes severe disease. Further study of these CD8+T cells may have therapeutic implications for preventing severe COPD.

**Keywords:** CD8 T cells; CITE-seq; COPD; scRNA-seq.

21

PLoS One

. 2023 Sep 27;18(9):e0290647.

doi: 10.1371/journal.pone.0290647. eCollection 2023.

# Systemic steroid therapy for pneumonic chronic obstructive pulmonary disease exacerbation: A retrospective cohort study

Akihiro Shiroshita[1 2 3 4], Keisuke Anan[4 5], Masafumi Takeshita[3], Yuki Kataoka[4 6 7 8]

Affiliations expand

- PMID: 37756275

- PMCID: PMC10529550

- DOI: 10.1371/journal.pone.0290647

**Free PMC article**

## Abstract

The effectiveness of systemic steroid therapy on mortality in patients with pneumonic chronic obstructive pulmonary disease (COPD) exacerbation is unclear. We evaluated the association between systemic steroid therapy and 30-day mortality after adjusting for known confounders, using data from the Health, Clinic, and Education Information Evaluation Institute in Japan, which longitudinally followed up patients in the same hospital. We selected patients aged ≥40 years admitted for pneumonic COPD exacerbation. The exclusion criteria were censoring within 24 h, comorbidity with other respiratory diseases, and daily steroid use. Systemic steroid therapy was defined as

oral/parenteral steroid therapy initiated within two days of admission. The primary outcome was the 30-day mortality rate. To account for known confounders, each patient was assigned an inverse probability of treatment weighting. The outcome was evaluated using logistic regression. Among 3,662 patients showing pneumonic COPD exacerbation, 30-day mortality in the steroid therapy and non-steroid therapy groups was 27.6% (169/612) and 21.9% (668/3,050), respectively. Systemic steroid therapy indicated a slightly higher estimated probability of 30-day mortality (difference in the estimated probabilities, 2.65%; 95% confidence interval, -1.23 to 6.54%, p-value = 0.181). Systemic steroid therapy within two days of admission was associated with higher 30-day mortality rates in pneumonic COPD exacerbation. Further validation studies based on chart reviews will be needed to cope with residual confounders.



# Conflict of interest statement

AS received a research grant from Real World Data, Co., Ltd (a profit organization). and the Japan Society for the Promotion of Science, a non-profit organization (Grants-in-Aid for Scientific Research [Kakenhi] for this study. This does not alter our adherence to PLOS ONE policies on sharing data and materials.

- 23 references
- 3 figures

supplementary info

Grants and fundingexpand

full text links

Proceed to details

Cite

Share

22

ERJ Open Res

. 2023 Sep 25;9(5):00409-2023.

doi: 10.1183/23120541.00409-2023. eCollection 2023 Sep.

# Effects of pharmacological and non-pharmacological interventions on physical activity outcomes in COPD: a systematic review and meta-analysis

Dimitrios Megaritis[1], Emily Hume[1], Nikolaos Chynkiamis[2], Christopher Buckley[1], Ashley M Polhemus[3], Henrik Watz[4], Thierry Troosters[5], Ioannis Vogiatzis[1]

Affiliations expand

- PMID: 37753290

- PMCID: PMC10518871

- DOI: 10.1183/23120541.00409-2023

**Free PMC article**

## Abstract

**Rationale:** The effect of pharmacological and non-pharmacological interventions on physical activity (PA) outcomes is not fully elucidated in patients with COPD. The objectives of the present study were to provide estimation of treatment effects of all available interventions on PA outcomes in patients with COPD and to provide recommendations regarding the future role of PA outcomes in pharmacological trials.

**Materials and methods:** This review was conducted according to the Cochrane Handbook for Systematic Reviews of Interventions and reported in line with PRISMA. Records were identified through searches of 12 scientific databases; the most updated search was performed in January 2023.

**Results:** 74 studies published from 2000 to 2021 were included, with a total of 8140 COPD patients. Forced expiratory volume in 1 s % predicted ranged between 31% and 74%, with a mean of 55%. Steps/day constituted the most frequently assessed PA outcome in interventional studies. Compared to usual care, PA behavioural modification interventions

resulted in improvements in the mean (95% CI) steps/day when implemented alone (by 1035 (576-1493); p<0.00001) or alongside exercise training (by 679 (93-1266); p=0.02). Moreover, bronchodilator therapy yielded a favourable difference of 396 (125-668; p=0.004) steps/day, compared to placebo.

**Conclusions:** PA behavioural modification and pharmacological interventions lead to significant improvements in steps/day, compared to control and placebo groups, respectively. Compared to bronchodilator therapy, PA behavioural modification interventions were associated with a 2-fold greater improvement in steps/day. Large-scale pharmacological studies are needed to establish an intervention-specific minimal clinically important difference for PA outcomes as well as their convergent validity to accelerate qualification as potential biomarkers and efficacy end-points for regulatory approval.



# Conflict of interest statement

Conflict of interest: A.M. Polhemus declares an employment contract with MSD International. Conflict of interest: T. Troosters declares involvement in studies funded by AstraZeneca and Boehringer Ingelheim. Conflict of interest: I. Vogiatzis is an associate editor of this journal. Conflict of interest: The remaining authors explicitly state that there are no conflicts of interest in connection with this article and that they have no relevant financial disclosures.

- 39 references
- 5 figures



23

ERJ Open Res

. 2023 Sep 25;9(5):00492-2023.

doi: 10.1183/23120541.00492-2023. eCollection 2023 Sep.

# Oral corticosteroid use and sarcopenia-related traits in older people with chronic airway disease: a population-based study

Elizabeth Benz[1,2], Lies Lahousse[1,3], Johnmary T Arinze[4,5], Sara Wijnant[1,4], Maria de Ridder[5], Fernando Rivadeneira[2], Guy Brusselle[1,4], Bruno H Stricker[1]

Affiliations expand

- PMID: 37753286
- PMCID: PMC10518877
- DOI: 10.1183/23120541.00492-2023

**Free PMC article**

## Abstract

**Background:** Sarcopenia is characterised by two major phenotypic components: low handgrip strength (HGS) and appendicular skeletal muscle index (ASMI). Oral corticosteroid (OCS) use is an important medication for acute respiratory exacerbations in patients with COPD and asthma. However, the association of OCS and sarcopenia components in older people is largely unexplored. The aim of this study was to examine the association between OCS use and HGS or ASMI in the general population and explore interactions with chronic airway diseases.

**Methods:** From the population-based Rotterdam Study, 5054 participants (age 69.0±8.8 years; 56% females) were included in the cross-sectional analysis and 1324 in the longitudinal analysis. Associations between OCS and muscle strength and mass were analysed using linear regression models adjusted for age, sex, fat %, height, kidney function, smoking and comorbidities.

**Results:** At baseline, ever-OCS users had lower handgrip strength (β= -0.48, 95% CI -0.84- -0.12) than never-OCS users, with cumulative frequency (≥10 OCS prescriptions)-dependent effects (β= -1.25, 95% CI -2.16- -0.33). COPD ever-OCS users, but not asthma, had lower handgrip strength (β= -0.98, 95% CI -1.91- -0.06) and lower lean mass (β= -0.14, 95% CI -0.27- -0.01) than never-OCS users. After 5.6 years of follow-up in those free of sarcopenia traits at baseline, COPD ever-OCS users developed lower handgrip strength (β=

-1.64, 95% CI -2.87- -0.40) with frequency (β= -3.64, 95% CI -6.57- -0.72) and duration (β= -1.51, 95% CI -2.87- -0.15) association compared to never-OCS users.

**Conclusions:** OCS use is associated with a decline in handgrip strength in people with COPD in a cumulative frequency and duration-dependent manner. Routine muscle examination may be necessary for patients with COPD.



# Conflict of interest statement

Conflict of interest: E. Benz, J.T. Arinze, S. Wijnant, M. de Ridder, F. Rivadeneira and B.H. Stricker have no conflicts of interest nothing to disclose. Conflict of interest: L. Lahousse reports financial support by the Fund for Scientific Research Flanders (Grant 3G037618), lecture honoraria from IPSA vzw and Chiesi (paid to her institution), an advisory board for AstraZeneca, and ERS membership (faculty board). Conflict of interest: G. Brusselle reports honoraria for lectures from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Merck Sharp & Dohme, Novartis and Sanofi, and ERS and GINA memberships.


- 39 references
- 3 figures

full text links

Proceed to details

Cite

Share

24


**Editorial**


ERJ Open Res

. 2023 Sep 25;9(5):00469-2023.

doi: 10.1183/23120541.00469-2023. eCollection 2023 Sep.

# Revisiting Peter Macklem's old dream through the PRISm of lung volumes

Engi Ahmed[1,2,3], Zakaria Mohamed Lahmar[1,2], Arnaud Bourdin[1,2]

Affiliations expand

- PMID: 37753277
- PMCID: PMC10518892
- DOI: 10.1183/23120541.00469-2023

**Free PMC article**

**Abstract**

**In healthy asymptomatic smokers with normal $FEV_1$/FVC, abnormal CT lung volumes that reflect small airway dysfunction and emphysema could be used as a biomarker to identify susceptible smokers at increased risk of progressing to COPD** https://bit.ly/3XZDj1s.



## Conflict of interest statement

Conflict of interest: E. Ahmed has nothing to disclose. Conflict of interest: Z.M. Lahmar has nothing to disclose. Conflict of interest: A. Bourdin has nothing to disclose.

## Comment on

- Lung volumes differentiate the predominance of emphysema *versus* airway disease phenotype in early COPD: an observational study of the COPDGene cohort.
  Zeng S, Luo G, Lynch DA, Bowler RP, Arjomandi M.ERJ Open Res. 2023 Sep 18;9(5):00289-2023. doi: 10.1183/23120541.00289-2023. eCollection 2023 Sep.PMID: 37727675 **Free PMC article.**

- 21 references

supplementary info

Publication typesexpand

25

ERJ Open Res

. 2023 Sep 25;9(5):00035-2023.

doi: 10.1183/23120541.00035-2023. eCollection 2023 Sep.

# High prevalence of interstitial lung abnormalities in middle-aged never-smokers

Ida Pesonen[1,2], Fredrik Johansson[3], Åse Johnsson[4,5], Anders Blomberg[6], Marianne Boijsen[4,5], John Brandberg[4,5], Kerstin Cederlund[7], Arne Egesten[8], Össur Ingi Emilsson[9,10], Jan E Engvall[11,12], Andreas Frølich[6], Emil Hagström[13,14], Eva Lindberg[10], Andrei Malinovschi[15], Nikolai Stenfors[6], Eva Swahn[16], Hanan Tanash[17], Raquel Themudo[18,19], Kjell Torén[20,21], Lowie E G W Vanfleteren[22,23], Per Wollmer[24], Suneela Zaigham[15,25], Carl Johan Östgren[11,26], C Magnus Sköld[1,2]

Affiliations expand

- PMID: 37753274

- PMCID: PMC10518870

- DOI: 10.1183/23120541.00035-2023

**Free PMC article**

## Abstract

**Background:** Interstitial lung abnormalities (ILA) are incidental findings on chest computed tomography (CT). These patterns can present at an early stage of fibrotic lung disease. Our aim was to estimate the prevalence of ILA in the Swedish population, in particular in never-smokers, and find out its association with demographics, comorbidities and symptoms.

**Methods:** Participants were recruited to the Swedish CArdioPulmonary BioImage Study (SCAPIS), a population-based survey including men and women aged 50-64 years performed at six university hospitals in Sweden. CT scan, spirometry and questionnaires were performed. ILA were defined as cysts, ground-glass opacities, reticular abnormality, bronchiectasis and honeycombing.

**Findings:** Out of 29 521 participants, 14 487 were never-smokers and 14 380 were men. In the whole population, 2870 (9.7%) had ILA of which 134 (0.5%) were fibrotic. In never-smokers, the prevalence was 7.9% of which 0.3% were fibrotic. In the whole population, age, smoking history, chronic bronchitis, cancer, coronary artery calcium score and high-sensitive C-reactive protein were associated with ILA. Both ILA and fibrotic ILA were associated with restrictive spirometric pattern and impaired diffusing capacity of the lung for carbon monoxide. However, individuals with ILA did not report more symptoms compared with individuals without ILA.

**Interpretation:** ILA are common in a middle-aged Swedish population including never-smokers. ILA may be at risk of being underdiagnosed among never-smokers since they are not a target for screening.



# Conflict of interest statement

Conflict of interest: I. Pesonen reports fees from Boehringer Ingelheim for lectures and participation on advisory boards. Conflict of interest: A. Egeston reports consulting fees from BioCryst, payment/honoraria from AstraZeneca and an unrestricted research grant from CSL-Behring. Conflict of interest: Ö.I. Emilsson reports payment from study work from Boehringer Ingelheim, unrelated to this publication. Conflict of interest: E. Hagström reports payments to institution from Pfizer and Amgen, small personal fees from Amgen, NovoNordisk, Bayer and AstraZeneca, and a small personal fee from Amarin AB for participation on an advisory board. He is the co-chair of the Swedish secondary prevention registry and the national coordinator for the trials DalCore DAL301 DalGne, Regeneron R1500-CL-1643 and Aegis II/Perfuse. Conflict of interest: L.E.G.W. Vanfleteren reports grants paid to his institution from the Swedish Heart and Lung Foundation and the family Kamprad foundation, and payments/honoraria from AstraZeneca, GSK, Boehringer, Novartis, Chiesi, Pulmonx for lectures and presentations. He also reports personal payments for participation on a data safety monitoring board or advisory board for AstraZeneca. He was member of the board for the Swedish National Airway registry. He is as associate editor of this journal. Conflict of interest: P. Wollmer received fees for lectures

from Chiesi Pharma outside the scope of the study. He also has a patent issued for a device and method for pulmonary function measurement outside the scope of the study. Conflict of interest: S. Zaigham reports a research project grant from Magnus Bergvalls Stiftelse, and support for meeting attendance from the Swedish Heart and Lung Foundation and Bror Hjerpstedts Stiftelse. Conflict of interest: C.M. Sköld reports research grants from Boehringer Ingelheim for pulmonary fibrosis research, payments for lectures and educational activities related to pulmonary fibrosis, and participation on advisory boards related to pulmonary fibrosis. Conflict of interest: All other authors declare no conflicts of interest.

- 31 references
- 3 figures

full text links

Proceed to details

Cite

Share

26

Intensive Care Med

- 
- 
- 

. 2023 Sep 26.

doi: 10.1007/s00134-023-07229-y. Online ahead of print.

# Different oxygenation targets for stable COPD and acute exacerbations in the ICU. Author's reply

Fang Qian[1], Willem van den Boom[2], Kay Choong See[3]

Affiliations expand

- PMID: 37750903

- DOI: 10.1007/s00134-023-07229-y

***No abstract available***

- 5 references

supplementary info

Publication types, Grants and fundingexpand

full text links

Proceed to details

Cite

Share

27

Respir Res

- 
- 
- 

. 2023 Sep 25;24(1):229.

doi: 10.1186/s12931-023-02523-1.

# Benefit of prompt initiation of single-inhaler fluticasone furoate, umeclidinium, and vilanterol (FF/UMEC/VI) in patients with COPD in England following an exacerbation: a retrospective cohort study

Afisi S Ismaila[1,2], Kieran J Rothnie[3], Robert P Wood[4], Victoria L Banks[#4,5], Lucinda J Camidge[4], Alexandrosz Czira[3], Chris Compton[6], Raj Sharma[6], Shannon N Millard[#4,7], Olivia Massey[4], David M G Halpin[8]

Affiliations expand


- PMID: 37749551

- PMCID: PMC10521462

- DOI: 10.1186/s12931-023-02523-1


**Free PMC article**

## Abstract


**Background:** Triple therapy is recommended for patients with chronic obstructive pulmonary disease (COPD) who remain symptomatic despite dual therapy. The optimal timing of triple therapy following an exacerbation of COPD is unknown. The outcomes of prompt (≤ 30 days) vs. delayed (31-180 days) initiation of single-inhaler triple therapy with fluticasone furoate, umeclidinium, and vilanterol (FF/UMEC/VI) following an exacerbation of COPD were examined.

**Methods:** This was a retrospective cohort study of linked English primary (Clinical Practice Research Datalink) and secondary (Hospital Episode Statistics) care data. Patients aged ≥ 35 years with COPD were indexed on the first and/or earliest date of exacerbation between November 15, 2017 and March 31, 2019 with subsequent FF/UMEC/VI initiation within 180 days. Patients were required to be continuously registered with a general practitioner for ≥ 12 months prior to and following index. Subsequent exacerbations, direct medical costs, and hospital readmissions were compared between prompt and delayed initiators. Inverse probability of treatment weighting was used to adjust for measured confounders between cohorts.

**Results:** Overall, 1599 patients were included (prompt: 393, delayed: 1206). After weighting, prompt initiators had numerically lower moderate/severe exacerbations compared with delayed initiators (rate ratio: 0.87, 95% confidence interval [CI]: 0.76-1.01, p = 0.0587). Both all-cause and COPD-related 30-day hospital readmissions were significantly lower among patients with prompt initiation compared with delayed initiators (all-cause: 23.6% vs. 34.6%, odds ratio [95% CI]: 0.58 [0.36-0.95], p = 0.0293; COPD-related: 20.3% vs. 30.6%, odds ratio [95% CI]: 0.58 [0.35-0.96], p = 0.0347). Prompt initiators also had numerically lower all-cause total costs and significantly lower COPD-related costs per-person-per year compared with delayed initiators (COPD-related: £742 vs. £801, p = 0.0016).

**Conclusion:** Prompt initiation of FF/UMEC/VI following a moderate/severe exacerbation was associated with fewer subsequent exacerbations, fewer hospital readmissions, and lower COPD-related medical costs compared with delayed initiation.

**Keywords:** Chronic obstructive pulmonary disease; Exacerbation; FF/UMEC/VI; Healthcare cost; SITT.

# Plain language summary

Triple therapy with an inhaled corticosteroid (ICS), a long-acting muscarinic antagonist (LAMA), and a long-acting β2-agonist (LABA) is recommended for patients with chronic obstructive pulmonary disease (COPD) who still experience symptoms while taking dual therapy (LABA/LAMA or ICS/LABA). Triple therapy can be taken using single or multiple inhalers. The best time to start triple therapy for patients who may benefit from it following a short-term worsening (flare-up) of their COPD symptoms is unknown. This study assesses the effect of starting treatment with triple therapy sooner compared with later in patients with COPD.Patients who experienced a flare-up of their COPD symptoms were split into two groups – those who started taking triple therapy (via a single inhaler) within 30 days of their symptom flare-up and those who started taking triple therapy 31–180 days following their symptom flare-up. Over the 12 months following the initial flare-up, patients who started triple therapy earlier (within 30 days) had fewer subsequent symptom flare-ups, fewer hospital admissions, and lower healthcare costs compared with patients who started triple therapy later (31–180 days). These findings suggest that doctors should consider prescribing triple therapy (via a single inhaler) to their patients with COPD straight away if they experience a flare-up of their symptoms.



# Conflict of interest statement

ASI, KJR, AC, CC, and RS are employees of GSK and/or hold stocks/shares in GSK. ASI is also an unpaid part-time member of the McMaster University faculty. RPW, VLB, LJC, SNM, and OM are/were employees of Adelphi Real World at the time of this study; Adelphi Real World received funds from GSK to complete the study. DMGH reports personal fees from Aerogen, AstraZeneca, Boehringer Ingelheim, Chiesi, CSL Behring, GSK, Novartis, Pfizer, and Sanofi. VLB is a current employee and shareholder for Bayer PLC (since January 2022). SNM is a current employee for P1vital Limited (since October 2021).

- 23 references
- 8 figures

supplementary info

MeSH terms, Substancesexpand

full text links

28

Environ Sci Pollut Res Int

. 2023 Sep 25.

doi: 10.1007/s11356-023-29688-y. Online ahead of print.

# Associations between environmental heavy metals exposure and preserved ratio impaired spirometry in the U.S. adults

Chen Chen[#1], Shunan Zhang[#1], Ting Yang[2], Chen Wang[3,4], Guiling Han[1]

Affiliations expand

- PMID: 37749472

- DOI: 10.1007/s11356-023-29688-y

**Abstract**

We examined 9556 individuals aged 18 to 79 years who had information on spirometry testing and heavy metals and used multivariable logistic or linear regression to evaluate associations between serum levels of cadmium, lead, and mercury and PRISm and lung function in U.S. adults, which were conducted first in all participants, and then separately in never/former smokers and current smokers. The overall prevalence of PRISm was 7.02%. High levels of serum cadmium were significantly associated with PRISm in all individuals, no matter in never/former smokers (quartile 4 vs 1, the OR = 2.517, 95% CI = 1.376-4.604, p-trend = 0.0077) and current smokers (quartile 4 vs 1, the OR = 2.201, 95% CI = 1.265-3.830, p-trend = 0.0020). Serum lead and mercury were not significantly correlated with

PRISm, regardless of smoking status. Serum cadmium was strongly correlated with lower $FEV_1$/FVC, regardless of smoking status. Besides, serum cadmium was also significantly related to lower FVC % predicted in never/former smokers and lower $FEV_1$% predicted in current smokers. Serum lead was strongly correlated with lower FVC % predicted and $FEV_1$/FVC in all individuals and never/former smokers. And serum mercury was significantly associated with decrements in FVC % predicted in all individuals and current smokers. These findings demonstrate that serum cadmium is associated with a higher risk of PRISm and lower lung function, with the most significant effect on $FEV_1$/FVC in particular. Our results also indicate that exposure to lead and mercury negatively affects lung function in never/former smokers and current smokers, respectively.

**Keywords:** Chronic obstructive pulmonary disease; Environmental pollutants; Heavy metals; Lung function; National Health and Nutrition Survey; Preserved ratio impaired spirometry.



- 71 references

## supplementary info

Grants and fundingexpand

## full text links

Proceed to details

Cite

Share

29

Am J Respir Crit Care Med

. 2023 Sep 25.

doi: 10.1164/rccm.202307-1268LE. Online ahead of print.

# Icenticaftor, A Novel Treatment for COPD: Needs Further Verification of Its Effectiveness

Qiming Gan[1], Kai Yang[2], Yanjuan Wu[1], Jingcun Wang[3 1], Haojie Zhang[4 5], Nuofu Zhang[6], Kang Wu[7]

Affiliations expand

- PMID: 37748186

- DOI: 10.1164/rccm.202307-1268LE

***No abstract available***

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



30

Am J Respir Crit Care Med

- 
- 
- 

. 2023 Sep 25.

doi: 10.1164/rccm.202309-1653LE. Online ahead of print.

# Reply to: Icenticaftor, A Novel Treatment for COPD: Needs Further Verification of Its Effectiveness

Fernando J Martinez[1]

Affiliations expand

- PMID: 37748176

- DOI: 10.1164/rccm.202309-1653LE

***No abstract available***



**Case Reports**

Respirol Case Rep

- 
- 
- 

. 2023 Sep 19;11(10):e01222.

doi: 10.1002/rcr2.1222. eCollection 2023 Oct.

# Immune checkpoint inhibitor-induced asthma and chronic obstructive pulmonary disease overlap in patient with adenocarcinoma

Yuki Hayakawa[1], Takako Kawaguchi[1], Kei Yamasaki[1], Miyu Endo[1], Masaya Komatsu[1], Yutaka Ishiguro[1], Yuichi Murata[1], Kazuhiro Yatera[1]

Affiliations expand

- PMID: 37736311
- PMCID: PMC10509402
- DOI: 10.1002/rcr2.1222


**Free PMC article**


**Abstract**

A 67-year-old current smoker Japanese man, with no history of asthma, was diagnosed with lung adenocarcinoma. He received first-line chemotherapy with carboplatin, pemetrexed, ipilimumab, and nivolumab in July 20XX-1, and subsequently a maintenance therapy with nivolumab. In October 20XX, he became aware of wheezy dyspnoea, and chest computed tomography demonstrated worsening bronchial wall thickenings. Eosinophilia was noted, and a pulmonary function test showed obstructive dysfunction insufficiently responding to beta-agonists, with 130 mL increase of forced expiratory volume in one second and high fractional exhaled nitric oxide level (85 ppb). He was clinically diagnosed with asthma and chronic obstructive pulmonary disease overlap, secondary to immune checkpoint inhibitors (ICIs). The inhibition of binding between programmed cell death-protein-1 (PD-1), expressed on T cells, and programmed cell death-ligand-2 (PD-L2), expressed on tumour and dendritic cells, can induce airway hyperresponsiveness. Physicians should be wary of asthmatic symptoms and chest image findings during ICIs therapy.



**Keywords:** adenocarcinoma; asthma; chronic obstructive pulmonary disease; immune checkpoint inhibitors.




# Conflict of interest statement

None declared.

- 5 references
- 2 figures

## supplementary info

Publication typesexpand

full text links

Proceed to details

Cite

Share

32

Respir Care

- 
- 
- 

. 2023 Oct;68(10):1479-1480.

doi: 10.4187/respcare.11380.

# Home Noninvasive Ventilation for COPD: The Trouble With the Mode

Umur Hatipoğlu [1], Joseph S Lewarski [2], Robert L Chatburn [3]

Affiliations expand

- PMID: 37722732

- PMCID: PMC10506649 (available on 2024-10-01)

- DOI: 10.4187/respcare.11380

***No abstract available***

supplementary info

Publication types, MeSH termsexpand

full text links

33

Eur Respir J

- 
- 
- 

. 2023 Sep 28;62(3):2300806.

doi: 10.1183/13993003.00806-2023. Print 2023 Sep.

# From pre-COPD to COPD: a Simple, Low cost and easy to IMplement (SLIM) risk calculator

Miguel J Divo[1], Congjian Liu[2], Francesca Polverino[3], Peter J Castaldi[4 5], Bartolome R Celli[2 6], Yohannes Tesfaigzi[2 6]

Affiliations expand

- PMID: 37678951

- PMCID: PMC10533946

- DOI: 10.1183/13993003.00806-2023

**Free PMC article**

## Abstract

**Background:** The lifetime risk of developing clinical COPD among smokers ranges from 13% to 22%. Identifying at-risk individuals who will develop overt disease in a reasonable timeframe may allow for early intervention. We hypothesised that readily available clinical and physiological variables could help identify ever-smokers at higher risk of developing chronic airflow limitation (CAL).

**Methods:** Among 2273 Lovelace Smokers' Cohort (LSC) participants, we included 677 (mean age 54 years) with normal spirometry at baseline and a minimum of three spirometries, each 1 year apart. Repeated spirometric measurements were used to determine incident CAL. Using logistic regression, demographics, anthropometrics, smoking history, modified Medical Research Council dyspnoea scale, St George's Respiratory Questionnaire, comorbidities and spirometry, we related variables obtained at baseline to incident CAL as defined by the Global Initiative for Chronic Obstructive Lung Disease and lower limit of normal criteria. The predictive model derived from the LSC was validated in subjects from the COPDGene study.

**Results:** Over 6.3 years, the incidence of CAL was 26 cases per 1000 person-years. The strongest independent predictors were forced expiratory volume in 1 s ($FEV_1$)/forced vital capacity (FVC) <0.75, having smoked ≥30 pack-years, body mass index (BMI) ≤25 $kg{\cdot}m^2$ and symptoms of chronic bronchitis. Having all four predictors increased the risk of developing CAL over 6 years to 85% (area under the receiver operating characteristic curve (AUC ROC) 0.84, 95% CI 0.81-0.89). The prediction model showed similar results when applied to subjects in the COPDGene study with a follow-up period of 10 years (AUC ROC 0.77, 95% CI 0.72-0.81).

**Conclusion:** In middle-aged ever-smokers, a simple predictive model with $FEV_1$/FVC, smoking history, BMI and chronic bronchitis helps identify subjects at high risk of developing CAL.



# Conflict of interest statement

Conflict of interest: The authors declare that they have no potential conflicts of interest to disclose. F. Polverino is a Section Editor of the European Respiratory Journal.

# Comment in

- All roads lead to COPD… or not?
Agusti A, Faner R.Eur Respir J. 2023 Sep 28;62(3):2301470. doi: 10.1183/13993003.01470-2023. Print 2023 Sep.PMID: 37770089 No abstract available.

- 57 references

- 3 figures

full text links

34

Eur Respir Rev

- 
- 
- 

. 2023 Sep 6;32(169):230034.

doi: 10.1183/16000617.0034-2023. Print 2023 Sep 30.

# The role of vaccination in COPD: influenza, SARS-CoV-2, pneumococcus, pertussis, RSV and varicella zoster virus

Susanne Simon[1], Oana Joean[1], Tobias Welte[2 3], Jessica Rademacher[1 3]

Affiliations expand

- PMID: 37673427

- PMCID: PMC10481333

- DOI: 10.1183/16000617.0034-2023

**Free PMC article**

## Abstract

Exacerbations of COPD are associated with worsening of the airflow obstruction, hospitalisation, reduced quality of life, disease progression and death. At least 70% of COPD exacerbations are infectious in origin, with respiratory viruses identified in approximately 30% of cases. Despite long-standing recommendations to vaccinate patients with COPD, vaccination rates remain suboptimal in this population.*Streptococcus pneumoniae* is one of the leading morbidity and mortality causes of lower respiratory tract infections. The Food and Drug Administration recently approved pneumococcal conjugate vaccines that showed strong immunogenicity against all 20 included serotypes. Influenza is

the second most common virus linked to severe acute exacerbations of COPD. The variable vaccine efficacy across virus subtypes and the impaired immune response are significant drawbacks in the influenza vaccination strategy. High-dose and adjuvant vaccines are new approaches to tackle these problems. Respiratory syncytial virus is another virus known to cause acute exacerbations of COPD. The vaccine candidate RSVPreF3 is the first authorised for the prevention of RSV in adults ≥60 years and might help to reduce acute exacerbations of COPD. The 2023 Global Initiative for Chronic Lung Disease report recommends zoster vaccination to protect against shingles for people with COPD over 50 years.



# Conflict of interest statement

Conflict of interest: T. Welte reports support for the present manuscript from German Ministry of Research and Education; grants or contracts from Bavaria Nordisk, outside the submitted work; payment or honoraria from Janssen, GSK, MSD and Pfizer, outside the submitted work; and is a current editorial board member for European Respiratory Review. J. Rademacher reports receiving payment or honoraria from GSK and MSD, outside the submitted work. The remaining authors have nothing to disclose.

# Comment in

- doi: 10.1183/16000617.0028-2023
- 146 references
- 1 figure

supplementary info

MeSH terms, Substancesexpand

full text links

Proceed to details

Cite

Share

35

Respirology

. 2023 Oct;28(10):962-963.

doi: 10.1111/resp.14577. Epub 2023 Aug 17.

# Whole lung health for the whole of life

Christine Jenkins[1]

Affiliations expand

- PMID: 37592458

- DOI: 10.1111/resp.14577

**Free article**

***No abstract available***

**Keywords:** COPD; air pollution; lung physiology; newborn; paediatrics.



**Observational Study**

Pulm Pharmacol Ther

. 2023 Oct;82:102248.

doi: 10.1016/j.pupt.2023.102248. Epub 2023 Aug 9.

# Effects of elexacaftor-tezacaftor-ivacaftor on daily treatment burden and airflow obstruction in adults with cystic fibrosis

Angelica Tiotiu[1], Iulia Ioan[2], Yves Billon[3]

Affiliations expand

- PMID: 37562640

- DOI: 10.1016/j.pupt.2023.102248

**Abstract**

**Background:** The drug combination elexacaftor-tezacaftor-ivacaftor (ETI) proved highly effective in the improvement of the respiratory symptoms, the percentage of predicted forced expiratory volume in 1 s (FEV1), and to reduce rates of pulmonary exacerbations in people with cystic fibrosis (CF) with at least one F508del mutation. The objectives of the study were to evaluate the impact of ETI on the daily treatment burden due to patient decision and the evolution of lung function parameters at 6 months of treatment in real life.

**Methods:** A single-center observational study was realized including adult patients starting ETI therapy from March 10, 2020 to April 5, 2022. Clinical characteristics were collected at initiation (T0) and at 6 months (T6) of treatment. Outcome measures included names and number of chronic daily medications, respectively lung function parameters: FEV1, forced vital capacity (FVC), FEV1/FVC ratio, peak expiratory flow (PEF), forced expiratory flow at 25-75% of FVC (FEF25-75), β-angle and FEF50/PEF ratio.

**Results:** Sixty-five patients were included with a mean age of 29.4 ± 8.5 years old, 48% of them F508del homozygous previously treated by lumacaftor-ivacaftor. At T6, the median number of daily medications decreased from 13 [2-24] to 9 [1-19] ($p < 0.001$). All the studied functional respiratory parameters were improved: FEV1 +18%, FVC +14%, FEF25-75% + 18% (all $p < 0.001$), as well the airflow obstruction: FEV1/FVC +6%, FEF50/PEF by 0.1 ± 0.1 and β-angle by 10° ± 13° (all $p \leq 0.007$).

**Conclusion:** ETI therapy can reduce the daily treatment burden in real-life at 6 months of treatment, increase a large number of lung function parameters and improve airflow obstruction.

**Keywords:** Cystic fibrosis; Daily treatment burden; Distal airways; Elexacaftor-tezacaftor-ivacaftor; List: airflow obstruction.



## Conflict of interest statement

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



**Review**

Eur Respir Rev

. 2023 Aug 9;32(169):220253.

doi: 10.1183/16000617.0253-2022. Print 2023 Sep 30.

# Post-COVID-19 dyspnoea and pulmonary imaging: a systematic review and meta-analysis

Elizabeth Guinto[1], Firoozeh V Gerayeli[1], Rachel L Eddy[1,2], Hyun Lee[1,3], Stephen Milne[1,2,4], Don D Sin[5,2]

Affiliations expand

- PMID: 37558261

- PMCID: PMC10410398

- DOI: 10.1183/16000617.0253-2022

**Free PMC article**

## Abstract

**Background:** A proportion of coronavirus disease 2019 (COVID-19) survivors experience persistent dyspnoea without measurable impairments in lung function. We performed a systematic review and meta-analysis to determine relationships between dyspnoea and imaging abnormalities over time in post-COVID-19 patients.

**Methods:** Using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, we analysed studies published prior to 15 September 2022 and indexed by Google Scholar, PubMed and LitCOVID which assessed chest imaging in adults ≥3 months after COVID-19. Demographic, chest imaging, spirometric and post-COVID-19 symptom data were extracted. The relationships between imaging abnormalities and dyspnoea, sex and age were determined using a random effects model and meta-regression.

**Results:** 47 studies were included in the meta-analysis (n=3557). The most prevalent computed tomography (CT) imaging abnormality was ground-glass opacities (GGOs) (44.9% (95% CI 37.0-52.9%) at any follow-up time-point). Occurrence of reticulations significantly decreased between early and late follow-up (p=0.01). The prevalence of imaging abnormalities was related to the proportion of patients with dyspnoea (p=0.012). The proportion of females was negatively correlated with the presence of reticulations (p=0.001), bronchiectasis (p=0.001) and consolidations (p=0.025). Age was positively correlated with imaging abnormalities across all modalities (p=0.002) and imaging abnormalities present only on CT (p=0.001) (GGOs (p=0.004) and reticulations (p=0.001)). Spirometric values improved during follow-up but remained within the normal range at all time-points.

**Conclusions:** Imaging abnormalities were common 3 months after COVID-19 and their occurrence was significantly related to the presence of dyspnoea. This suggests that CT imaging is a sensitive tool for detecting pulmonary abnormalities in patients with dyspnoea, even in the presence of normal spirometric measurements.

# Conflict of interest statement

Conflict of interest: R.L. Eddy receives personal consulting fees from VIDA Diagnostics Inc., and lecture honoraria from AstraZeneca, outside the submitted work. S. Milne reports grants from British Columbia Lung Association, CHEST Foundation, Genome British Columbia, Mitacs and Michael Smith Health Research BC, and financial support from Chiesi Australia, outside the submitted work. D.D. Sin has received an honorarium for speaking engagements for COPD from GSK, AstraZeneca and Boehringer Ingelheim, and chairs a DSMB for an NHLBI-sponsored clinical trial in COPD, outside the submitted work. E. Guinto, F.V. Gerayeli and H. Lee do not declare any conflicts of interest.


- 88 references
- 4 figures

supplementary info

Publication types, MeSH termsexpand

full text links

Proceed to details

Cite

Share

38


**Review**


Adv Ther

. 2023 Oct;40(10):4236-4263.

doi: 10.1007/s12325-023-02609-8. Epub 2023 Aug 4.

# Implementing an Evidence-Based COPD Hospital Discharge Protocol: A Narrative Review and Expert Recommendations

Marc Miravitlles[1], Mohit Bhutani[2], John R Hurst[3], Frits M E Franssen[4], Job F M van Boven[5], Ee Ming Khoo[6,7], Jing Zhang[8], Stephen Brunton[9], Daiana Stolz[10], Tonya Winders[11], Kazuhisa Asai[12], Jane E Scullion[13]

Affiliations expand

- PMID: 37537515
- PMCID: PMC10499689
- DOI: 10.1007/s12325-023-02609-8

**Free PMC article**

## Abstract

Discharge bundles, comprising evidence-based practices to be implemented prior to discharge, aim to optimise patient outcomes. They have been recommended to address high readmission rates in patients who have been hospitalised for an exacerbation of chronic obstructive pulmonary disease (COPD). Hospital readmission is associated with increased morbidity and healthcare resource utilisation, contributing substantially to the economic burden of COPD. Previous studies suggest that COPD discharge bundles may result in fewer hospital readmissions, lower risk of mortality and improvement of patient quality of life. However, evidence for their effectiveness is inconsistent, likely owing to variable content and implementation of these bundles. To ensure consistent provision of high-quality care for patients hospitalised with an exacerbation of COPD and reduce readmission rates following discharge, we propose a comprehensive discharge protocol, and provide evidence highlighting the importance of each element of the protocol. We then review care bundles used in COPD and other disease areas to understand how they affect patient outcomes, the barriers to implementing these bundles and what strategies have been used in other disease areas to overcome these barriers. We identified four evidence-based care bundle items for review prior to a patient's discharge from hospital, including (1) smoking cessation and assessment of environmental exposures, (2) treatment optimisation, (3) pulmonary rehabilitation, and (4) continuity of care. Resource constraints, lack of staff engagement and knowledge, and complexity of the COPD population were some of the key barriers inhibiting effective bundle implementation. These barriers can be addressed by applying learnings on successful bundle implementation from other disease areas, such as healthcare practitioner education and audit and feedback. By utilising the

relevant implementation strategies, discharge bundles can be more (cost-)effectively delivered to improve patient outcomes, reduce readmission rates and ensure continuity of care for patients who have been discharged from hospital following a COPD exacerbation.

**Keywords:** Care bundles; Chronic obstructive pulmonary disease; Discharge protocol; Exacerbation; Hospital readmission; Implementation strategies.



# Conflict of interest statement

Marc Miravitlles has received speaker fees from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, CSL Behring, GlaxoSmithKline, Grifols, Janssen, Kamada, Menarini, Novartis, Specialty Therapeutics, Takeda and Zambon; consulting fees from AstraZeneca, Atriva Therapeutics, Boehringer Ingelheim, Chiesi, CSL Behring, Ferrer, GlaxoSmithKline, Grifols, Inhibrx, Menarini, Mereo BioPharma, Novartis, Novo Nordisk, ONO Pharmaceutical, Palobiofarma S.L, Sanofi, Specialty Therapeutics, Spin Therapeutics, Takeda and Zambon; and research grants from Grifols. Mohit Bhutani has received speaker/consultancy fees from AstraZeneca, Boehringer Ingelheim, Covis, GlaxoSmithKline, Sanofi and Valeo; grants from Alberta Lung, AstraZeneca, Canadian Institute of Health Research, GlaxoSmithKline, Mereo and Sanofi; and is an Executive of the Canadian Thoracic Society. John R Hurst has received speaker/consultancy fees from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Novartis and Takeda. Frits ME Franssen has received speaker/consultancy fees and/or grants from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Merck Sharp & Dohme, Novartis and Teva. Job FM van Boven has received consultancy fees and/or grants from Aardex, AstraZeneca, Chiesi, European Commission COST (COST Action 19,132), GlaxoSmithKline, Novartis, Pfizer, Pill Connect, Teva, Trudell Medical and Vertex (all paid to his institution). Ee Ming Khoo has received speaker/consultancy fees from AstraZeneca and grants from the National Institute for Health Research Global Health Research Unit on Respiratory Health (RESPIRE), and is the President of the International Primary Care Respiratory Group and the Primary Care Respiratory Group Malaysia. Jing Zhang has received speaker/consultancy fees from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline and Pfizer. Stephen Brunton has received speaker/consultancy fees from AstraZeneca and Boehringer Ingelheim. Daiana Stolz reports grants from The Swiss National Foundation (SNF 189280), and unrestricted grants from AstraZeneca, Boston Scientific, and Curetis AG; as well as honoraria from, and participation on data safety monitoring boards, talks or advisory boards for, AstraZeneca, Berlin-Chemie/Menarini, Boehringer Ingelheim, Chiesi, CSL Behring, Curetis AG, GlaxoSmithKline, Merck, Merck Sharp & Dohme, Novartis, Sanofi and Vifor. Daiana Stolz is the current GOLD representative for Switzerland, the immediate past Education Council Chair of the European Respiratory Society and past President of the Education Committee of the Swiss Respiratory Society. Tonya Winders has received speaker/consultancy fees from Amgen, AstraZeneca, GlaxoSmithKline, Novartis and Sanofi Regeneron. Kazuhisa Asai has received speaker/consultancy fees from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline,

Novartis and Sanofi. Jane E Scullion has received speaker fees and honoraria for attending congresses or educational events from AstraZeneca, Boehringer Ingelheim, Chiesi, Let's Talk Respiratory, Monthly Index of Medical Specialties, Mundipharma, Napp and Teva.

- 138 references
- 1 figure

supplementary info

Publication types, MeSH termsexpand

full text links

Proceed to details

Cite

Share

39

Int J Biometeorol

. 2023 Oct;67(10):1543-1553.

doi: 10.1007/s00484-023-02504-5. Epub 2023 Jul 31.

# Global Chronic obstructive pulmonary disease burden attributable to air pollution from 1990 to 2019

Guixia Pan[1], Jian Cheng[1], Hai-Feng Pan[1], Yin-Guang Fan[1], Dong-Qing Ye[2]

Affiliations expand

- PMID: 37522974
- DOI: 10.1007/s00484-023-02504-5

## Abstract

**Background:** The disease burden attributable to chronic obstructive pulmonary disease (COPD) is significant worldwide. Some studies have linked exposure to air pollution to COPD, but there has been little research on this.

**Methods:** We aimed to assess the COPD-related disease burden attributable to air pollution from multiple epidemiological perspectives. This study conducted a three-stage analysis. Firstly, we reported on the burden of disease worldwide in 2019 by different subgroups including sex, age, region, and country. Secondly, we studied the trends in disease burden from 1990 to 2019. Finally, we explored the association of some national indicators with disease burden to look for risk factors.

**Results:** In 2019, the death number of COPD associated with air pollution accounted for 2.32% of the total global death, and the number of DALY accounted for 1.12% of the global DALY. From 1990 to 2019, the death number of COPD associated with air pollution increased peaked at 1.41 million in 1993, fluctuated, and then declined. We found the same temporal pattern of DALY. The corresponding age-standardized rates had been falling. At the same time, the burden of COPD associated with air pollution was also affected by some national indicators.

**Conclusions:** This study indicated that air pollution-related COPD contributed to a significant global disease burden. We called for health policymakers to take action and interventions targeting vulnerable countries and susceptible populations.

**Keywords:** Air pollution; COPD; Disease burden; Global; Trend.

40

**Meta-Analysis**

Eur J Clin Pharmacol

. 2023 Oct;79(10):1321-1332.

doi: 10.1007/s00228-023-03543-y. Epub 2023 Jul 29.

# LABA/LAMA versus LABA/ICS fixed-dose combinations in the prevention of COPD exacerbations: a modeling analysis of literature aggregate data

Yiwen Gong[1], Zichao Sui[1], Yinghua Lv[1], Qingshan Zheng[1], Lujin Li[2]

Affiliations expand

- PMID: 37507595

- DOI: 10.1007/s00228-023-03543-y

**Abstract**

**Objectives:** This study aimed to quantitatively compare the efficacy and safety of long-acting $\beta_2$-agonist (LABA)/long-acting muscarinic antagonist (LAMA) and LABA/inhaled corticosteroid (ICS) fixed-dose combinations (FDCs) in preventing moderate or severe chronic obstructive pulmonary disease (COPD) exacerbations.

**Methods:** A literature search was performed using public databases. The time course characteristics of the probability of a moderate or severe exacerbation in stable COPD patients treated with LABA/LAMA and LABA/ICS FDCs were described by the parametric survival function. A random-effects model in a single-arm meta-analysis was used to analyze the incidence of serious adverse events (SAEs) and pneumonia.

**Results:** Twenty studies including 23,955 participants were included. The proportion of participants with a history of COPD exacerbation (%) in the previous year and the postbronchodilator forced expiratory volume in the first second ($FEV_1$) (%predicted) were

important factors affecting drug efficacy. After adjusting the above factors to median levels of 100% and 45.5%, respectively, the moderate or severe exacerbation rates at 52 weeks for olodaterol/tiotropium, formoterol/budesonide, indacaterol/glycopyrronium, formoterol/glycopyrronium, vilanterol/fluticasone, salmeterol/fluticasone, and vilanterol/umeclidinium were 38.3%, 41.0%, 42.6%, 47.0%, 47.5%, 47.9%, and 53.0%, respectively. In terms of safety, significant differences were observed among drugs containing different LABA/LAMA FDCs.

**Conclusions:** This study showed that not all LABA/LAMA FDCs were superior to LABA/ICS FDCs in safety and in preventing moderate or severe exacerbations in patients with stable COPD, providing important quantitative information for COPD-related guidelines.

**Keywords:** COPD exacerbations; Chronic obstructive pulmonary disease; LABA/ICS fixed-dose combinations; LABA/LAMA fixed-dose combinations; Model-based meta-analysis.



- 41 references

supplementary info

Publication types, MeSH terms, Substances, Grants and fundingexpand

full text links

Proceed to details

Cite

Share

41

**Published Erratum**

Adv Ther

- 
- 
- 

. 2023 Oct;40(10):4689-4690.

doi: 10.1007/s12325-023-02613-y. Epub 2023 Jul 28.

# Correction to: DElaying Disease Progression In COPD with Early Initiation of Dual Bronchodilator or Triple Inhaled PharmacoTherapy (DEPICT): A Predictive Modelling Approach

Dave Singh[1,2], Diego Litewka[3], Rafael Páramo[4], Adrian Rendon[5], Abdullah Sayiner[6], Suzana E Tanni[7], Sudeep Acharya[8], Bhumika Aggarwal[8], Afisi S Ismaila[9,10], Raj Sharma[11], Peter Daley-Yates[12]

Affiliations expand

- PMID: 37505374
- PMCID: PMC10500000
- DOI: 10.1007/s12325-023-02613-y

**Free PMC article**

***No abstract available***

## Erratum for

- DElaying Disease Progression In COPD with Early Initiation of Dual Bronchodilator or Triple Inhaled PharmacoTherapy (DEPICT): A Predictive Modelling Approach.
  Singh D, Litewka D, Páramo R, Rendon A, Sayiner A, Tanni SE, Acharya S, Aggarwal B, Ismaila AS, Sharma R, Daley-Yates P.Adv Ther. 2023 Oct;40(10):4282-4297. doi: 10.1007/s12325-023-02583-1. Epub 2023 Jun 29.PMID: 37382864 **Free PMC article.**

supplementary info

Publication typesexpand

full text links

42

Respir Physiol Neurobiol

. 2023 Oct;316:104124.

doi: 10.1016/j.resp.2023.104124. Epub 2023 Jul 25.

# A comparative study of dynamic lung hyperinflation and tidal volume to total lung capacity ratios during exercise in patients with chronic respiratory disease and healthy individuals

Ming-Lung Chuang[1]

Affiliations expand

- PMID: 37499989

- DOI: 10.1016/j.resp.2023.104124

**Abstract**

**Background:** Current measures of tidal volume/forced vital capacity (VT/FVC) and VT/inspiratory capacity (VT/IC) at peak exercise cannot differentiate restrictive from obstructive ventilation patterns. This study aimed to investigate the utility of VT/total lung capacity (VT/TLC) as a marker for dynamic lung hyperinflation (DH) in patients with chronic obstructive pulmonary disease (COPD) and interstitial lung disease (ILD).

**Methods:** 267 subjects were screened: 23 ILD, 126 COPD, and 33 healthy individuals were enrolled. Lung function tests and cardiopulmonary exercise tests with repeated IC maneuver were conducted and compared at three exercise efforts: unloaded, middle of exercise, and peak exercise.

**Results:** During exercise, ILD patients demonstrated normal end-expiratory lung volume/TLC (EELV/TLC) ratios, but elevated end-inspiratory lung volume/TLC (EILV/TLC) ratios, except for peak exercise. COPD patients exhibited elevated ratios for both EELV/TLC and EILV/TLC during exercise with a larger EELV/TLC ratio compared to ILD patients at peak exercise ($p < 0.05$). The VT/TLC ratio distinguished ILD, COPD, and healthy controls at peak exercise ($p < 0.05$). A VT/TLC ratio of ≤ 0.22 or ≥ 0.30 indicated airflow obstruction with hyperinflation or normal lung expansion, respectively (AUC: 0.74 or 0.88). Furthermore, VT/TLC outperformed VT/FVC and VT/IC in differentiating lung expansion between ILD and COPD during exercise (all $p < 0.05$).

**Conclusion:** Exercise-induced DH was absent in ILD patients but observed in COPD patients. Excessive lung expansion occurred in all patients during exercise, except for limited expansion in ILD at peak exercise probably due to specific lung properties. VT/TLC can distinguish between restrictive, obstructive, and normal ventilatory patterns.

**Keywords:** Dynamic lung hyperinflation; End-expiratory lung volume; End-inspiratory lung volume; Lung expandability; Ratio of tidal volume to inspiratory capacity; Ratio of tidal volume to total lung capacity.



# Conflict of interest statement

Declaration of Competing Interest The authors declare no competing interests.

supplementary info

Publication types, MeSH termsexpand

full text links

. 2023 Oct;20(10):1389-1396.

doi: 10.1513/AnnalsATS.202304-384CME.

# Personalizing Selection of Inhaled Delivery Systems in Chronic Obstructive Pulmonary Disease

Donald A Mahler[1,2], David M G Halpin[3]

Affiliations expand

- PMID: 37499210

- DOI: 10.1513/AnnalsATS.202304-384CME

**Abstract**

It can be challenging for healthcare professionals (HCPs) to prescribe inhaled therapy for patients with chronic obstructive pulmonary disease (COPD) because of the multiple individual and combinations of inhaled medications available in numerous delivery systems. Guidance on the selection of an inhaled delivery system has received limited attention compared with the emphasis on prescribing the class of the inhaled molecule(s). Although numerous recommendations and algorithms have been proposed to guide the selection of an inhaled delivery system for patients with COPD, no specific approach has been endorsed in COPD guidelines/strategies or by professional organizations. To provide recommendations for an inhaler selection strategy at initial and follow-up appointments, we examined the impact of patient errors using handheld inhalers on clinical outcomes and performed a focused narrative review to consider patient factors (continuity of the inhaled delivery system, cognitive function, manual function/dexterity, and peak inspiratory flow) when selecting an inhaled delivery system. On the basis of these findings, five questions are proposed for HCPs to consider in the initial selection of an inhaler delivery system and three questions to consider at follow-up. We propose that HCPs consider the inhaled medication delivery system as a unit and to match appropriate medication(s) with the unique features of the delivery system to individual patient factors. Assessment of inhaler technique and adherence together with patient outcomes/satisfaction at each visit is essential to determine whether the inhaled medication delivery system is providing benefits. Continued and repeated education on device features and correct technique is warranted to optimize efficacy.

**Keywords:** dyspnea; exacerbations; inhaled bronchodilators; inhaled delivery systems; shared decision making.

**Review**

Eur Respir Rev

. 2023 Jul 26;32(169):220223.

doi: 10.1183/16000617.0223-2022. Print 2023 Sep 30.

# Regenerative and translational medicine in COPD: hype and hope

Lucas Pires Guarnier[1,2], Lincoln Gozzi Moro[2,3], Francislaine Aparecida Dos Reis Lívero[4], Carolina Arruda de Faria[5], Mauricio Fogaça Azevedo[2], Beatriz Pizoni Roma[2], Edilson Rodrigues Albuquerque[4], Maria José Malagutti-Ferreira[2], Alessandra Gomes Duarte Rodrigues[6], Adelson Alves da Silva[7], Eliseo Joji Sekiya[7], João Tadeu Ribeiro-Paes[8,2]

Affiliations expand

- PMID: 37495247

- PMCID: PMC10369169

- DOI: 10.1183/16000617.0223-2022

**Free PMC article**

**Abstract**

COPD is a common, preventable and usually progressive disease associated with an enhanced chronic inflammatory response in the airways and lung, generally caused by exposure to noxious particles and gases. It is a treatable disease characterised by persistent respiratory symptoms and airflow limitation due to abnormalities in the airways and/or alveoli. COPD is currently the third leading cause of death worldwide, representing a serious public health problem and a high social and economic burden. Despite significant advances, effective clinical treatments have not yet been achieved. In this scenario, cell-based therapies have emerged as potentially promising therapeutic approaches. However, there are only a few published studies of cell-based therapies in human patients with COPD and a small number of ongoing clinical trials registered on clinicaltrials.gov Despite the advances and interesting results, numerous doubts and questions remain about efficacy, mechanisms of action, culture conditions, doses, timing, route of administration and conditions related to homing and engraftment of the infused cells. This article presents the state of the art of cell-based therapy in COPD. Clinical trials that have already been completed and with published results are discussed in detail. We also discuss the questions that remain unanswered about cell-based regenerative and translational medicine for COPD.



# Conflict of interest statement

Conflict of interest: The authors declare no conflicts of interest.

- 142 references
- 4 figures

## supplementary info

Publication types, MeSH termsexpand

## full text links

Proceed to details

Cite

Share

45

Thorax

. 2023 Oct;78(10):1039-1042.

doi: 10.1136/thorax-2023-220065. Epub 2023 Jul 14.

# Pulmonary telerehabilitation vs. conventional pulmonary rehabilitation - a secondary responder analysis

Henrik Hansen[1,2], Andre Torre[3], Thomas Kallemose[3], Charlotte Suppli Ulrik[4,5], Nina Skavlan Godtfredsen[5,6]

Affiliations expand

- PMID: 37451863

- PMCID: PMC10511950

- DOI: 10.1136/thorax-2023-220065

**Free PMC article**

## Abstract

Home-based pulmonary telerehabilitation (PTR) has been proposed to be equivalent to supervised outpatient pulmonary rehabilitation (PR) but available randomised trials have failed to reach the minimal important changes (MIC). The purpose of this study was to analyse the proportion of MIC responders and non-responders on short-term (10 weeks from baseline) and long-term (62 weeks from baseline) in total and between groups in 134 patients with COPD randomised (1:1) to either home-based PTR or traditional hospital-based outpatient PR. Difference between PTR and PR on 6MWD response proportion could not be shown at 10 (OR=0.72, CI=0.34 to 1.51, p=0.381) or 62 weeks (OR=1.12, CI=0.40 to 3.14, p=0.834). While the evidence and knowledge of PTR accumulate, outpatient supervised PR for now remains the standard of care, with home-based PTR as a strong secondary option for those unable to attend out-patient programmes.

**Keywords:** Exercise; Pulmonary Rehabilitation.

## Conflict of interest statement

Competing interests: AT, TK, CSU and NSG have no competing interests to report in relation to the presented work. HH received personal grants from the Danish Lung Foundation (charitable funding), Telemedical Center, Regional Capital Copenhagen (governmental funding), TrygFonden Foundation (charitable funding) during the conduct of this study. The grants covered expenses conducting the trial, salary and university fee for the PhD study.



**Review**


Eur Respir Rev

. 2023 Jul 12;32(169):230013.

doi: 10.1183/16000617.0013-2023. Print 2023 Sep 30.


# Performance-based outcome measures to assess functionality in hospitalised patients with COPD exacerbations: a

# systematic review of the measurement properties

Naiara Tais Leonardi[1], Débora Mayumi Oliveira Kawakami[1], John R Hurst[2], Joana Cruz[3], Renata Gonçalves Mendes[4]

Affiliations expand

- PMID: 37437913
- PMCID: PMC10336549
- DOI: 10.1183/16000617.0013-2023

**Free PMC article**

## Abstract

**Introduction:** Hospitalised patients with exacerbations of COPD (ECOPD) may have physical and functional impairments that impact morbidity and readmission. Therefore, it is crucial to properly identify reduced functionality in these patients to support a personalised rehabilitation. The objective of this study is to summarise and compare the measurement properties of functionality performance-based outcome measures for hospitalised patients with ECOPD.

**Methods:** A systematic review based on the Consensus-based Standards for the selection of health Measurement Instruments (COSMIN) was performed. The PubMed, Embase, PEDro and Cochrane databases were searched using terms related to functionality, hospitalised patients with ECOPD and measurement properties. Studies were selected and extracted by two researchers. The COSMIN Risk of Bias checklist was applied to assess the methodological quality of the studies and measurement property results were compared with the criteria for good measurement properties. Quality of evidence was graded using a modified Grades of Recommendation, Assessment, Development and Evaluation approach.

**Results:** 13 studies were included with nine outcome measures, namely the 6-min pegboard ring test, the de Morton mobility index, the incremental shuttle walk test (ISWT), the 6-min walk test (6MWT), maximum inspiratory pressure (MIP), the Berg balance scale, 4-m gait speed, handgrip strength and the 6-min stepper test. Construct validity was rated as sufficient, except for the ISWT. Responsiveness, assessed only for MIP, was considered insufficient and measurement errors for the ISWT and 6MWT were insufficient, with a very low quality of evidence for all measurement properties.

**Conclusion:** Measurement properties of performance-based outcome measures to assess functionality in patients hospitalised with ECOPD are still scarce, with very low evidence supporting validity and a lack of evidence of responsiveness and reliability. Further studies are needed to address this topic and guide assertive and personalised management.



# Conflict of interest statement

Conflict of interest: N.T. Leonardi reports support for the present manuscript from FAPESP (São Paulo Research Foundation) in the form of English review and article processing charges, as well as support in attending meetings and travels to present products/results of the project. J.R. Hurst reports consulting fees from AstraZeneca, GSK; lecture honoraria from Boehringer Ingelheim, Chiesi, Sanofi, Takeda; travel support and advisory board participation from AstraZeneca; donation of oximeters from Nonin; outside the submitted work. J. Cruz reports travel support to attend the European Respiratory Society Congress 2022 as the representative of the Early Career Members of Assembly 9; and is a member of the Editorial Board of ERJ Open Research (unpaid); outside the submitted work. R.G. Mendes reports support for the present manuscript from FAPESP (São Paulo Research Foundation), in the form of project funding providing support for buying laboratory consumables materials and equipment and also article processing charges and maintenance costs, as well as attending meetings and travels to present products/results of the project. All other authors have nothing to disclose.


- 68 references

supplementary info

Publication types, MeSH termsexpand

full text links

Proceed to details

Cite

Share

47

Respirology

. 2023 Oct;28(10):942-953.

doi: 10.1111/resp.14553. Epub 2023 Jul 11.

# Supranormal lung function: Prevalence, associated factors and clinical manifestations across the lifespan

Caspar Schiffers[1], Rosa Faner[2,3,4], Alina Ofenheimer[1,5], Owat Sunanta[1], Patricia Puchhammer[1], Tobias Mraz[1,6], Marie-Kathrin Breyer[1,6], Otto Chris Burghuber[1,7], Sylvia Hartl[1,6,7], Alvar Agustí[2,3,4,8], Robab Breyer-Kohansal[1,6]

Affiliations expand

- PMID: 37434280

- DOI: 10.1111/resp.14553

**Abstract**

**Background and objective:** It is now well established that there are different life-long lung function trajectories in the general population, and that some are associated with better or worse health outcomes. Yet, the prevalence, clinical characteristics and risk factors of individuals with supranormal $FEV_1$ or FVC values (above the upper-limit of normal [ULN]) in different age-bins through the lifetime in the general population are poorly understood.

**Method:** To address these questions, we investigated the prevalence of supranormal $FEV_1$ and FVC values in the LEAD (Lung, hEart, sociAl and boDy) study, a general population cohort in Austria that includes participants from 6 to 82 years of age.

**Results:** We found that: (1) the prevalence of supranormal pre-bronchodilator $FEV_1$ and FVC values was 3.4% and 3.1%, respectively, and that these figures remained relatively stable through different age-bins except for participants >60 years., in whom they increased (5.0% and 4.2%, respectively). Approximately 50% of supranormal individuals had both increased $FEV_1$ and FVC values; (2) supranormal spirometric values were consistently accompanied by higher static lung volumes and lower specific airway resistance through the lifespan, indicating better overall lung function; and (3) multivariate regression analysis identified that female sex, higher muscle mass (FFMI), less diabetes and fewer respiratory symptoms were consistently associated with supranormal $FEV_1$ and FVC values.

**Conclusion:** Supranormal $FEV_1$ and/or FVC values occur in about 3% of the general population in different age bins and are associated with better health markers.

**Keywords:** COPD; asthma; chronic obstructive pulmonary disease; diabetes; lung function trajectories; lung health; smoking; spirometry.




- 25 references

supplementary info

MeSH terms, Grants and fundingexpand

full text links

Proceed to details

Cite

Share


48

Qual Life Res

. 2023 Oct;32(10):2875-2886.

doi: 10.1007/s11136-023-03447-5. Epub 2023 Jul 10.

# Measuring skill-based health literacy in chronic airway disease patients: the development and psychometric evaluation of the Vancouver airways health literacy tool (VAHLT)

Richard E Hohn[1], Jacek A Kopec[2], Richard Sawatzky[3 4], Iraj Poureslami[5 6 7], J Mark FitzGerald[5 7]

Affiliations expand

- PMID: 37428406

- DOI: 10.1007/s11136-023-03447-5

**Abstract**

**Purpose:** This article describes the development of the Vancouver airways health literacy tool (VAHLT), a novel measure of skill-based health literacy specific to chronic airway diseases (CADs). Across several phases, psychometric characteristics of the VAHLT were examined and used to guide its development.

**Methods:** An initial pool of 46 items was developed using input from patients, clinicians, researchers, and policy-makers. An initial patient sample (N = 532) was evaluated and used to inform item revisions. A revised 44-item pool was then evaluated using a second sample, the results of which aided in the selection of a final set of 30 items. The finalized 30-item VAHLT was then psychometrically evaluated using the second sample (N = 318). An item response theory approach was utilized to evaluate the VAHLT by assessing model fit, item parameter estimates, test and item information curves, and item characteristic curves. Reliability was assessed using ordinal coefficient alpha. We additionally assessed differential item functioning between asthma and COPD diagnoses.

**Results:** The VAHLT demonstrated a unidimensional structure and reasonably discriminated patients in the lower range of health literacy estimates. The tool demonstrated strong reliability (α = .920). Two of the 30 items were found to exhibit non-negligible differential item functioning.

**Conclusions:** This study presents compelling evidence of validity in several areas for the VAHLT, including content and structural validity. Further external validation studies are needed and forthcoming. Overall, this work represents a strong first step towards a novel, skill-based, and disease-specific measure of CAD-related health literacy.

**Keywords:** Assessment; Chronic respiratory disease; Disease management; Health competencies; Health literacy; Psychometrics.



- 31 references

supplementary info

MeSH terms, Supplementary concepts, Grants and fundingexpand

full text links

**Observational Study**

Pulm Pharmacol Ther

- 
- 
- 

. 2023 Oct;82:102231.

doi: 10.1016/j.pupt.2023.102231. Epub 2023 Jul 4.

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

Paola Rogliani[1], Dejan Radovanovic[2], Josuel Ora[3], Nadia Starc[3], Stefano Verri[3], Elena Pistocchini[3], Luigino Calzetta[4]

Affiliations expand

- PMID: 37414133

- DOI: 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 ≥22 pulmonary centres in Italy and that enrols ≥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.



# Conflict of interest statement

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

## supplementary info

Publication types, MeSH terms, Supplementary concepts, Associated dataexpand

## full text links



50

Ann Am Thorac Soc

- 
- 
- 

. 2023 Oct;20(10):1425-1434.

doi: 10.1513/AnnalsATS.202304-303OC.

# Dynamic Ventilatory Reserve During Incremental Exercise: Reference Values and Clinical Validation in Chronic Obstructive Pulmonary Disease

Danilo C Berton[1], Franciele Plachi[1], Matthew D James[2], Sandra G Vincent[2], Reginald M Smyth[2], Nicolle J Domnik[2], Devin B Phillips[2,3], Juan P de-Torres[2], Luiz E Nery[4], Denis E O'Donnell[2], J Alberto Neder[2]

Affiliations expand

- PMID: 37413694

- DOI: 10.1513/AnnalsATS.202304-303OC

**Abstract**

**Rationale:** Ventilatory demand-capacity imbalance, as inferred based on a low ventilatory reserve, is currently assessed only at peak cardiopulmonary exercise testing (CPET). Peak ventilatory reserve, however, is poorly sensitive to the submaximal, dynamic mechanical ventilatory abnormalities that are key to dyspnea genesis and exercise intolerance. **Objectives:** After establishing sex- and age-corrected norms for dynamic ventilatory reserve at progressively higher work rates, we compared peak and dynamic ventilatory reserve for their ability to expose increased exertional dyspnea and poor exercise tolerance in mild to very severe chronic obstructive pulmonary disease (COPD). **Methods:** We analyzed resting functional and incremental CPET data from 275 controls (130 men, aged 19-85 yr) and 359 Global Initiative for Chronic Obstructive Lung Disease patients with stage 1-4 obstruction (203 men) who were prospectively recruited for previous ethically approved studies in three research centers. In addition to peak and dynamic ventilatory reserve (1 - [ventilation / estimated maximal voluntary ventilation] × 100), operating lung volumes and dyspnea scores (0-10 on the Borg scale) were obtained. **Results:** Dynamic ventilatory reserve was asymmetrically distributed in controls; thus, we calculated its centile distribution at every 20 W. The lower limit of normal (lower than the fifth centile) was consistently lower in women and older subjects. Peak and dynamic ventilatory reserve disagreed significantly in indicating an abnormally low test result in patients: whereas approximately 50% of those with a normal peak ventilatory reserve showed a reduced dynamic ventilatory reserve, the opposite was found in approximately 15% ($P < 0.001$). Irrespective of peak ventilatory reserve and COPD severity, patients who had a dynamic ventilatory reserve below the lower limit of normal at an isowork rate of 40 W had greater ventilatory requirements, prompting earlier attainment of critically low inspiratory reserve. Consequently, they reported higher dyspnea scores, showing poorer exercise tolerance compared with those with preserved dynamic

ventilatory reserve. Conversely, patients with preserved dynamic ventilatory reserve but reduced peak ventilatory reserve reported the lowest dyspnea scores, showing the best exercise tolerance. **Conclusions:** Reduced submaximal dynamic ventilatory reserve, even in the setting of preserved peak ventilatory reserve, is a powerful predictor of exertional dyspnea and exercise intolerance in COPD. This new parameter of ventilatory demand-capacity mismatch may enhance the yield of clinical CPET in the investigation of activity-related breathlessness in individual patients with COPD and other prevalent cardiopulmonary diseases.

**Keywords:** COPD; cardiopulmonary exercise testing; dyspnea; lung mechanics; ventilation.



51

Respir Med

. 2023 Oct;217:107347.

doi: 10.1016/j.rmed.2023.107347. Epub 2023 Jul 3.

# Underdiagnosis and misclassification of COPD in Sweden - A Nordic Epilung study

Malin Axelsson[1], Helena Backman[2], Bright I Nwaru[3], Caroline Stridsman[4], Lowie Vanfleteren[5], Linnea Hedman[2], Päivi Piirilä[6], Juuso Jalasto[6], Arnulf Langhammer[7], Hannu Kankaanranta[8], Madeleine Rådinger[9], Linda Ekerljung[9], Eva Rönmark[2], Anne Lindberg[4]

Affiliations expand

- PMID: 37406781

- DOI: 10.1016/j.rmed.2023.107347

**Free article**

**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. $COPD_{GOLD}$ 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 $COPD_{GOLD}$, 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.




52

Respir Med

. 2023 Oct;217:107309.

doi: 10.1016/j.rmed.2023.107309. Epub 2023 Jun 30.


# Dyspnea-induced Limitation (DYSLIM), a new self-administered concise questionnaire to evaluate dyspnea-related

# activity limitation in chronic respiratory diseases

Thierry Perez[1], Nicolas Roche[2], Hilario Nunes[3], Pierre-Régis Burgel[2], Ari Chaouat[4], Pascale Surpas[5], Frédéric Herengt[6], Gilles Garcia[7], Jean-Marie Grosbois[8], Sandrine Stelianides[9], Philippe de Rigal[10], Philippe Guérin[11], Benoît Arnould[12], Joël Coste[13]

Affiliations expand

- PMID: 37394196

- DOI: 10.1016/j.rmed.2023.107309

**Abstract**

**Background and aim:** Few questionnaires are available for routine assessment of dyspnea. The study aimed to design a self-administered questionnaire assessing the impact of chronic dyspnea on daily activities, named DYSLIM (Dyspnea-induced Limitation).

**Methods:** The development followed 4 steps: 1: selection of relevant activities and related questions (focus groups); 2: clinical study: internal and concurrent validity vs. modified Medical Research Council (mMRC), Baseline Dyspnea Index (BDI) and Saint George Respiratory Questionnaire (SGRQ); 3: item reduction; 4: responsiveness. Eighteen activities (from eating to climbing stairs) were considered with 5 modalities for each: doing the task slowly, taking breaks, seeking assistance, changing habits, and activity avoidance. Each modality was graded from 5 (never) to 1 (very often). Validation study included 194 patients: COPD (FEV1 ≥ 50% pred: n = 40; FEV1 < 50% pred: n = 65); cystic fibrosis (n = 30), interstitial lung disease (n = 30), pulmonary hypertension (n = 29). Responsiveness was evaluated by post-pulmonary rehabilitation data in 52 COPD patients.

**Results:** Acceptability was high and short term (7 days) reproducibility was satisfactory (Kappa mostly above 0.7). Concurrent validity was high vs. mMRC (Spearman correlation coefficient, r = 0.71), BDI (r = - 0.75) and SGRQ (r = - 0.79). The reduced questionnaire with 8 activities (from cleaning to climbing stairs) and 3 modalities (slowly, seeking help, changing habits) showed a comparable validity and was chosen as the final short version. Effect size of rehabilitation was good for both the full (0.57) and short (0.51) versions. A significant correlation was also found between changes of SGRQ and DYSLIM post rehabilitation: r = - 0.68 and r = - 0.60 for full and reduced questionnaires, respectively.

**Conclusion:** The DYSLIM questionnaire appears promising for the evaluation of dyspnea-induced limitations in chronic respiratory diseases and seems suitable for use in various contexts.

**Keywords:** COPD; Cystic fibrosis; Dyspnea; Interstitial lung disease; Pulmonary hypertension; Questionnaire.



## Conflict of interest statement

Declaration of competing interest No Conflict of interest.



doi: 10.1007/s12325-023-02583-1. Epub 2023 Jun 29.

# DElaying Disease Progression In COPD with Early Initiation of Dual Bronchodilator or Triple Inhaled PharmacoTherapy (DEPICT): A Predictive Modelling Approach

Dave Singh[1,2], Diego Litewka[3], Rafael Páramo[4], Adrian Rendon[5], Abdullah Sayiner[6], Suzana E Tanni[7], Sudeep Acharya[8], Bhumika Aggarwal[8], Afisi S Ismaila[9,10], Raj Sharma[11], Peter Daley-Yates[12]

Affiliations expand

- PMID: 37382864

- PMCID: PMC10499693

- DOI: 10.1007/s12325-023-02583-1

**Free PMC article**

**Erratum in**

- Correction to: DElaying Disease Progression In COPD with Early Initiation of Dual Bronchodilator or Triple Inhaled PharmacoTherapy (DEPICT): A Predictive Modelling Approach.
  Singh D, Litewka D, Páramo R, Rendon A, Sayiner A, Tanni SE, Acharya S, Aggarwal B, Ismaila AS, Sharma R, Daley-Yates P.Adv Ther. 2023 Oct;40(10):4689-4690. doi: 10.1007/s12325-023-02613-y. Epub 2023 Jul 28.PMID: 37505374 **Free PMC article.** No abstract available.

# Abstract

**Introduction:** Clinical studies demonstrate an accelerated decline in lung function in patients with moderate chronic obstructive pulmonary disease (COPD) (Global Initiative for Chronic Obstructive Lung Disease [GOLD] grade 2) versus severe and very severe COPD (GOLD grades 3 and 4). This predictive modelling study assessed the impact of initiating pharmacotherapy earlier versus later on long-term disease progression in COPD.

**Methods:** The modelling approach used data on decline in forced expiratory volume in 1 s ($FEV_1$) extracted from published studies to develop a longitudinal non-parametric superposition model of lung function decline with progressive impact of exacerbations from 0 per year to 3 per year and no ongoing pharmacotherapy. The model simulated decline in $FEV_1$ and annual exacerbation rates from age 40 to 75 years in COPD with initiation of long-acting anti-muscarinic antagonist (LAMA)/long-acting $beta_2$-agonist (LABA) (umeclidinium (UMEC)/vilanterol (VI)) or triple (inhaled corticosteroid (ICS)/LAMA/LABA; fluticasone furoate (FF)/UMEC/VI) therapy at 40, 55 or 65 years of age.

**Results:** Model-predicted decline in $FEV_1$ showed that, compared with 'no ongoing' therapy, initiation of triple or LAMA/LABA therapy at age 40, 55 or 65 years preserved an additional 469.7 mL or 236.0 mL, 327.5 mL or 203.3 mL, or 213.5 mL or 137.5 mL of lung function, respectively, by the age of 75. The corresponding average annual exacerbation rates were reduced from 1.57 to 0.91, 1.06 or 1.23 with triple therapy or to 1.2, 1.26 and 1.4 with LAMA/LABA therapy when initiated at 40, 55 or 65 years of age, respectively.

**Conclusions:** This modelling study suggests that earlier initiation of LAMA/LABA or triple therapy may have positive benefits in slowing disease progression in patients with COPD. Greater benefits were demonstrated with early initiation therapy with triple versus LAMA/LABA.

**Keywords:** COPD exacerbation; Chronic obstructive pulmonary disease (COPD); Dual bronchodilator therapy (LAMA/LABA); GOLD grades; Lung function decline; Triple therapy (ICS/LAMA/LABA).



# Conflict of interest statement

Dave Singh has received consulting fees from Aerogen, AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, CSL Behring, Epiendo, Genentech, GSK, Glenmark, Gossamerbio, Kinaset, Menarini, Novartis, Orion, Pulmatrix, Sanofi, Synairgen, Teva, Theravance and Verona. Diego Litewka has received honoraria for lectures, presentations, speakers' bureaus or educational events and participation in an advisory board from GSK; and support for travel/attending meetings from Boehringer Ingelheim and Tuteur. Rafael Páramo has received consulting fees from Chiesi and GSK; payment for lectures and presentations at medical meetings from AstraZeneca, Boehringer Ingelheim, GSK and Novartis; and support for travel/attending meetings from AstraZeneca, Boehringer Ingelheim, Chiesi, GSK and Novartis. Adrian Rendon has received consulting fees, honoraria for lectures, presentations, speakers' bureaus or educational events, and participation in advisory boards from AstraZeneca, Boehringer Ingelheim, Chiesi, GSK and Sanofi; and has received support for travel/attending meetings from Chiesi. Abdullah Sayiner has received honoraria for lectures, presentations, speakers' bureaus or educational events from Abdi Ibrahim, Bilim, Deva and GSK; and fees for participation in advisory boards from Abdi Ibrahim and GSK. Suzana Erico Tanni has received honoraria for educational events from Gilead. Sudeep Acharya, Bhumika Aggarwal, Afisi S Ismaila and Raj Sharma are employees of GSK and hold GSK shares. Afisi S Ismaila is also an unpaid part-time faculty member at the McMaster University in Canada. Peter Daley-Yates is a former employee of GSK and holds GSK shares. Peter Daley-Yates is currently an independent clinical pharmacology consultant.

- 65 references
- 3 figures

supplementary info

Publication types, MeSH terms, Substancesexpand

full text links

**Editorial**

Thorax

. 2023 Oct;78(10):951-952.

doi: 10.1136/thorax-2023-220411. Epub 2023 Jun 28.

# Getting the best from pulmonary rehabilitation

Sara C Buttery[1,2]

Affiliations expand

- PMID: 37380355

- DOI: 10.1136/thorax-2023-220411

***No abstract available***

**Keywords:** exercise; pulmonary rehabilitation.

## Conflict of interest statement

Competing interests: None declared.

## supplementary info

Publication types, MeSH termsexpand

55

Ann Am Thorac Soc

. 2023 Oct;20(10):1397-1399.

doi: 10.1513/AnnalsATS.202304-366VP.

# Pulmonary Rehabilitation in Chronic Obstructive Pulmonary Disease: Medicine's Best-kept Secret That Could Save Medicare a Billion Dollars a Year

Christopher L Mosher[1,2], Michael Belman[3], Chris Garvey[3], Richard Casaburi[4]

Affiliations expand

- PMID: 37364287

- DOI: 10.1513/AnnalsATS.202304-366VP

***No abstract available***

full text links

Proceed to details

Cite

Ann Am Thorac Soc

- 
- 
- 

. 2023 Oct;20(10):1435-1444.

doi: 10.1513/AnnalsATS.202211-964OC.

# Cardiovascular Autonomic Function and Incident Chronic Obstructive Pulmonary Disease Hospitalizations in Atherosclerosis Risk in Communities

David M MacDonald[1,2], Yuekai Ji[3], Selcuk Adabag[4,5], Alvaro Alonso[6], Lin Yee Chen[5], Benjamin E Henkle[1,2], Stephen P Juraschek[7], Faye L Norby[8], Pamela L Lutsey[3], Ken M Kunisaki[1,2]

Affiliations expand

- PMID: 37364277

- DOI: 10.1513/AnnalsATS.202211-964OC

**Abstract**

**Rationale:** The autonomic nervous system extensively innervates the lungs, but its role in chronic obstructive pulmonary disease (COPD) outcomes has not been well studied. **Objective:** We assessed relationships between cardiovascular autonomic nervous system measures (heart rate variability [HRV] and orthostatic hypotension [OH]) and incident COPD hospitalization in the multicenter ARIC (Atherosclerosis Risk In Communities) study. **Methods:** We used Cox proportional hazards regression models to estimate hazard ratios and 95% confidence intervals between baseline (1987-1989) autonomic function measures (HRV measures from 2-minute electrocardiograms and OH variables) and incident COPD hospitalizations through 2019. Adjusted analyses included demographic data, smoking status, lung function, comorbidities, and physical activity. We also performed analyses stratified by baseline airflow obstruction. **Results:** Of the 11,625 participants, (mean age, 53.8 yr), 56.5% were female and 26.3% identified as Black. Baseline mean percentage predicted forced expiratory volume in 1 second was 94 ± 17% (standard

deviation), and 2,599 participants (22.4%) had airflow obstruction. During a median follow-up time of 26.9 years, there were 2,406 incident COPD hospitalizations. Higher HRV (i.e., better autonomic function) was associated with a lower risk of incident COPD hospitalization. Markers of worse autonomic function (OH and greater orthostatic changes in systolic and diastolic blood pressure) were associated with a higher risk of incident COPD hospitalization (hazard ratio for the presence of OH, 1.5; 95% confidence interval, 1.25-1.92). In stratified analyses, results were more robust in participants without airflow obstruction at baseline. **Conclusions:** In this large multicenter prospective community cohort, better cardiovascular autonomic function at baseline was associated with a lower risk of subsequent hospitalization for COPD, particularly among participants without evidence of lung disease at baseline.

**Keywords:** autonomic nervous system; chronic obstructive; cohort studies; disease exacerbation; pulmonary disease.

# Comment in

- The Autonomous Nervous System: A Novel and Potentially Modifiable Risk Factor for Chronic Obstructive Pulmonary Disease in the Population?
Hamrefors V.Ann Am Thorac Soc. 2023 Oct;20(10):1402-1403. doi: 10.1513/AnnalsATS.202307-618ED.PMID: 37772941 No abstract available.



. 2023 Oct;53(10):e14043.

doi: 10.1111/eci.14043. Epub 2023 Jun 20.

# Association between spirometry pattern, left ventricular diastolic function, and mortality

Wei-Ming Huang[1,2,3,4], Hao-Chih Chang[2,5], Ching-Wei Lee[1,2], Chi-Jung Huang[6], Wen-Chung Yu[1,2], Hao-Min Cheng[2,3,6,7,8], Chao-Yu Guo[3], Chern-En Chiang[1,2,7], Chen-Huan Chen[2,3,6], Shih-Hsien Sung[1,2,8,9]

Affiliations expand

- PMID: 37340550

- DOI: 10.1111/eci.14043

**Abstract**

**Background:** Spirometric abnormalities have been related to incident heart failure in general population, who generally have preserved left ventricular ejection fraction (LVEF). We aimed to investigate the association between spirometric indices, cardiac functions and clinical outcomes.

**Methods:** Subjects presenting with exertional dyspnoea and received spirometry and echocardiography were eligible for this study. Forced vital capacity (FVC) and forced expiratory volume in the first second (FEV1)/FVC ratio were measured to define the spirometry patterns: normal (FEV1/FVC ≥ 70%, FVC ≥ 80%), obstructive (FEV1/FVC < 70%, FVC ≥ 80%), restrictive pattern (FEV1/FVC ≥ 70%, FVC < 80%) and mixed (FEV1/FVC < 70%, FVC < 80%). The diastolic dysfunction index (DDi) was the counts of the indicators, including septal e' velocity <7 cm/s, septal E/e' > 15, pulmonary artery systolic pressure > 35 mmHg and left atrial dimension >40 mm.

**Results:** Among a total of 8669 participants (65.8 ± 16.3 years, 56% men), 3739 (43.1%), 829 (9.6%), 3050 (35.2%) and 1051 (12.1%) had normal, obstructive, restrictive and mixed spirometry pattern, respectively. Subjects with restrictive or mixed spirometry pattern had higher DDi and worse long-term survival than those with obstructive or normal ventilation. FVC but not FEV1/FVC was predictive of 5-year mortality, independent of age, sex, renal function, LVEF, DDi, body mass index, and comorbidities (hazard ratio, 95% confidence intervals: .981, .977-.985). Furthermore, there was an inverse nonlinear relationship between FVC and DDi, suggesting the declined FVC may mediate 43% of the prognostic hazard of left ventricular diastolic dysfunction.

**Conclusions:** The restrictive spirometry pattern or the declined FVC was associated with left ventricular diastolic dysfunction, which aggravated the long-term mortality in the ambulatory dyspnoeic subjects.

**Keywords:** left ventricular diastolic dysfunction; long-term survival; pulmonary function test; spirometry.




- 39 references

supplementary info

MeSH terms, Grants and fundingexpand

full text links

Proceed to details

Cite

Share

58

**Meta-Analysis**


Thorax

- 
- 
- 

. 2023 Oct;78(10):1004-1010.

doi: 10.1136/thorax-2023-219988. Epub 2023 May 22.

# Acetazolamide for metabolic alkalosis complicating respiratory failure with chronic obstructive pulmonary disease or obesity hypoventilation syndrome: a systematic review

Timothy John Bemand[1 2 3], Richard Chatoor[4 2 5], Patrizia Natale[3 6 7], Giovanni Strippoli[3 6], Anthony Delaney[5 8 9 10]

Affiliations expand

- PMID: 37217290

- DOI: 10.1136/thorax-2023-219988

## Abstract

**Background:** Metabolic alkalosis may lead to respiratory inhibition and increased need for ventilatory support or prolongation of weaning from ventilation for patients with chronic respiratory disease. Acetazolamide can reduce alkalaemia and may reduce respiratory depression.

**Methods:** We searched Medline, EMBASE and CENTRAL from inception to March 2022 for randomised controlled trials comparing acetazolamide to placebo in patients with chronic obstructive pulmonary disease, obesity hypoventilation syndrome or obstructive sleep apnoea, hospitalised with acute respiratory deterioration complicated by metabolic alkalosis. The primary outcome was mortality and we pooled data using random-effects meta-analysis. Risk of bias was assessed using the Cochrane RoB 2 (Risk of Bias 2) tool, heterogeneity was assessed using the $I^2$ value and $\chi^2$ test for heterogeneity. Certainty of evidence was assessed using GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) methodology.

**Results:** Four studies with 504 patients were included. 99% of included patients had chronic obstructive pulmonary disease. No trials recruited patients with obstructive sleep apnoea. 50% of trials recruited patients requiring mechanical ventilation. Risk of bias was overall low to some risk. There was no statistically significant difference with acetazolamide in mortality (relative risk 0.98 (95% CI 0.28 to 3.46); p=0.95; 490 participants; three studies; GRADE low certainty) or duration of ventilatory support (mean difference -0.8 days (95% CI -7.2 to 5.6); p=0.36; 427 participants; two studies; GRADE: low certainty).

**Conclusion:** Acetazolamide may have little impact on respiratory failure with metabolic alkalosis in patients with chronic respiratory diseases. However, clinically significant benefits or harms are unable to be excluded, and larger trials are required.

**Prospero registration number:** CRD42021278757.

**Keywords:** Assisted Ventilation; COPD Exacerbations; Critical Care.

## Conflict of interest statement

Competing interests: None declared.

supplementary info

Publication types, MeSH terms, Substancesexpand

full text links

Proceed to details

Cite

Share

59

Ann Biomed Eng

. 2023 Oct;51(10):2100-2102.

doi: 10.1007/s10439-023-03238-6. Epub 2023 May 15.

# Revolutionizing Chronic Obstructive Pulmonary Disease Care with the Open AI Application: ChatGPT

Muhammad Hasnain[1], Asad Hayat[2], Akbar Hussain[3]

Affiliations expand

- PMID: 37184746

- DOI: 10.1007/s10439-023-03238-6

**Abstract**

Chronic Obstructive Pulmonary Disease (COPD) is one of the major and leading threats to human being. To cope with this health challenge, several studies have been undertaken in the literature. However, COPD is not paid close attention to eliminate it entirely. The current study aims to examine the role of ChatGPT application to bring improvement in controlling and managing COPD in patients. ChatGPT is used to give prompt answers of text-based questions in a variety of fields. It has potential role in knowing the symptoms of COPD, and letting individuals to modify their life styles. ChatGPT suggests medications for COPD individuals based on the established medical guidelines. Compared to the literature, ChatGPT provides a comprehensive list of COPD test and evaluation methods. ChatGPT has the potential to help physicians to take decisions in diagnosing, treating, and managing COPD among individuals in its upcoming versions. More researches can be conducted to identify the limits of ChatGPT application in future works.

**Keywords:** COPD tests; Medication; Pulmonary rehabilitation.



- 16 references

## supplementary info

Publication types, MeSH termsexpand

## full text links

Proceed to details

Cite

Share

60

Thorax

- 
- 
- 

. 2023 Oct;78(10):974-982.

doi: 10.1136/thorax-2022-219619. Epub 2023 May 5.

# Short-term air pollution exposure and exacerbation events in mild to moderate COPD: a case-crossover study within the CanCOLD cohort

Bryan A Ross[1,2], Dany Doiron[1], Andrea Benedetti[1], Shawn D Aaron[3], Kenneth Chapman[4], Paul Hernandez[5], François Maltais[6], Darcy Marciniuk[7], Denis E O'Donnell[8], Don D Sin[9], Brandie L Walker[10], Wan Tan[9], Jean Bourbeau[11,2]; CanCOLD Collaborative Research Group and the Canadian Respiratory Research Network

Affiliations expand

- PMID: 37147124

- DOI: 10.1136/thorax-2022-219619

**Abstract**

**Background:** Infections are considered as leading causes of acute exacerbations of chronic obstructive pulmonary disease (COPD). Non-infectious risk factors such as short-term air pollution exposure may play a clinically important role. We sought to estimate the relationship between short-term air pollutant exposure and exacerbations in Canadian adults living with mild to moderate COPD.

**Methods:** In this case-crossover study, exacerbations ('symptom based': ≥48 hours of dyspnoea/sputum volume/purulence; 'event based': 'symptom based' plus requiring antibiotics/corticosteroids or healthcare use) were collected prospectively from 449 participants with spirometry-confirmed COPD within the Canadian Cohort Obstructive Lung Disease. Daily nitrogen dioxide ($NO_2$), fine particulate matter ($PM_{2.5}$), ground-level ozone ($O_3$), composite of $NO_2$ and $O_3$ ($O_x$), mean temperature and relative humidity estimates were obtained from national databases. Time-stratified sampling of hazard and control periods on day '0' (day-of-event) and Lags ('-1' to '-6') were compared by fitting generalised estimating equation models. All data were dichotomised into 'warm' (May-October) and 'cool' (November-April) seasons. ORs and 95% CIs were estimated per IQR increase in pollutant concentrations.

**Results:** Increased warm season ambient concentration of $NO_2$ was associated with symptom-based exacerbations on Lag-3 (1.14 (1.01 to 1.29), per IQR), and increased cool season ambient $PM_{2.5}$ was associated with symptom-based exacerbations on Lag-1 (1.11 (1.03 to 1.20), per IQR). There was a negative association between warm season ambient $O_3$ and symptom-based events on Lag-3 (0.73 (0.52 to 1.00), per IQR).

**Conclusions:** Short-term ambient $NO_2$ and $PM_{2.5}$ exposure were associated with increased odds of exacerbations in Canadians with mild to moderate COPD, further heightening the awareness of non-infectious triggers of COPD exacerbations.

**Keywords:** COPD epidemiology; COPD exacerbations; COPD exacerbations mechanisms; Clinical epidemiology.



# Conflict of interest statement

Competing interests: BAR reports grants/contracts from the Canadian Institutes of Health Research (CIHR), Réseau de Recherche en Santé Respiratoire du Québec (RSRQ), Research Institute of the MUHC (RI MUHC), Ministère de l'Économie et de l'Innovation (MEI) Québec, McGill University Health Centre (MUHC) Foundation Grant, Fonds de Recherche Santé Québec (FRSQ), and CHEST Foundation Grant; and payments/honoraria from the Canadian Thoracic Society (CTS), CHEST/ACCP, Respiplus (non-profit), Alberta Kinesiology Association (AKA), and McGill University Continuing Professional Development (CPD). SDA reports payments/honoraria from AstraZeneca, GSK; and participation on Data Safety Monitoring/Advisory Board for AstraZeneca, GSK, and Sanofi. PH reports grants/contracts from Boehringer Ingelheim, Cyclomedica, Grifols, Vertex; consulting fees from Acceleron, AstraZeneca, Boehringer Ingelheim, Covis, GlaxoSmithKline, Janssen, Novartis, Sanofi, Teva, Takeda, Valeo; and leadership/fiduciary role in the Canadian Thoracic Society. FM reports grants/contracts from GlaxoSmithKline, AstraZeneca, Sanofi, Novartis, Boehringer Ingelheim, Grifols; consulting fees from AstraZeneca; payment/honoraria from GlaxoSmithKline, Boehringer Ingelheim, Grifols, Novartis; and stock/stock options from Oxynov. DM reports grants/contracts from AstraZeneca, Boehringer Ingelheim, Canadian Institute of Health Research, GlaxoSmithKline, Grifols, Lung Association—Saskatchewan, Novartis, Sanofi, Saskatchewan Health Research Foundation, Schering-Plough; consulting fees from Alberta Health Services, Canadian Foundation for Healthcare Improvement, Health Canada, Lung Association—Saskatchewan, Ontario Ministry of Health and Long-Term Care, Saskatchewan Health Authority, Yukon Health and Social Services; payment/honoraria from the Lung Association—Saskatchewan, American College of Chest Physicians; leadership/fiduciary role in the CHEST journal, Canadian Thoracic Society, American Thoracic Society and AARC; and is an employee of the University of Saskatchewan. DE O'D reports grants/contracts from AstraZeneca, Lung Health Foundation and Boehringer Ingelheim Canada; and payment/honoraria from GSK and Viajes Pacifico. BLW reports payment/honoraria from AstraZeneca, GSK, Sanofi; and Data Safety Monitoring/Advisory Board participation for AstraZeneca, GSK, and Sanofi. JB reports grants/contracts from the Canadian Institute of Health Research (CIHR), Réseau en santé respiratoire du FRQS, McGill University, McGill University Health Centre Foundation, AstraZeneca Canada Ltd, Boehringer Ingelheim Canada Ltd, GSK, Grifols, Novartis, Sanofil,

Trudell Canada Ltd; and payment/honoraria from AstraZeneca Canada Ltd, Boehringer Ingelheim Canada Ltd, GSK, Pfizer Canada Ltd, and Trudell Canada Ltd.

- Cited by 1 article

supplementary info

MeSH terms, Substancesexpand

full text links

Proceed to details

Cite

Share

61

**Review**

Physiol Rev

- 
- 
- 

. 2023 Oct 1;103(4):2349-2422.

doi: 10.1152/physrev.00058.2021. Epub 2023 Apr 6.

# Mitochondria in health, disease, and aging

John S Harrington[1], Stefan W Ryter[2], Maria Plataki[1], David R Price[1], Augustine M K Choi[1]

Affiliations expand

- PMID: 37021870

- PMCID: PMC10393386 (available on 2024-10-01)

- DOI: 10.1152/physrev.00058.2021

**Abstract**

Mitochondria are well known as organelles responsible for the maintenance of cellular bioenergetics through the production of ATP. Although oxidative phosphorylation may be their most important function, mitochondria are also integral for the synthesis of metabolic precursors, calcium regulation, the production of reactive oxygen species, immune signaling, and apoptosis. Considering the breadth of their responsibilities, mitochondria are fundamental for cellular metabolism and homeostasis. Appreciating this significance, translational medicine has begun to investigate how mitochondrial dysfunction can represent a harbinger of disease. In this review, we provide a detailed overview of mitochondrial metabolism, cellular bioenergetics, mitochondrial dynamics, autophagy, mitochondrial damage-associated molecular patterns, mitochondria-mediated cell death pathways, and how mitochondrial dysfunction at any of these levels is associated with disease pathogenesis. Mitochondria-dependent pathways may thereby represent an attractive therapeutic target for ameliorating human disease.

**Keywords:** inflammation; mitochondria; mitochondrial dynamics; mitochondrial dysfunction; mitophagy.

# Conflict of interest statement

S.W.R. is a current employee and stockholder of Proterris Inc. and a former Weill Cornell employee. A.M.K.C. is a cofounder and equity stockholder of Proterris, which develops therapeutic uses for carbon monoxide. A.M.K.C. has a use patent on CO. Additionally, A.M.K.C. has a patent in COPD. None of the other authors has any conflicts of interest, financial or otherwise, to disclose.

62

Thorax

. 2023 Oct;78(10):983-989.

doi: 10.1136/thorax-2022-219382. Epub 2023 Apr 3.

# Estimating individual treatment effects on COPD exacerbations by causal machine learning on randomised controlled trials

Kenneth Verstraete[1,2], Iwein Gyselinck[1], Helene Huts[1,2], Nilakash Das[1], Marko Topalovic[3], Maarten De Vos[2,4], Wim Janssens[5]

Affiliations expand

- PMID: 37012070
- PMCID: PMC10511983
- DOI: 10.1136/thorax-2022-219382

**Free PMC article**

## Abstract

**Rationale:** Estimating the causal effect of an intervention at individual level, also called individual treatment effect (ITE), may help in identifying response prior to the intervention.

**Objectives:** We aimed to develop machine learning (ML) models which estimate ITE of an intervention using data from randomised controlled trials and illustrate this approach with prediction of ITE on annual chronic obstructive pulmonary disease (COPD) exacerbation rates.

**Methods:** We used data from 8151 patients with COPD of the Study to Understand Mortality and MorbidITy in COPD (SUMMIT) trial (NCT01313676) to address the ITE of fluticasone furoate/vilanterol (FF/VI) versus control (placebo) on exacerbation rate and developed a novel metric, Q-score, for assessing the power of causal inference models. We then validated the methodology on 5990 subjects from the InforMing the PAthway of COPD Treatment (IMPACT) trial (NCT02164513) to estimate the ITE of FF/umeclidinium/VI

(FF/UMEC/VI) versus UMEC/VI on exacerbation rate. We used Causal Forest as causal inference model.

**Results:** In SUMMIT, Causal Forest was optimised on the training set (n=5705) and tested on 2446 subjects (Q-score 0.61). In IMPACT, Causal Forest was optimised on 4193 subjects in the training set and tested on 1797 individuals (Q-score 0.21). In both trials, the quantiles of patients with the strongest ITE consistently demonstrated the largest reductions in observed exacerbations rates (0.54 and 0.53, $p<0.001$). Poor lung function and blood eosinophils, respectively, were the strongest predictors of ITE.

**Conclusions:** This study shows that ML models for causal inference can be used to identify individual response to different COPD treatments and highlight treatment traits. Such models could become clinically useful tools for individual treatment decisions in COPD.

**Keywords:** COPD Exacerbations.



# Conflict of interest statement

Competing interests: KV has nothing to disclose. IG receives personal funding from Research Foundation Flanders (FWO). HH has nothing to disclose. ND has nothing to disclose. MT is CEO and co-founder of ArtiQ but received no payments related to the manuscript. MDV received funding from the AI in Flanders project. WJ received grants from AstraZeneca and Chiesi and obtained fees from AstraZeneca, Chiesi and GlaxoSmithKline. He is chairman of Board of Flemish Society for TBC prevention and board member of ArtiQ.


- 25 references
- 7 figures

supplementary info

MeSH terms, Substancesexpand

full text links

Proceed to details

Cite

Share

63

**Observational Study**

Anesth Analg

. 2023 Oct 1;137(4):806-818.

doi: 10.1213/ANE.0000000000006235. Epub 2022 Nov 1.

# Preoperative Spirometry in Patients With Known or Suspected Chronic Obstructive Pulmonary Disease Undergoing Major Surgery: The Prospective Observational PREDICT Study

André Dankert[1], Benedikt Neumann-Schirmbeck[1], Thorsten Dohrmann[1], Gillis Greiwe[1], Lili Plümer[1], Benjamin Löser[2], Susanne Sehner[3], Christian Zöllner[1], Martin Petzoldt[1]

Affiliations expand

- PMID: 36730893

- DOI: 10.1213/ANE.0000000000006235

## Abstract

**Background:** Pulmonary function tests (PFTs) such as spirometry and blood gas analysis have been claimed to improve preoperative pulmonary risk assessment, but the scientific literature is conflicting. The Preoperative Diagnostic Tests for Pulmonary Risk Assessment in Chronic Obstructive Pulmonary Disease (PREDICT) study aimed to determine whether preoperative PFTs improve the prediction of postoperative pulmonary complications (PPCs) in patients with known or suspected chronic obstructive pulmonary disease (COPD) undergoing major surgery. A secondary aim was to determine whether the Global Initiative for Chronic Obstructive Lung Diseases (GOLD) classification of airflow limitation severity (grades I-IV) is associated with PPC.

**Methods:** In this prospective, single-center study, patients with GOLD key indicators for COPD scheduled for major surgery received PFTs. Patients with confirmed COPD (forced

expiratory volume in 1 second [FEV1]/forced vital capacity [FVC] ≤0.7) were included in the COPD cohort and compared with a reference cohort without COPD. We developed 3 multivariable risk prediction models and compared their ability to predict PPC: the "standard model" (medical preconditions, and sociodemographic and surgical data), the "COPD assessment model" (additional GOLD key indicators, pack-years, and poor exercise capacity), and the "PFT model" (additional PFT parameters selected by adaptive least absolute shrinkage and selection operator [LASSO] regression). Multiple LASSO regressions were used for cross-validation.

**Results:** A total of 31,714 patients were assessed for eligibility; 1271 individuals received PFTs. Three hundred twenty patients (240 with confirmed COPD: 78 GOLD I, 125 GOLD II, 28 GOLD III, 9 GOLD IV, and 80 without COPD) completed follow-up. The diagnostic performance was similar among the standard model (cross-validated area under the curve [cvAUC], 0.723; bias-corrected bootstrapped [bc-b] 95% confidence interval [CI], 0.663-0.775), COPD assessment model (cvAUC, 0.724; bc-b 95% CI, 0.662-0.777), and PFT model (cvAUC, 0.729; bc-b 95% CI, 0.668-0.782). Previously known COPD was an independent predictor in the standard and COPD assessment model. %FEV1 PRED was the only PFT parameter selected by LASSO regression and was an independent predictor in the PFT model (adjusted odds ratios [OR], 0.98; 95% CI, 0.967-.0.998; P = .030). The risk for PPC significantly increased with GOLD grades ( P < .001). COPD was newly diagnosed in 53.8% of the patients with confirmed COPD; however, these individuals were not at increased risk for PPC ( P = .338).

**Conclusions:** COPD is underdiagnosed in surgical patients. Patients with newly diagnosed COPD commonly presented with low GOLD severity grades and were not at higher risk for PPC. Neither a structured COPD-specific assessment nor preoperative PFTs added incremental diagnostic value to the standard clinical preassessment in patients with known or suspected COPD. Unnecessary postponement of surgery and undue health care costs can be avoided.



# Conflict of interest statement

Conflicts of Interest: See Disclosures at the end of the article.

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

1

J Am Geriatr Soc

.
. 2023 Sep 29.

doi: 10.1111/jgs.18608. Online ahead of print.

# The impact of dual VA-Medicare use on a data-driven clinical management tool for older Veterans with multimorbidity

Franya Hutchins[1], Ann-Marie Rosland[1,2], Xinhua Zhao[1], Hongwei Zhang[1], Joshua M Thorpe[1,3]

Affiliations expand

- PMID: 37775961

- DOI: 10.1111/jgs.18608

**Abstract**

**Background:** Healthcare systems are increasingly turning to data-driven approaches, such as clustering techniques, to inform interventions for medically complex older adults. However, patients seeking care in multiple healthcare systems may have missing diagnoses across systems, leading to misclassification of resulting groups. We evaluated the impact of multi-system use on the accuracy and composition of multimorbidity groups among older adults in the Veterans Health Administration (VA).

**Methods:** Eligible patients were VA primary care users aged ≥65 years and in the top decile of predicted 1-year hospitalization risk in 2018 (n = 558,864). Diagnoses of 26 chronic conditions were coded using a 24-month lookback period and input into latent

class analysis (LCA) models. In a random 10% sample (n = 56,008), we compared the resulting model fit, class profiles, and patient assignments from models using only VA system data versus VA with Medicare data.

**Results:** LCA identified six patient comorbidity groups using VA system data. We labeled groups based on diagnoses with higher within-group prevalence relative to the average: Substance Use Disorders (7% of patients), Mental Health (15%), Heart Disease (22%), Diabetes (16%), Tumor (14%), and High Complexity (10%). VA with Medicare data showed improved model fit and assigned more patients with high accuracy. Over 70% of patients assigned to the Substance, Mental Health, High Complexity, and Tumor groups using VA data were assigned to the same group in VA with Medicare data. However, 41.9% of the Heart Disease group and 14.7% of the Diabetes group were reassigned to a new group characterized by multiple cardiometabolic conditions.

**Conclusions:** The addition of Medicare data to VA data for older high-risk adults improved clustering model accuracy and altered the clinical profiles of groups. Accessing or accounting for multi-system data is key to the success of interventions based on empiric grouping in populations with dual-system use.

**Keywords:** Veterans health; chronic disease; electronic health records; latent class analysis; patient care management.



- 47 references

## supplementary info

Grants and fundingexpand

## full text links

Proceed to details

Cite

Share

2

BMC Health Serv Res

-

. 2023 Sep 29;23(1):1041.

doi: 10.1186/s12913-023-09970-y.

# Economic evaluation of a multimorbidity patient centered care model implemented in the Chilean public health system

Paula Zamorano[1,2], Manuel Antonio Espinoza[3,4], Teresita Varela[1], Tomas Abbott[2], Alvaro Tellez[1,5], Nicolás Armijo[2], Francisco Suarez[6]

Affiliations expand

- PMID: 37773153

- DOI: 10.1186/s12913-023-09970-y

**Abstract**

Multimorbidity and patient-centered care approaches are growing challenges for health systems and patients. The cost of multimorbidity patients and the transition to a new care strategy is still sightly explored. In Chile, more than 70% of the adult population suffer from multimorbidity, opening an opportunity to implement a Multimorbidity patient-centered care model. The objective of this study was to perform an economic evaluation of the model from the public health system perspective.The methodology used a cost-consequence evaluation comparing seven exposed with seven unexposed primary care centers, and their reference hospitals. It followed three steps. First, we performed a Time-Driven Activity-Based Costing with routinely collected data routinely collected. Second, we run a comparative analysis through a propensity score matching and an estimation of the attributable costs to health services utilization at primary, secondary and tertiary care and health outcomes. Third, we estimated implementation and transaction costs.Results showed savings in aggregate costs of the total population (-0.12 (0.03) $p < 0.01$) during the period under evaluation. Costs in primary care showed a significant increase, whereas tertiary care showed significant savings. Health outcomes were associated with higher survival in patients under the new care model (HR 0.70 (0.05) $p < 0.01$). Implementation and transaction costs increased as the number of pilot intervention centers increased, and they represented 0,07% of the total annual budget of the Servicio de Salud Metropolitano Sur Oriente. After three years of piloting, the implementation and transaction cost for the total period was USD 1,838,767 and 393,775, respectively.The study's findings confirm the purpose of the new model to place primary health care at the center of care for people with non-communicable chronic diseases. Thus, it is necessary to consider implementation

and transaction costs to introduce a broad health system multimorbidity approach. The health system should assume some of them permanently to guarantee sustainability and facilitate scale-up.

**Keywords:** Chile; Economic evaluation; Implementation science; Multimorbidity; Transactional analysis.



- 44 references

full text links

Proceed to details

Cite

Share

3

**Comment**

Br J Gen Pract

- 
- 
- 

. 2023 Sep 28;73(735):443-444.

doi: 10.3399/bjgp23X735045. Print 2023 Oct.

# Multimorbidity: a problem in the body, or a problem of the system?

Esca van Blarikom[1], Nina Fudge[2], Deborah Swinglehurst[3]

Affiliations expand

- PMID: 37770224

- DOI: 10.3399/bjgp23X735045

***No abstract available***

# Comment on

- Overdiagnosis and overtreatment: generalists--it's time for a grassroots revolution.

Treadwell J, McCartney M.Br J Gen Pract. 2016 Mar;66(644):116-7. doi: 10.3399/bjgp16X683881.PMID: 26917633 **Free PMC article.** No abstract available.

- The polypharmacy challenge: time for a new script?

Swinglehurst D, Fudge N.Br J Gen Pract. 2017 Sep;67(662):388-389. doi: 10.3399/bjgp17X692189.PMID: 28860279 **Free PMC article.** No abstract available.

- Defining and measuring complex multimorbidity: a critical analysis.

Pati S, MacRae C, Henderson D, Weller D, Guthrie B, Mercer S.Br J Gen Pract. 2023 Jul 27;73(733):373-376. doi: 10.3399/bjgp23X734661. Print 2023 Aug.PMID: 37500453 No abstract available.

## supplementary info

Publication typesexpand

## full text links

Proceed to details

Cite

Share

4

JAMA Cardiol

- 
- 
- 

. 2023 Sep 27;e233241.

doi: 10.1001/jamacardio.2023.3241. Online ahead of print.

# Prevalence and Overlap of Cardiac, Renal, and Metabolic Conditions in US Adults, 1999-2020

John W Ostrominski[1], Suzanne V Arnold[2], Javed Butler[3,4], Gregg C Fonarow[5], Jamie S Hirsch[6], Swetha R Palli[7], Bonnie M K Donato[7], Christina M Parrinello[8], Thomas O'Connell[9], Eric B Collins[10], Jonathan J Woolley[9], Mikhail N Kosiborod[2], Muthiah Vaduganathan[1]

Affiliations expand

- PMID: 37755728
- PMCID: PMC10535010
- DOI: 10.1001/jamacardio.2023.3241

**Free PMC article**

## Abstract

**Importance:** Individually, cardiac, renal, and metabolic (CRM) conditions are common and leading causes of death, disability, and health care-associated costs. However, the frequency with which CRM conditions coexist has not been comprehensively characterized to date.

**Objective:** To examine the prevalence and overlap of CRM conditions among US adults currently and over time.

**Design, setting, and participants:** To establish prevalence of CRM conditions, nationally representative, serial cross-sectional data included in the January 2015 through March 2020 National Health and Nutrition Examination Survey (NHANES) were evaluated in this cohort study. To assess temporal trends in CRM overlap, NHANES data between 1999-2002 and 2015-2020 were compared. Data on 11 607 nonpregnant US adults (≥20 years) were included. Data analysis occurred between November 10, 2020, and November 23, 2022.

**Main outcomes and measures:** Proportion of participants with CRM conditions, overall and stratified by age, defined as cardiovascular disease (CVD), chronic kidney disease (CKD), type 2 diabetes (T2D), or all 3.

**Results:** From 2015 through March 2020, of 11 607 US adults included in the analysis (mean [SE] age, 48.5 [0.4] years; 51.0% women), 26.3% had at least 1 CRM condition, 8.0%

had at least 2 CRM conditions, and 1.5% had 3 CRM conditions. Overall, CKD plus T2D was the most common CRM dyad (3.2%), followed by CVD plus T2D (1.7%) and CVD plus CKD (1.6%). Participants with higher CRM comorbidity burden were more likely to be older and male. Among participants aged 65 years or older, 33.6% had 1 CRM condition, 17.1% had 2 CRM conditions, and 5.0% had 3 CRM conditions. Within this subset, CKD plus T2D (7.3%) was most common, followed by CVD plus CKD (6.0%) and CVD plus T2D (3.8%). The CRM comorbidity burden was disproportionately high among participants reporting non-Hispanic Black race or ethnicity, unemployment, low socioeconomic status, and no high school degree. Among participants with 3 CRM conditions, nearly one-third (30.5%) did not report statin use, and only 4.8% and 3.0% used glucagon-like peptide-1 receptor agonists and sodium-glucose cotransporter 2 inhibitors, respectively. Between 1999 and 2020, the proportion of US adults with multiple CRM conditions increased significantly (from 5.3% to 8.0%; P < .001 for trend), as did the proportion having all 3 CRM conditions (0.7% to 1.5%; P < .001 for trend).

**Conclusions and relevance:** This cohort study found that CRM multimorbidity is increasingly common and undertreated among US adults, highlighting the importance of collaborative and comprehensive management strategies.

# Conflict of interest statement

Conflict of Interest Disclosures: Dr Butler reported receiving personal fees from Abbott, American Regent, Amgen, Applied Therapeutic, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Cardiac Dimension, Cardior, CVRx, Cytokinetics, Edwards, Element Science, Innolife, Impulse Dynamics, Imbria, Inventiva, Lexicon, Lilly, LivaNova, Janssen, Medtronics, Merck, Occlutech, Novartis, Novo Nordisk, Pfizer, Pharmacosmos, Pharmain, Roche, Sequana, SQ Innovation, and Vifor. Dr Fonarow reported receiving personal fees from Abbott, Amgen, AstraZeneca, Bayer, Cytokinetics, Eli Lilly, Janssen, Medtronic, Merck, Novartis, and Pfizer outside the submitted work; and serving as an associate section editor for JAMA Cardiology. Dr Hirsch reported receiving personal fees from Boehringer Ingelheim outside the submitted work. Ms Palli reported being employed by Boehringer Ingelheim, which has a product indicated for managing cardiac, renal, and metabolic conditions, during the conduct of the study. Dr Donato reported being employed by Boehringer Ingelheim, which has a product indicated for managing CRM conditions. Dr Parrinello reported receiving personal fees from Medicus Economics during the conduct of the study; personal fees from Medicus Economics, Collective Acumen, ConcertAI, EQRx, Evidation Health, Canopy Care, Flatiron Health, Greenleaf Health, Jazz Pharmaceuticals, Sensorum Health, TTi Health Research & Economics, and Clue by Biowink outside the submitted work. Messrs O'Connell, Collins, and Woolley are employees of Medicus Economics, a health economics and outcomes research consultancy that received consulting fees from Boehringer Ingelheim during the course of the study and have received consulting fees from other biopharmaceutical industry clients. Dr Kosiborod reported receiving personal fees from Alnylam, AstraZeneca, Amgen, Bayer, Boehringer Ingelheim, Cytokinetics, Dexcom, Eli Lilly, Janssen, Lexicon, Merck, Novo Nordisk, Pharmacosmos, Pfizer, scPharmaceuticals, Esperion Therapeutics, Structure Therapeutics, Vifor Pharma, Youngene Therapeutics, 35Pharma, and Applied Therapeutics to his institution; and grants from Boehringer Ingelheim and AstraZeneca to his institution outside the submitted work. Dr Vaduganathan reported receiving grants from Amgen, AstraZeneca, American Regent, Bayer, Boehringer Ingelheim, and Roche Diagnostics; receiving consulting fees from Amgen, AstraZeneca, American Regent, Baxter HealthCare, Bayer,

Boehringer Ingelheim, Cytokinetics, Relypsa, Lexicon Pharmaceuticals, Tricog Health, Novo Nordisk, and Chiesi; serving on the advisory board for Amgen, AstraZeneca, American Regent, Baxter HealthCare, Bayer, Boehringer Ingelheim, Cytokinetics, Relypsa, Lexicon Pharmaceuticals, Tricog Health, Novo Nordisk, and Chiesi; receiving speaker fees AstraZeneca, Novartis, and Roche Diagnostics; and serving on a clinical trial committee for AstraZeneca, Novartis, Galmed, Occlutech, and Impulse Dynamics outside the submitted work. No other disclosures were reported.



5

Sci Data

. 2023 Sep 25;10(1):655.

doi: 10.1038/s41597-023-02513-4.

# Integrative GWAS and co-localisation analysis suggests novel genes associated with age-related multimorbidity

Clare E West[1,2], Mohd Karim[3,4], Maria J Falaguera[3,4], Leo Speidel[5,6], Charlotte J Green[7], Lisa Logie[7,8], Jeremy Schwartzentruber[4,9], David Ochoa[3,9], Janet M Lord[10,11], Michael A J Ferguson[7], Chas Bountra[12], Graeme F Wilkinson[8], Beverley Vaughan[12], Andrew R Leach[3,4], Ian Dunham[3,4,9], Brian D Marsden[12,13]

Affiliations expand

- PMID: 37749083

- PMCID: PMC10520009

- DOI: 10.1038/s41597-023-02513-4

**Free PMC article**



**Abstract**

Advancing age is the greatest risk factor for developing multiple age-related diseases. Therapeutic approaches targeting the underlying pathways of ageing, rather than individual diseases, may be an effective way to treat and prevent age-related morbidity while reducing the burden of polypharmacy. We harness the Open Targets Genetics Portal to perform a systematic analysis of nearly 1,400 genome-wide association studies (GWAS) mapped to 34 age-related diseases and traits, identifying genetic signals that are shared between two or more of these traits. Using locus-to-gene (L2G) mapping, we identify 995 targets with shared genetic links to age-related diseases and traits, which are enriched in mechanisms of ageing and include known ageing and longevity-related genes. Of these 995 genes, 128 are the target of an approved or investigational drug, 526 have experimental evidence of binding pockets or are predicted to be tractable, and 341 have no existing tractability evidence, representing underexplored genes which may reveal novel biological insights and therapeutic opportunities. We present these candidate targets for exploration and prioritisation in a web application.




# Conflict of interest statement

J.S. is now an employee of Illumina. M.K. is now an employee of Variant Bio. The authors declare no other competing interests.


- 73 references
- 3 figures

supplementary info

MeSH terms, Grants and fundingexpand

full text links

Proceed to details

Cite

**Meta-Analysis**

Crit Care Med

. 2023 Oct 1;51(10):1373-1385.

doi: 10.1097/CCM.0000000000005936. Epub 2023 May 30.

# Responsiveness of Critically Ill Adults With Multimorbidity to Rehabilitation Interventions: A Patient-Level Meta-Analysis Using Individual Pooled Data From Four Randomized Trials

Jennifer R A Jones[1,2,3], Amalia Karahalios[4], Zudin A Puthucheary[5,6], Michael J Berry[7], D Clark Files[8,9], David M Griffith[10,11], Luke A McDonald[2], Peter E Morris[12], Marc Moss[13], Amy Nordon-Craft[14], Timothy Walsh[10,15,16], Sue Berney[1,2], Linda Denehy[1,17,18]

Affiliations expand

- PMID: 37246922

- DOI: 10.1097/CCM.0000000000005936

## Abstract

**Objective:** To explore if patient characteristics (pre-existing comorbidity, age, sex, and illness severity) modify the effect of physical rehabilitation (intervention vs control) for the coprimary outcomes health-related quality of life (HRQoL) and objective physical performance using pooled individual patient data from randomized controlled trials (RCTs).

**Data sources:** Data of individual patients from four critical care physical rehabilitation RCTs.

**Study selection:** Eligible trials were identified from a published systematic review.

**Data extraction:** Data sharing agreements were executed permitting transfer of anonymized data of individual patients from four trials to form one large, combined dataset. The pooled trial data were analyzed with linear mixed models fitted with fixed effects for treatment group, time, and trial.

**Data synthesis:** Four trials contributed data resulting in a combined total of 810 patients (intervention n = 403, control n = 407). After receiving trial rehabilitation interventions, patients with two or more comorbidities had HRQoL scores that were significantly higher and exceeded the minimal important difference at 3 and 6 months compared with the similarly comorbid control group (based on the Physical Component Summary score (Wald test p = 0.041). Patients with one or no comorbidities who received intervention had no HRQoL outcome differences at 3 and 6 months when compared with similarly comorbid control patients. No patient characteristic modified the physical performance outcome in patients who received physical rehabilitation.

**Conclusions:** The identification of a target group with two or more comorbidities who derived benefits from the trial interventions is an important finding and provides direction for future investigations into the effect of rehabilitation. The multimorbid post-ICU population may be a select population for future prospective investigations into the effect of physical rehabilitation.



# Conflict of interest statement

Dr. Puthucheary reports honorarium and speaker fees from Baxter, Faraday Pharmaceuticals, Lyric Pharmaceuticals, Fresenius-Kabi, Nestle, Orion, GlaxoSmithKline, and Nutritica. Dr. Files reports consulting fees from Cytovale. The remaining authors have disclosed that they do not have any potential conflicts of interest.

# Comment in

- Physical Therapy in the ICU-Is It Time to Consider Individualized Therapy Plans?
  Rewa OG.Crit Care Med. 2023 Oct 1;51(10):1445-1447. doi: 10.1097/CCM.0000000000005966. Epub 2023 Sep 14.PMID: 37707385 No abstract available.

- 48 references

supplementary info

Publication types, MeSH terms, Grants and fundingexpand

7

Psychol Med

. 2023 Oct;53(13):6212-6222.

doi: 10.1017/S0033291722003488. Epub 2022 Nov 24.

# Ethnic differences in physical and mental multimorbidity in working age adults with a history of depression and/or anxiety

Amy Ronaldson[1], Jorge Arias de la Torre[1,2,3], Matthew Broadbent[4], Mark Ashworth[5], David Armstrong[5], Ioannis Bakolis[1], Stephani L Hatch[1,6], Matthew Hotopf[1,7], Alex Dregan[1]

Affiliations expand

- PMID: 36420618

- PMCID: PMC10520586

- DOI: 10.1017/S0033291722003488

**Free PMC article**

## Abstract

**Background:** The current study used data from an ethnically diverse population from South London to examine ethnic differences in physical and mental multimorbidity among working age (18-64 years) adults in the context of depression and anxiety.

**Method:** The study included 44 506 patients who had previously attended Improving Access to Psychological Therapies services in the London Borough of Lambeth. Multinomial logistic regression examined cross-sectional associations between ethnicity with physical and mental multimorbidity. Patterns of multimorbidity were identified using hierarchical cluster analysis.

**Results:** Within 44 056 working age adults with a history of depression or anxiety from South London there were notable ethnic differences in physical multimorbidity. Adults of Black Caribbean ethnicity were more likely to have physical multimorbidity [adjusted relative risk ratio (aRRR) = 1.25, 95% confidence interval (CI) 1.15-1.36] compared to adults of White ethnicity. Relative to adults of White ethnicity, adults of Asian ethnicity were more likely to have physical multimorbidity at higher thresholds only (e.g. 4 + conditions; aRRR = 1.53, 95% CI 1.17-2.00). Three physical (atopic, cardiometabolic, mixed) and three mental (alcohol/substance use, common/severe mental illnesses, personality disorder) multimorbidity clusters emerged. Ethnic minority groups with multimorbidity had a higher probability of belonging to the cardiometabolic cluster.

**Conclusion:** In an ethnically diverse population with a history of common mental health disorders, we found substantial between- and within-ethnicity variation in rates of physical, but not mental, multimorbidity. The findings emphasised the value of more granular definitions of ethnicity when examining the burden of physical and mental multimorbidity.

**Keywords:** Anxiety; cluster analysis; common mental health disorders; depression; ethnicity; multimorbidity.

# Conflict of interest statement

This study represents independent research part-funded by the National Institute for Health and Care Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care. AR, JAT, MB, MA, DA, IB, MH, and AD have nothing to disclose. SH is a member of the following: Expert Review Group (ERG) of the UK Prevention Research Partnership (UKPRP) Ethnic inequalities in health care among people with multiple conditions (University of Sussex) – Advisory Board NHS Race and Health Observatory, Co-Chair Academic Reference Group and Board Member The Royal Foundation – Mental Health Research Group NHS England and NHS Improvement – The Mental Health Equalities Data Quality and Research Subgroup NHS England and NHS Improvement – Patient and Carers Race Equalities Framework [PCREF] Steering Group NHS England and NHS Improvement – Advancing Mental Health Equalities Taskforce Health Education England – Mental Health Workforce Equalities Subgroup Maudsley Learning – Maudsley Learning Advisory Board South London and Maudsley NHS Foundation Trust (SLaM) – Independent Advisory Groups, the SLaM Partnership Group Lambeth Public Health – Serious Youth Violence Public Health Task and Finish Group Thrive London – Thrive

London Advisory Board Black Thrive – Black Thrive Advisory Board NHS England and NHS Improvement – The Mental Health Workforce Equalities Subgroup Commissions: Welsh Government's Race Equality Plan; contribution to the evidence review for Health and Social Care and Employment and Income policy areas.

- 49 references

supplementary info

MeSH termsexpand

full text links

Proceed to details

Cite

Share

8

**Review**

Community Dent Oral Epidemiol

. 2023 Oct;51(5):705-717.

doi: 10.1111/cdoe.12812. Epub 2022 Nov 15.

# Periodontitis and risk of immune-mediated systemic conditions: A systematic review and meta-analysis

Harriet Larvin[1], Jing Kang[2], Vishal R Aggarwal[1], Susan Pavitt[1], Jianhua Wu[1,3]

Affiliations expand

- PMID: 36377800

- DOI: 10.1111/cdoe.12812

**Free article**

## Abstract

**Introduction:** The aim of this review is to examine and quantify the long-term risk of immune-mediated systemic conditions in people with periodontitis compared to people without periodontitis.

**Methods:** Medline, EMBASE and Cochrane databases were searched up to June 2022 using keywords and MeSH headings. The 'Risk of Bias in Non-Randomised Studies of Interventions' tool was used to assess bias. Cohort studies comparing incident metabolic/autoimmune/inflammatory diseases in periodontitis to healthy controls were included. Meta-analysis and meta-regression quantified risks and showed impact of periodontitis diagnosis type and severity.

**Results:** The search retrieved 3354 studies; 166 studies were eligible for full-text screening, and 30 studies were included for review. Twenty-seven studies were eligible for meta-analysis. The risks of diabetes, rheumatoid arthritis (RA) and osteoporosis were increased in people with periodontitis compared to without periodontitis (diabetes-relative risk [RR]: 1.22, 95% CI: 1.13-1.33; RA-RR: 1.27, 95% CI: 1.07-1.52; osteoporosis-RR: 1.40, 95% CI: 1.12-1.75). Risk of diabetes showed gradient increase by periodontitis severity (moderate-RR = 1.20, 95% CI = 1.11-1.31; severe-RR = 1.34, 95% CI = 1.10-1.63).

**Conclusion:** People with moderate-to-severe cases of periodontitis have the highest risk of developing diabetes, while the effect of periodontal severity on risk of other immune-mediated systemic conditions requires further investigation. More homologous evidence is required to form robust conclusions regarding periodontitis-multimorbidity associations.

**Keywords:** arthritis; cohort studies; diabetes; immune response; periodontitis; systematic review; systemic disease.



- Cited by 4 articles
- 91 references

supplementary info

Publication types, MeSH termsexpand

full text links

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

1

BMC Pulm Med

- 
- 
- 

. 2023 Sep 30;23(1):365.

doi: 10.1186/s12890-023-02668-1.

# Association of cigarette smoking with increased use of heated tobacco products in middle-aged and older adults with self-reported chronic obstructive pulmonary disease, asthma, and asthma-COPD overlap in Japan, 2022: the JASTIS study

Shingo Noguchi[1,2], Tomohiro Ishimaru[3], Yoshihisa Fujino[3], Kazuhiro Yatera[4], Takahiro Tabuchi[5]

Affiliations expand

- PMID: 37777737

- DOI: 10.1186/s12890-023-02668-1

**Abstract**

**Background:** Smoking cessation is the most important intervention in chronic obstructive pulmonary disease (COPD), asthma, and asthma-COPD overlap (ACO); however, high rates of current cigarette smoking are observed in adults with these respiratory diseases. Meanwhile, rapidly increasing use of heated tobacco products (HTPs) is observed in Japan; however, the status of HTPs use has not been fully understood in adults with COPD, asthma, and ACO. This study aimed to reveal the association between COPD, asthma, and ACO and HTPs use in adults.

**Methods:** Data on Japanese individuals ≥ 40 years old obtained from the Japan Society and New Tobacco Internet Survey were analyzed. The prevalence of HTPs use in adults with COPD, asthma, and ACO, among individuals categorized into three groups according to cigarette smoking (never, former, and current), was calculated and the relationship between each disease and HTPs use were evaluated. The clinical diagnosis of these diseases was based on the self-reported diagnosis, as obtained from questionnaires.

**Results:** A total of 19,308 individuals were included. The proportions of never, past, and current cigarettes smokers were 10,900 (56.5%), 4,903 (25.4%), and 3,505 (18.2%), respectively, and that of HTPs use was 1,813 (9.4%). In current cigarettes smokers, the adjusted odds ratios (ORs) of HTPs use was 2.88 (95% CI [confidence interval], 1.86-4.47), 1.23 (95% CI, 0.99-1.52), and 5.81 (95% CI, 3.12-10.82) in adults with COPD, asthma, and ACO compared to those without these respiratory diseases, respectively. Meanwhile, in past cigarettes smokers, the adjusted ORs of HTPs use was 0.51 (95% CI, 0.24-1.08), 0.69 (95% CI, 0.53-0.88), and 0.25 (95% CI, 0.06-1.07) in adults with COPD, asthma, and ACO, respectively.

**Conclusions:** HTPs use is more prevalent among current cigarettes smokers with COPD, asthma, and ACO compared to those without these respiratory diseases. Complete cessation of smoking both cigarettes and HTPs is the only way to achieve complete smoking cessation, therefore, adults with COPD, asthma, and ACO need to make greater efforts to quit smoking.

**Keywords:** Asthma-COPD overlap; Chronic obstructive pulmonary disease; Dual use; Heated tobacco products; Smoking cessation.



- 42 references

. 2023 Oct 1;44(10):537-550.

doi: 10.1542/pir.2022-005618.

# Allergic Rhinitis

Barrie Cohen[1]

Affiliations expand

- PMID: 37777655

- DOI: 10.1542/pir.2022-005618

**Abstract**

Allergic rhinitis (AR) affects more than 400 million people worldwide, making it 1 of the most prevalent chronic diseases. Childhood AR is increasing, and almost half of patients with AR develop symptoms before age 6 years. Although a diagnosis of AR is associated with higher socioeconomic status, underserved and urban populations have more indoor aeroallergen sensitizations and are likely underdiagnosed with AR, further exacerbating health-care disparities. AR negatively impacts quality of life, school performance, and overall health outcomes. Untreated AR in children increases the risk for poor asthma control, increased asthma severity, and exacerbations. Many patients believe that they have seasonal allergies only but in reality have both perennial and seasonal AR, which may change the approach to allergen avoidance measures and treatment recommendations. Pharmacotherapy of AR has expanded, with many intranasal corticosteroids, intranasal antihistamines, and second-generation oral antihistamines approved for pediatric use. Allergen immunotherapy, including both subcutaneous and sublingual forms, are approved for children and are disease modifying, potentially reducing further allergen sensitization and progression to asthma. Many of the currently available biological therapies indicated for pediatric asthma and/or atopic diseases reduce AR symptoms as well. Children with moderate to severe or refractory AR or those with comorbidities should be referred to allergists for diagnostic testing and expanded management options, including immunotherapy and potential biological treatment.

3

Respir Med

. 2023 Sep 28;107414.

doi: 10.1016/j.rmed.2023.107414. Online ahead of print.

# Biologics in severe asthma: A pragmatic approach for choosing the right treatment for the right patient

Linda Rogers[1], Milos Jesenak[2], Leif Bjermer[3], Nicola A Hanania[4], Sven Seys[5], Zuzana Diamant[6]

Affiliations expand

- PMID: 37776915

- DOI: 10.1016/j.rmed.2023.107414

**Abstract**

The development of monoclonal antibody therapies targeting specific components of the pathways relevant to asthma pathophysiology has revolutionized treatment of severe asthma both in adults and children and helped to further unravel the heterogeneity of this disease. However, the availability of multiple agents, often with overlapping eligibility criteria, creates a need for pragmatic guidance for specialists undertaking care of patients with severe asthma. In this review, we provide an overview of the data supporting the clinical efficacy of biologics in distinct asthma phenotypes/endotypes. We also focus on the role of biomarkers and treatable traits, including comorbidities, in the choice of asthma biologics, highlight which treatments have been demonstrated to be steroid sparing in corticosteroid dependent asthma, and provide practical guidance that can drive shared decision making on treatment choice with patients. In addition, we summarize what is known to date regarding long-term safety of these drugs, and lastly, discuss future directions in biologics research.

**Keywords:** Asthma; Asthma management; Biologics; Biomarkers; Comorbidities; Type 2 inflammation.



# Conflict of interest statement

Declaration of competing interest Dr. Linda Rogers receives research funding including salary support from Sanofi (Global) and Gene DX (formerly Sema 4). She has served on advisory boards and performed consulting work for Astra Zeneca, Sanofi (US) and Teva Pharmaceuticals. She has received travel funding and lecture honoraria from the American College of Chest Physicians. Dr. Sven Seys company receives grants/contracts from Sanofi, Novartis, GSK, and speakers fee from Teva Pharmaceuticals. Dr. Milos Jenesak has performed consulting for Novartis, Sanofi Genzyme, Astra Zeneca, and GSK, has received payment/honoraria for lectures, presentatinos, speakers bureaus, manuscript writing or educational events from Sanofi Genzyme and Novartis. Dr. Hanania's institution receives grants or contract from Astra Zeneca, GSK, Sanofi, Genentech, and Teva and consulting fees from Astra Zeneca, GSK, Sanofi, Genentech, Teva, and Amgen, andspeaking fees from Regeneron. Dr. Bjermer has no conflicts to declare in relation to this manuscript. Dr Zuzana Diamant as served on advisory boards and performed consulting for GSK (UK), Sanofi-Genzyme (USA)



J Allergy Clin Immunol Pract

. 2023 Sep 27;S2213-2198(23)01047-4.

doi: 10.1016/j.jaip.2023.09.015. Online ahead of print.

# Increased Risk of New-onset Asthma after COVID-19 Infection: A Nationwide Population-based Cohort Study

Bo-Guen Kim[1], Hyun Lee[1], Sang Woo Yeom[2], Cho Yun Jeong[2], Dong Won Park[1], Tai Sun Park[1], Ji-Yong Moon[1], Tae-Hyung Kim[1], Jang Won Sohn[1], Ho Joo Yoon[1], Jong Seung Kim[3], Sang-Heon Kim[4]

Affiliations expand

- PMID: 37774780

- DOI: 10.1016/j.jaip.2023.09.015

**Abstract**

**Background:** Previous studies have suggested that respiratory virus infections may be associated with new-onset asthma. However, whether coronavirus disease 2019 (COVID-19) is associated with an increased risk of new-onset asthma remains unclear.

**Objective:** We aimed to evaluate whether recent COVID-19 infection increases the risk of new-onset asthma and whether COVID-19 vaccination could mitigate this risk.

**Methods:** We constructed three different study designs using the Korean National Health Insurance claim-based database: Study 1: COVID-19 diagnosed participants (COVID-19 cohort) and their matched controls; Study 2: COVID-19 vaccinated participants (vaccination cohort) and their matched controls; Study 3: vaccination cohort and their matched controls, excluding participants diagnosed with COVID-19.

**Results:** In Study 1, 1.6% of the COVID-19 cohort and 0.7% of the matched cohort developed new-onset asthma, with incidences of 31.28 and 14.55 per 1,000 person-years, respectively ($p<0.001$). COVID-19 cohort had a higher risk of new-onset asthma (adjusted hazard ratio [aHR], 2.14; 95% confidence interval [CI], 1.88-2.45) than matched controls. In Study 2, vaccination cohort had a lower risk of new-onset asthma than matched controls (aHR, 0.82; 95% CI, 0.76-0.89). However, among participants without a COVID-19 diagnosis, COVID-19 vaccination was not associated with a reduced risk of new-onset asthma in Study 3 (aHR, 0.95; 95% CI, 0.87-1.04). In subgroup analysis, the risk of new-onset asthma was significantly lower in fully vaccinated participants and higher in older individuals and in those with diabetes mellitus compared to their counterparts.

**Conclusion:** COVID-19 was associated with a higher incidence of new-onset asthma, which might be preventable by COVID-19 vaccination.

**Keywords:** COVID-19; asthma; vaccination.





**Review**

Respir Res

- 
- 
- 

. 2023 Sep 29;24(1):238.

doi: 10.1186/s12931-023-02529-9.

# Rhinovirus induces airway remodeling: what are the physiological consequences?

Cassandra Spector[1], Camden M De Sanctis[1], Reynold A Panettieri Jr[1], Cynthia J Koziol-White[2]

Affiliations expand

- PMID: 37773065

- DOI: 10.1186/s12931-023-02529-9

**Abstract**

**Background:** Rhinovirus infections commonly evoke asthma exacerbations in children and adults. Recurrent asthma exacerbations are associated with injury-repair responses in the

airways that collectively contribute to airway remodeling. The physiological consequences of airway remodeling can manifest as irreversible airway obstruction and diminished responsiveness to bronchodilators. Structural cells of the airway, including epithelial cells, smooth muscle, fibroblasts, myofibroblasts, and adjacent lung vascular endothelial cells represent an understudied and emerging source of cellular and extracellular soluble mediators and matrix components that contribute to airway remodeling in a rhinovirus-evoked inflammatory environment.

**Main body:** While mechanistic pathways associated with rhinovirus-induced airway remodeling are still not fully characterized, infected airway epithelial cells robustly produce type 2 cytokines and chemokines, as well as pro-angiogenic and fibroblast activating factors that act in a paracrine manner on neighboring airway cells to stimulate remodeling responses. Morphological transformation of structural cells in response to rhinovirus promotes remodeling phenotypes including induction of mucus hypersecretion, epithelial-to-mesenchymal transition, and fibroblast-to-myofibroblast transdifferentiation. Rhinovirus exposure elicits airway hyperresponsiveness contributing to irreversible airway obstruction. This obstruction can occur as a consequence of sub-epithelial thickening mediated by smooth muscle migration and myofibroblast activity, or through independent mechanisms mediated by modulation of the $\beta_2$ agonist receptor activation and its responsiveness to bronchodilators. Differential cellular responses emerge in response to rhinovirus infection that predispose asthmatic individuals to persistent signatures of airway remodeling, including exaggerated type 2 inflammation, enhanced extracellular matrix deposition, and robust production of pro-angiogenic mediators.

**Conclusions:** Few therapies address symptoms of rhinovirus-induced airway remodeling, though understanding the contribution of structural cells to these processes may elucidate future translational targets to alleviate symptoms of rhinovirus-induced exacerbations.

**Keywords:** Airway epithelium; Airway hyperresponsiveness; Airway remodeling; Airway smooth muscle; Asthma; Fibroblasts; Myofibroblasts; Rhinovirus.



- 193 references

supplementary info

Publication types, Grants and fundingexpand

full text links

Proceed to details

Cite

6

Pediatr Pulmonol

- 
- 
- 

. 2023 Sep 29.

doi: 10.1002/ppul.26704. Online ahead of print.

# Metformin use is associated with decreased asthma exacerbations in adolescents and young adults

Erhan Ararat[1], Reid D Landes[2], Erick Forno[3], Emir Tas[4], Tamara T Perry[5]

Affiliations expand

- PMID: 37772681

- DOI: 10.1002/ppul.26704

**Abstract**

**Rationale:** Metformin is a commonly used antidiabetes medication with suggested anti-inflammatory and antioxidative effects. Metformin use has been associated with lower risk of asthma exacerbations and hospitalizations in adults. Here, we aimed to evaluate how asthma exacerbation rates changed after adolescents and young adults were prescribed metformin, and to learn if those changes were related to metformin prescription adherence.

**Methods:** Using secondary data of patients between 12 and 20 years old with asthma diagnosis and a metformin prescription from the Arkansas All Payers Claim Database and Arkansas School body mass index (BMI) database, we estimated the change in annualized asthma exacerbation rates after metformin prescription. We also evaluated the association of prescription adherence to the changes in those rates using univariate and multivariate regression models.

**Results:** A total of 464 patients met inclusion criteria. Outpatient exacerbation rates decreased after metformin prescription (13.4% only before vs. 7.8% only after, p = .009),

and the annualized rate decreased more after metformin prescription as adherence increased (rank r = -.165, p < .001). After adjusting for potential confounders-age, sex, BMI, and inhaled corticoid steroid use-the strength of the association was attenuated.

**Conclusions:** Asthma exacerbation rates decreased after metformin prescription, but a larger sample of patients who have experienced exacerbations and including patients with asthma who have not been prescribed metformin is needed to better know whether these decreases are driven by metformin use.

**Keywords:** diabetes; obesity.



- 19 references

## supplementary info

Grants and fundingexpand

## full text links

Proceed to details

Cite

Share

7

**Review**

Immunotherapy

- 
- 
- 

. 2023 Sep 29.

doi: 10.2217/imt-2023-0109. Online ahead of print.

# Tezepelumab for the treatment of severe asthma: a plain language summary of the PATHWAY and NAVIGATOR studies

Jonathan Corren[1], Andrew Menzies-Gow[2], Johan Bimmel[3], Anthony McGuinness[4], Gun Almqvist[5], Karin Bowen[6], Janet M Griffiths[7], Sandhia Ponnarambil[8], Arnaud Bourdin[9], Elliot Israel[10], Gene Colice[6], Christopher E Brightling[11], Michael E Wechsler[12]; PATHWAY and NAVIGATOR study investigators

Affiliations expand

- PMID: 37772607

- DOI: 10.2217/imt-2023-0109

**Abstract**

**What is this summary about?:** This is a summary of the results of 2 clinical studies that looked at a medicine called **tezepelumab**. Tezepelumab is approved in the United States of America (USA), the European Union (EU) and several other countries for the treatment of severe, uncontrolled asthma in people aged 12 and above. The results of these 2 studies, called **PATHWAY** and **NAVIGATOR**, formed the basis for tezepelumab's approval for use. Tezepelumab is a type of biologic treatment called an antibody. Biologics are treatments that target certain cells or proteins in the body and often in the immune system - the body's natural defence system against infections and diseases - to reduce patients' disease. It works by blocking a key first step in the body's chain reaction leading to inflammation in the airways of people with severe asthma. The clinical studies were done to learn if tezepelumab can be used to treat people with severe, uncontrolled asthma and to find out about its safety. In both studies, tezepelumab was compared to placebo. A placebo is a dummy treatment that looked like tezepelumab but did not have any medicine in it.

**What were the main conclusions reported by the researchers?:** In both studies, tezepelumab reduced the number of severe asthma attacks that the participants had per year compared with placebo. It also increased the volume of air that the participants could breathe out in 1 second compared with placebo. Tezepelumab was well-tolerated, and a similar number of participants had health issues in the tezepelumab and placebo treatment groups. The most common health issues that the participants had during the PATHWAY study were: Worsening of asthma, common cold, headache, and inflammation of the airways. The most common health issues that the participants had during the NAVIGATOR study were: Common cold, infection of the sinuses, throat and airways, headache, worsening of asthma, and inflammation of the airways.

**What are the key takeaways?:** The results showed that participants who had monthly doses of tezepelumab had fewer severe asthma attacks and better lung function than those who had placebo. In both studies, the health issues that the participants had were similar between the tezepelumab and placebo treatment groups. Overall, the studies showed that tezepelumab worked in a broad population of people with severe asthma and that the study participants had an acceptable level of health issues during the studies. These results led to the approval of tezepelumab for people with severe asthma aged 12 and above in the USA, EU and other countries. **Clinical Trial Registration:** PATHWAY study: NCT02054130; NAVIGATOR study: NCT03347279 (ClinicalTrials.gov).

**Keywords:** Antibody therapeutics; Clinical immunology; Cytokines and cell signaling.



8

BMC Pulm Med

. 2023 Sep 28;23(1):363.

doi: 10.1186/s12890-023-02661-8.

# Relationship between early life asthma and chronic airway disease in adult life - in search for disease trajectories over the life span- the RELATE study based on the Kongsberg cohort

Osman Savran[1], Klaus Bønnelykke[2,3], Charlotte Suppli Ulrik[4,2]

Affiliations expand

- PMID: 37770870

- PMCID: PMC10540471

- DOI: 10.1186/s12890-023-02661-8

**Abstract**

**Background:** Chronic airway disease in adults may have its origin in early life. The purpose of this study is to investigate the long-term prognosis of severe childhood asthma in search for an association between asthma in early life and obstructive lung disease in adulthood.

**Methods:** This study is based on the Kongsberg cohort, which includes approximately 5000 children with severe asthma with a 4-month stay at the asthma care facility in Kongsberg, Norway during the years 1950 to 1979. An on average 60-year observational study based on a follow-up examination will be performed including questionnaires, blood samples, and tests of lung function and bronchial responsiveness. Blood samples will be stored in a biobank. In addition, we will conduct further analyses of the cohort based on nationwide register data, including socio-economic parameters and mortality.

**Discussion:** Chronic airway disease is associated with substantial burden for both the individual patient and society. Our knowledge of early life origins of chronic airway disease later in life has been increasing in recent decades but is still limited. By exploring early life risk factors for chronic airway disease in adulthood, we may gain insights paving the way for future reduction in the burden of chronic airway diseases.

**Keywords:** Asthma; Childhood; Chronic airway diseases; Early life; Prognosis.



# Conflict of interest statement

The authors declare no competing interests.

- 53 references

full text links

9

J Clin Psychol Med Settings

. 2023 Sep 28.

doi: 10.1007/s10880-023-09976-y. Online ahead of print.

# Psychometric Properties of the Short Scale Anxiety Sensitivity Index Among Adults with Chronic Respiratory Disease

Heather L Clark[1], Laura J Dixon[1], Sujith Ramachandran[2], Patric J Leukel[2], Aaron A Lee[3]

Affiliations expand

- PMID: 37770802

- DOI: 10.1007/s10880-023-09976-y

**Abstract**

Approximately one-third of adults with chronic respiratory disease (CRD) have comorbid depressive and anxiety disorders; yet these disorders are often unrecognized in this patient population. Transdiagnostic processes such as anxiety sensitivity (AS) are useful for identifying mechanisms underlying psychological and heath conditions. The Short-Scale AS Index (SSASI) is a brief self-report measure of AS which has potential clinical utility among CRD populations to evaluate psychological distress and inform comprehensive care. The present study investigated the psychometric properties of the SSASI among adults with CRDs. Participants were recruited from a web-based panel of adults with CRDs (n = 768; 49.3% female; 57.8% White) including adults with asthma only (n = 230), COPD only (n = 321), or co-occurring asthma and COPD (n = 217). Participants completed a battery of self-report questionnaires assessing psychological and medical symptoms. Analyses were

conducted to examine the factor structure and measurement invariance across CRD groups. Convergent validity and criterion validity of the SSASI were assessed within each group. Results supported partial measurement invariance across CRD groups. The SSASI demonstrated high reliability, convergent validity, and criterion validity with each CRD group. Findings from this study and existing work indicate that the SSASI is an effective and economical assessment tool for identifying patients CRD who may benefit from psychological interventions to reduce AS.

**Keywords:** Anxiety sensitivity; Asthma; Chronic obstructive pulmonary disease; Respiratory disease.



- 78 references

full text links

Proceed to details

Cite

Share

10

Occup Environ Med

- 
- 
- 

. 2023 Sep 28;oemed-2023-108884.

doi: 10.1136/oemed-2023-108884. Online ahead of print.

# Irritant asthma and work: cases from the UK SWORD reporting scheme from 1999 to 2018

David Fishwick[1,2], Melanie Carder[2], Ireny Iskandar[2], Beth Charlotte Fishwick[3], Martie van Tongeren[2]

Affiliations expand

- PMID: 37770178

- DOI: 10.1136/oemed-2023-108884

**Abstract**

**Background:** Acute irritant asthma is a preventable health consequence of a workplace exposure and has a number of adverse outcomes. While cases and case series are reported, little is known about the causes and incidence of this condition over prolonged periods of time.

**Aims:** We aimed to estimate the reported incidence of irritant asthma referred to a national reporting scheme, and how this has changed over time.

**Methods:** Cases of irritant asthma reported to SWORD, the UK-based Surveillance of Work-related Occupational Respiratory Diseases scheme, were grouped into four 5-year time periods from 1999 onwards. Likely causative exposures, job, work sector and incidence rates were analysed over time.

**Results:** 307 actual cases equated to 1066 estimated cases; actual cases had a mean age of 46 years (SD 17.8); 70.7% were male. The annual incidence fell from 1.98 per million employed in the first 5-year period, to 0.56 in the most recent. Eleven occupational codes were associated with six or more attributed cases, and between them accounted for 38% of all cases. Thirteen exposure categories were associated with five or more cases. These were formaldehyde (n=5), cutting oils and coolants (n=6), isocyanates (n=6), pesticides and herbicides (n=6), welding fumes (n=7), paints (n=7), solder and colophony (n=7), solvents (n=9), fuel oil, diesel and ill-defined fumes (n=10), chlorine and hypochlorites (n=15), acids (n=23), smoke (n=25) and cleaning products and sterilising agents (n=39).

**Conclusions:** While the incidence of irritant asthma may have fallen, cases are persistently attributed to well-described causes. A persistence of cases attributed to cleaning agents was seen.

**Keywords:** asthma; epidemiology; occupational health; respiratory; respiratory function tests.



# Conflict of interest statement

Competing interests: None declared.

11

PLoS One

. 2023 Sep 28;18(9):e0292185.

doi: 10.1371/journal.pone.0292185. eCollection 2023.

# An efficient machine learning framework to identify important clinical features associated with pulmonary embolism

Baiming Zou[1,2], Fei Zou[1], Jianwen Cai[1]

Affiliations expand

- PMID: 37768933
- PMCID: PMC10538737
- DOI: 10.1371/journal.pone.0292185

**Free PMC article**

## Abstract

A misdiagnosis of pulmonary embolism (PE) can have severe consequences such as disability or death. It's crucial to accurately identify key clinical features of PE in clinical practice to promptly identify potential PE patients who may present asymptomatically, and to prevent misdiagnosing PE as asthma exacerbation in patients with symptoms like dyspnea or chest pain. However, reliably identifying these important features can be challenging due to many factors influencing the likelihood of PE development in complex

fashions (e.g., the interactions among these factors). To address this difficulty, we presented an effective framework using the deep neural network (DNN) model and the permutation-based feature importance test (PermFIT) procedure, i.e., PermFIT-DNN. We applied the PermFIT-DNN framework to the analysis of data from a PE study for asthma exacerbation patients. Our analysis results show that the PermFIT-DNN framework can robustly identify key features for classifying PE status. The important features identified can also aid in accurately predicting the PE risk.



# Conflict of interest statement

The authors have declared that no competing interests exist.

- 46 references



12

Thorax

. 2023 Sep 27;thorax-2022-219696.

doi: 10.1136/thorax-2022-219696. Online ahead of print.

# Spirometric patterns in young and middle-aged adults: a 20-year European study

Anne-Elie Carsin[1 2 3 4], Judith Garcia-Aymerich[5 2 3], Simone Accordini[6], Shyamali Dharmage[7], Bénédicte Leynaert[8], Marti de Las Heras[5 2 3], Lidia Casas[9 10], Seraina Caviezel[11], Pascal Demoly[12 13], Bertil Forsberg[14], Thorarinn Gislason[15 16], Angelo Guido Corsico[17 18], Christer Janson[19], Rain Jogi[20], Jesús Martínez-Moratalla[21], Dennis Nowak[22], Leopoldo Palacios Gómez[23], Isabelle Pin[24 25], Nicole Probst-Hensch[11], Chantal Raherison-Semjen[26], Giulia Squillacioti[27], Cecilie Svanes[28 29], Kjell Torén[30 31], Isabel Urrutia[32], Ismael Huerta[33], Josep Maria Anto[5 2 3], Debbie Jarvis[34], Stefano Guerra[5 35]

Affiliations expand

- PMID: 37758456

- DOI: 10.1136/thorax-2022-219696

**Abstract**

**Background:** Understanding the natural history of abnormal spirometric patterns at different stages of life is critical to identify and optimise preventive strategies. We aimed to describe characteristics and risk factors of restrictive and obstructive spirometric patterns occurring before 40 years (young onset) and between 40 and 61 years (mid-adult onset).

**Methods:** We used data from the population-based cohort of the European Community Respiratory Health Survey (ECRHS). Prebronchodilator forced expiratory volume in one second ($FEV_1$) and forced vital capacity (FVC) were assessed longitudinally at baseline (ECRHS1, 1993-1994) and again 20 years later (ECRHS3, 2010-2013). Spirometry patterns were defined as: restrictive if $FEV_1/FVC \geq LLN$ and FVC<10th percentile, obstructive if $FEV_1/FVC < LLN$ or normal otherwise. Five spirometry patterns were derived depending on whether participants never developed restrictive/obstructive (normal), developed restrictive/obstructive at baseline (young onset) or at last follow-up (mid-adult onset). The characteristics and risk factors associated with these patterns were described and assessed using multilevel multinomial logistic regression analysis adjusting for age, sex, sample (random or symptomatic) and centre.

**Results:** Among 3502 participants (mean age=30.4 (SD 5.4) at ECRHS1, 50.4 (SD 5.4) at ECRHS3), 2293 (65%) had a normal, 371 (11%) a young restrictive, 301 (9%) a young obstructive, 187 (5%) a mid-adult onset restrictive and 350 (10%) a mid-adult onset obstructive spirometric pattern. Being lean/underweight in childhood and young adult life was associated with the occurrence of the young spirometric restrictive pattern (relative risk ratio (RRR)=1.61 95% CI=1.21 to 2.14, and RRR=2.43 95% CI=1.80 to 3.29;

respectively), so were respiratory infections before 5 years (RRR=1.48, 95% CI=1.05 to 2.08). The main determinants for young obstructive, mid-adult restrictive and mid-adult obstructive patterns were asthma, obesity and smoking, respectively.

**Conclusion:** Spirometric patterns with onset in young and mid-adult life were associated with distinct characteristics and risk factors.

**Keywords:** COPD epidemiology; Clinical Epidemiology.



## Conflict of interest statement

Competing interests: None declared.



13

ERJ Open Res

. 2023 Sep 25;9(5):00492-2023.

doi: 10.1183/23120541.00492-2023. eCollection 2023 Sep.

# Oral corticosteroid use and sarcopenia-related traits in older people with chronic airway disease: a population-based study

Elizabeth Benz[1,2], Lies Lahousse[1,3], Johnmary T Arinze[4,5], Sara Wijnant[1,4], Maria de Ridder[5], Fernando Rivadeneira[2], Guy Brusselle[1,4], Bruno H Stricker[1]

Affiliations expand

- PMID: 37753286

- PMCID: PMC10518877

- DOI: 10.1183/23120541.00492-2023


**Free PMC article**


### Abstract

**Background:** Sarcopenia is characterised by two major phenotypic components: low handgrip strength (HGS) and appendicular skeletal muscle index (ASMI). Oral corticosteroid (OCS) use is an important medication for acute respiratory exacerbations in patients with COPD and asthma. However, the association of OCS and sarcopenia components in older people is largely unexplored. The aim of this study was to examine the association between OCS use and HGS or ASMI in the general population and explore interactions with chronic airway diseases.

**Methods:** From the population-based Rotterdam Study, 5054 participants (age 69.0±8.8 years; 56% females) were included in the cross-sectional analysis and 1324 in the longitudinal analysis. Associations between OCS and muscle strength and mass were analysed using linear regression models adjusted for age, sex, fat %, height, kidney function, smoking and comorbidities.

**Results:** At baseline, ever-OCS users had lower handgrip strength (β= -0.48, 95% CI -0.84- -0.12) than never-OCS users, with cumulative frequency (≥10 OCS prescriptions)-dependent effects (β= -1.25, 95% CI -2.16- -0.33). COPD ever-OCS users, but not asthma, had lower handgrip strength (β= -0.98, 95% CI -1.91- -0.06) and lower lean mass (β= -0.14, 95% CI -0.27- -0.01) than never-OCS users. After 5.6 years of follow-up in those free of sarcopenia traits at baseline, COPD ever-OCS users developed lower handgrip strength (β= -1.64, 95% CI -2.87- -0.40) with frequency (β= -3.64, 95% CI -6.57- -0.72) and duration (β= -1.51, 95% CI -2.87- -0.15) association compared to never-OCS users.

**Conclusions:** OCS use is associated with a decline in handgrip strength in people with COPD in a cumulative frequency and duration-dependent manner. Routine muscle examination may be necessary for patients with COPD.




# Conflict of interest statement

Conflict of interest: E. Benz, J.T. Arinze, S. Wijnant, M. de Ridder, F. Rivadeneira and B.H. Stricker have no conflicts of interest nothing to disclose. Conflict of interest: L. Lahousse

reports financial support by the Fund for Scientific Research Flanders (Grant 3G037618), lecture honoraria from IPSA vzw and Chiesi (paid to her institution), an advisory board for AstraZeneca, and ERS membership (faculty board). Conflict of interest: G. Brusselle reports honoraria for lectures from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Merck Sharp & Dohme, Novartis and Sanofi, and ERS and GINA memberships.

- 39 references
- 3 figures



14

ERJ Open Res

- 
- 
- 

. 2023 Sep 25;9(5):00239-2023.

doi: 10.1183/23120541.00239-2023. eCollection 2023 Sep.

# The Anti-Inflammatory Reliever (AIR) Algorithm Study: a protocol for a single-group study of an AIR stepwise approach to the treatment of adult asthma

Pepa Bruce[1], Lee Hatter[1], Claire Houghton[1], Ciléin Kearns[1], Mark Holliday[1], Augustus J Anderson[1], Allie Eathorne[1], John Martindale[1], Alex Semprini[1], Mark Weatherall[2], Ian Pavord[3], Tim Harrison[4,5], Alberto Papi[6], Rob Horne[7], Richard Beasley[1,8,9]

Affiliations expand

- PMID: 37753283

- PMCID: PMC10518889

- DOI: 10.1183/23120541.00239-2023

**Free PMC article**

**Abstract**

**Background:** The stepwise approach to long-term asthma management, which traditionally incorporates short-acting $\beta_2$-agonist reliever therapy, has been a core feature of asthma guidelines for over 30 years. There have been no studies, however, directly investigating the use of an entire guideline-recommended track. Recently, inhaled corticosteroid-formoterol has been recommended as the preferred reliever therapy in adult asthma, in accordance with a stepwise "Anti-Inflammatory Reliever" (AIR) treatment track.

**Objective:** The aim of this study was to evaluate the AIR stepwise approach recommended by the New Zealand adolescent and adult asthma guidelines, in combination with a novel algorithm for transitioning between treatment steps.

**Methods:** This 52-week, open-label, single-group study will recruit 100 adults aged 18 to 75 years with mild, moderate and moderate-severe asthma (ACTRN12620001010987). Participants will be allocated to budesonide-formoterol 200/6 µg, one actuation as needed (Step 1), one actuation twice daily and as needed (Step 2), or two actuations twice daily and one as needed (Step 3). Treatment steps will be adjusted throughout the study, in response to reliever use and asthma attacks, according to a stepwise AIR algorithm. Following a 26-week period of investigator-led transitions, participants will adjust their own treatment step. The primary outcome is participant satisfaction as measured by the Global Satisfaction score of the Treatment Satisfaction Questionnaire for Medication. Secondary outcomes will assess efficacy and safety, and describe patterns of medication use and participant flow through the treatment steps.

**Conclusion:** This is the first trial to assess the AIR treatment track and algorithm. The results will provide knowledge to guide the clinical use of this approach.



# Conflict of interest statement

Conflict of interest: M. Holliday reports support for the present manuscript from AstraZeneca (to the Medical Research Institute of New Zealand) for inhaler monitor devices and associated costs and study drugs provided free of charge. Conflict of interest: A. Semprini reports grants or contracts from the Health Research Council of New Zealand, and NZ Pharmacy Education and Research Foundation, outside the submitted work. Conflict of interest: I. Pavord reports support for manuscript writing from GSK and

Fishawack Health, outside the submitted work; grants or contracts from Chiesi, outside the submitted work; payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from AstraZeneca, Boehringer Ingelheim, Aerocrine, Almirall, Novartis, Teva, Chiesi, Sanofi/Regeneron, Menarini and GSK; payment for expert testimony from AstraZeneca and Teva; support for attending meetings and/or travel from GSK, Boehringer Ingelheim, AstraZeneca, Teva and Chiesi, outside the submitted work; patents planned, issued or pending for Merck Co. (patent holder of right to Leicester Cough Questionnaire), Bayer and Insmed, outside the submitted work; and participation on a data safety monitoring board or advisory board for Genentech, Sanofi/Regeneron, AstraZeneca, Boehringer Ingelheim, GSK, Novartis, Teva, Merck, Circassia and Chiesi, outside the submitted work. Conflict of interest: T. Harrison is an employee of AstraZeneca and owns stock. Conflict of interest: A. Papi reports grants or contracts from Chiesi, AstraZeneca, GSK, Sanofi and Agenzia Italiana del Farmaco, outside the submitted work; consulting fees from Chiesi, AstraZeneca, GSK, Novartis, Sanofi, Avillion and Elpen Pharmaceutica, outside the submitted work; payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from Chiesi, AstraZeneca, GSK, Menarini, Novartis, Zambon, Mundipharma, Sanofi, Edmond Pharma, Iqvia, Avillion and Elpen Pharmaceuticals, outside the submitted work; and participation on advisory boards for Chiesi, AstraZeneca, GSK, MSD, Novartis, Sanofi, Iqvia, Avillion and Elpen Pharmaceuticals, outside the submitted work. Conflict of interest: R. Horne reports royalties or licences from GSK, AstraZeneca, TEVA, Novartis, UCB, Eli Lilly, Sanofi, Pfizer and Gilead, outside the submitted work; consulting fees from AstraZeneca, UCB, Daiichi, Sciencus, Esai and Vertex, outside the submitted work; payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from AbbVie, Abbott, Amgen, Astellas, AstraZeneca, Boehringer Ingelheim, Biogen, Gilead Sciences, GlaxoSmithKline, Janssen, Merck Sharp Dohme, Merck, Novartis, Pfizer, Procter & Gamble, Roche, Sanofi, Shire, TEVA and UCB, outside the submitted work; participation on advisory boards for AstraZeneca, UCB, Abbott and Novartis, outside the submitted work; and stock or stock options as Founding Director of a UCL-Business company (Spoonful of Sugar Ltd) providing consultancy on treatment engagement and patient support programmes to healthcare policy makers, providers and pharmaceutical industry. Conflict of interest: R. Beasley reports support for the present manuscript form AstraZeneca and the Health Research Council of New Zealand; grants or contracts from AstraZeneca, Genentech and the Health Research Council New Zealand Cure Kids (NZ), outside the submitted work; consulting fees from AstraZeneca, Cipla, Avillion, the Health Research Council New Zealand, CSL Seqirus and Teva Pharmaceuticals, outside the submitted work; payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from AstraZeneca, Cipla, Avillion, the Health Research Council New Zealand, CSL Seqirus and Teva Pharmaceuticals, outside the submitted work; support for attending meetings and/or travel from AstraZeneca, Cipla, Avillion, the Health Research Council New Zealand, CSL Seqirus and Teva Pharmaceuticals, outside the submitted work; participation on a data safety monitoring board or advisory board for AstraZeneca, Cipla, Avillion, the Health Research Council New Zealand, CSL Seqirus and Teva Pharmaceuticals, outside the submitted work; and is Chair for Asthma and Respiratory Foundation NZ

adolescent and adult asthma guidelines, a Member of the GOLD Board, and a Consultant for GINA. All other authors have no conflicts to declare.

- 44 references
- 1 figure

full text links

Proceed to details

Cite

Share

15

Clin Exp Allergy

- 
- 
- 

. 2023 Sep 26.

doi: 10.1111/cea.14389. Online ahead of print.

# Efficacy of dupilumab in patients with uncontrolled, moderate-to-severe asthma with fungal sensitization

Jonathan Corren[1], Nicola A Hanania[2], William W Busse[3], Lawrence D Sher[4], Arman Altincatal[5], Megan Hardin[5], Leda P Mannent[6], Nikhil Amin[7], David J Lederer[7], Xavier Soler[7], Juby A Jacob-Nara[8], Paul J Rowe[8], Yamo Deniz[7]

Affiliations expand

- PMID: 37752621

- DOI: 10.1111/cea.14389

**Abstract**

**Background:** Fungal sensitization (FS) exacerbates asthma in patients who have elevated type 2 inflammatory response. Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for interleukin (IL)-4 and IL-13, key and central drivers of type 2 inflammation in multiple diseases.

**Objective:** This post hoc analysis, funded by the manufacturers of dupilumab, was conducted to assess dupilumab efficacy in patients from the phase 3 LIBERTY ASTHMA QUEST trial (NCT02414854) and TRAVERSE open-label extension (NCT02134028) study who had uncontrolled, moderate-to-severe asthma with type 2 inflammatory phenotype (defined as blood eosinophil count ≥150 cells/μL or FeNO ≥25 ppb) and with FS (defined as IgE specific to Alternaria alternata, Aspergillus fumigatus or Cladosporium herbarum >0.35 IU/mL).

**Methods:** We evaluated annualized rate of severe exacerbations (AER), change from baseline in pre-bronchodilator (BD) forced expiratory volume in 1 s ($FEV_1$), asthma control (per 5-item Asthma Control Questionnaire [ACQ-5]) and biomarker levels (blood eosinophil count, fractional exhaled nitric oxide [FeNO], total IgE, fungal-specific IgEs, thymus and activation-regulated chemokine [TARC] and eotaxin-3).

**Results:** Dupilumab vs. placebo reduced AER, improved pre-BD $FEV_1$ and asthma control (ACQ-5), and reduced serum IgE levels, blood eosinophil count, TARC, eotaxin-3 and FeNO in patients both with and without FS after 52 weeks of treatment in QUEST. Reductions in asthma exacerbation rates and improvements in all other variables were sustained over the TRAVERSE open-label extension study.

**Conclusion:** Dupilumab demonstrated efficacy during prolonged treatment in patients with uncontrolled, moderate-to-severe asthma with FS.

**Keywords:** asthma; dupilumab; fungal sensitization.



- 24 references

## supplementary info

Grants and fundingexpand

## full text links

Proceed to details

Cite

16

Orphanet J Rare Dis

. 2023 Sep 26;18(1):302.

doi: 10.1186/s13023-023-02918-9.

# Low-dose anti-IL 5 treatment in idiopathic hypereosinophilic syndrome: towards a precision medicine approach for remission maintenance

Marco Caminati[#1], Matteo Maule[#2], Roberto Benoni[3], Claudio Micheletto[4], Cristina Tecchio[5], Rachele Vaia[2], Lucia De Franceschi[6], Gabriella Guarnieri[7], Andrea Vianello[7], Gianenrico Senna[6 2]

Affiliations expand

- PMID: 37752586

- PMCID: PMC10521477

- DOI: 10.1186/s13023-023-02918-9

**Free PMC article**

## Abstract

Mepolizumab at the dose of 300 mg/4 weeks has been recently approved as an add-on therapy for patients with uncontrolled hypereosinophilic syndrome (HES) without any identifiable non-hematologic secondary cause. According to the available real-life evidence mepolizumab 300 mg and 100 mg, licensed for severe eosinophilic asthma, are comparable in terms of drug efficacy. However, the clinical rationale for selecting one dose or the other has not been explored. We investigated the efficacy and safety of mepolizumab 100 mg in idiopathic HES (I-HES) patients as a steroid sparing strategy for disease remission maintenance by assessing clinical conditions, blood eosinophil count

(BEC) and adverse events at baseline and at 3-6-12 months follow-up. Overall, 11 patients were enrolled (females 4-36%) with a median age of 62 years (IQR 55.0-72.0). At 3-month visit both prednisone daily dose and BEC significantly decreased from baseline, whilst a substantial improvement of Brief fatigue inventory score (BFI) was not recorded before the 6 months assessment. More than 70% of patients completely stopped prednisone at 12-months follow-up, without any flare in terms of BEC and BFI. No adverse event was registered. Although larger studies are needed, our report firstly describes that in a well-defined population, diagnosed with I-HES and in disease remission, low dose mepolizumab is a safe and effective steroid-sparing option for remission maintenance. It suggests that a personalized treatment dose might be explored according to the disease classification and activity at the time of biologic treatment start.

**Keywords:** Hypereosinophilic syndrome; Mepolizumab; Remission maintenance.



# Conflict of interest statement

The authors declare that they have no competing interests.

- 17 references
- 1 figure

supplementary info

Publication typesexpand

full text links

Proceed to details

Cite

Share

17

Clin Exp Allergy

- 
- 
- 

. 2023 Sep 26.

doi: 10.1111/cea.14395. Online ahead of print.

# Visceral adipose tissue: A relevant inflammatory compartment in obesity-related asthma?

Y Türk[1], J A Witte[1], A van Huisstede[2], B N Melgert[3,4], A van Schadewijk[5], C Taube[5,6], P S Hiemstra[5], J H Kappen[1,7], G J Braunstahl[1,8]

Affiliations expand

- PMID: 37752320

- DOI: 10.1111/cea.14395

***No abstract available***

- 9 references

supplementary info

Grants and fundingexpand

full text links

Proceed to details

Cite

Share

18

JMIR Public Health Surveill

- 
- 
- 

. 2023 Sep 26;9:e50085.

doi: 10.2196/50085.

# Trajectories of Controller Therapy Use Before and After Asthma-Related Hospitalization in Children and Adults: Population-Based Retrospective Cohort Study

Manon Belhassen[1], Maeva Nolin[1], Flore Jacoud[1], Claire Marant Micallef[1], Eric Van Ganse[1,2,3]

Affiliations expand

- PMID: 37751244

- DOI: 10.2196/50085

**Free article**

## Abstract

**Background:** Inappropriate use of inhaled corticosteroids (ICSs) for asthma impairs control and may cause exacerbation, including asthma-related hospitalization (ARH). In prospective studies, ICS use peaked around ARH, but information on routine care use is limited. Since ARH is a major outcome, controller therapy use in routine care before and after ARH should be documented.

**Objective:** This study aimed to distinguish ICS use typologies (trajectories) before and after ARH, and assess their relationships with sociodemographic, disease, and health care characteristics.

**Methods:** A retrospective cohort study was performed using a 1% random sample of the French claims database. All patients hospitalized for asthma between January 01, 2013, and December 31, 2015, were classified as either children (aged 1-10 years) or teens/adults (aged ≥11 years). Health care resource use was assessed between 24 and 12 months before ARH. ICS use was computed with the Continuous Measures of Medication Acquisition-7 (CMA7) for the 4 quarters before and after ARH. Initially, the overall impact of hospitalization on the CMA7 value was studied using a segmented regression analysis in both children and teens/adults. Then, group-based trajectory modeling differentiated the groups with similar ICS use. We tested different models having 2 to 5 distinct trajectory groups before selecting the most appropriate trajectory form. We finally selected the model with the lowest Bayesian Information Criterion, the highest proportion of patients in each group, and the maximum estimated probability of assignment to a specific group.

**Results:** Overall, 863 patients were included in the final study cohort, of which 447 (51.8%) were children and 416 (48.2%) were teens/adults. In children, the average CMA7 value was 12.6% at the start of the observation period, and there was no significant quarter-to-quarter change in the value (P=.14) before hospitalization. Immediately after hospitalization, the average CMA7 value rose by 34.9% (P=.001), before a significant decrease (P=.01) of 7.0% per quarter. In teens/adults, the average CMA7 value was 31.0% at the start, and there was no significant quarter-to-quarter change in the value (P=.08) before hospitalization. Immediately after hospitalization, the average CMA7 value rose by 26.9% (P=.002), before a significant decrease (P=.01) of 7.0% per quarter. We identified 3 and 5 trajectories before ARH in children and adults, respectively, and 5 after ARH for both groups. Trajectories were related to sociodemographic characteristics (particularly, markers of social deprivation) and to potentially inappropriate health care, such as medical management and choice of therapy.

**Conclusions:** Although ARH had an overall positive impact on ICS use trajectories, the effect was often transient, and patient behaviors were heterogeneous. Along with overall trends, distinct trajectories were identified, which were related to specific patients and health care characteristics. Our data reinforce the evidence that inappropriate use of ICS paves the way for ARH.

**Keywords:** asthma; clustering; hospitalization; inhaled corticosteroids; quality of care; trajectories.

. 2023 Sep 26;e0118123.

doi: 10.1128/spectrum.01181-23. Online ahead of print.

# Interactive effects between *CDHR3* genotype and rhinovirus species for diagnosis and severity of respiratory tract infections in hospitalized children

Yu P Song[1], Man F Tang[1,2], Agnes S Y Leung[1,2], Kin P Tao[1,2,3], Oi M Chan[1], Gary W K Wong[1], Paul K S Chan[4], Renee W Y Chan[1,2,3], Ting F Leung[1,2,3]

Affiliations expand

- PMID: 37750685

- DOI: 10.1128/spectrum.01181-23

**Free article**

**Abstract**

Rhinovirus (RV) is the leading pathogen causing childhood wheezing, with rhinovirus C (RV-C) species reported to cause asthma exacerbation. Allele A of single-nucleotide polymorphism (SNP) *CDHR3*_rs6967330 upregulates epithelial expression of RV-C receptors which results in more severe asthma exacerbations in children. Nevertheless, there are limited data on interactions between *CDHR3* variants and their impact on severity of RV-related pediatric respiratory tract infections (RTIs). Medical records of RV-related RTIs in children aged below 18 years who were hospitalized in two public hospitals in 2015-2016 were independently reviewed by two paediatricians. Archived nasopharyngeal aspirates were retrieved for RV detection and sequencing as well as *CDHR3* genotyping. HaploView v.5.0 and generalized multifactor dimensionality reduction (GMDR) analysis were employed for haplotypic assignment and gene-environment interaction analyses. Among 1019 studied cases, our results confirmed the relationship between RV-C species and more severe RTIs. Besides the top risk variant rs6967330-A, we identified rs140154310-T to be associated with RV-C susceptibility under the additive model [odds ratio (OR) 2.53, 95% CI 1.15-5.56; *P* = 0.021]. Rs140154310 was associated with wheezing illness (OR 2.38, 95% CI 1.12-5.04; *P* = 0.024), with such association being stronger in subjects who wheezed due to RV-C infections (OR 2.71, 95% CI 1.32-5.58; *P* = 0.007). Haplotype GAG

constructed from rs4730125, rs6967330, and rs73195665 was associated with increased risk of RV-C infection (OR 1.71, 95% CI 1.11-2.65; *P* = 0.016) and oxygen supplementation (OR 1.93, 95% CI 1.13-3.30; *P* = 0.016). GMDR analyses revealed epistatic interaction between rs140154310 and rs6967330 of *CDHR3* for RV-C infection (*P* = 0.001), RV-C-associated lower RTI (*P* = 0.004), and RV-C-associated wheeze (*P* = 0.007). There was synergistic gene-environmental interaction between rs3887998 and RV-C for more severe clinical outcomes (*P* < 0.001). To conclude, rs140154310-T is another risk variant for RV-C susceptibility and more severe RTIs. Synergistic epistatic interaction is found between *CDHR3* SNPs and RV-C for RTI severity, which is likely mediated by susceptibility to RV-C. Haplotypic analysis and GMDR should be included in identifying prediction models of *CDHR3* for childhood asthma and RTIs. IMPORTANCE This case-control study investigated the interaction between CDHR3 genotypes and rhinovirus (RV) species on disease severity in Hong Kong children hospitalized for respiratory tract infection (RTI). There were synergistic effects between RV-C and CDHR3 SNPs for RTI severity, which was mainly driven by RV-C. Specifically, rs6967330 and rs140154310 alone and their epistatic interaction were associated with RV-C-related and severe RTIs in our subjects. Therefore, genotyping of CDHR3 SNPs may help physicians formulate prediction models for severity of RV-associated RTIs.

**Keywords:** CDHR3; children; gene-environment interaction; respiratory tract infection; rhinovirus; wheezing.

# Effect of dupilumab on sputum eosinophils in patients with moderate-to-severe asthma

Sarah Svenningsen[1,2], Melanie Kjarsgaard[1,2], Kayla Zhang[1], Hana Serajeddini[1,2], Carmen Venegas Garrido[1,2], Anurag Bhalla[1,2], Katherine Radford[1], Chynna Huang[1], Terence Ho[1,2], Nandhitha Ragunayakam[1], Ashutosh Thakar[1], Nisarg Radadia[1], Manali Mukherjee[1,2], Parameswaran Nair[1,2]

Affiliations expand

- PMID: 37750593

- DOI: 10.1111/all.15901

***No abstract available***

- 6 references

supplementary info

Grants and fundingexpand

full text links

Proceed to details

Cite

Share

21

**Review**

Expert Rev Respir Med

. 2023 Sep 25.

doi: 10.1080/17476348.2023.2262920. Online ahead of print.

# Epithelial alarmins: a new target to treat chronic respiratory diseases

Denislava Nedeva[1], Krzysztof Kowal[2], Stefan Mihaicuta[3,4], Guillermo Guidos Fogelbach[5], Paschalis Steiropoulos[6], Herberto Jose Chong-Neto[7], Angelica Tiotiu[8,9]

Affiliations expand

- PMID: 37746733

- DOI: 10.1080/17476348.2023.2262920

**Abstract**

**Introduction:** In response to injury, epithelial cells release alarmins including thymic stromal lymphopoietin (TSLP), high mobility group-box-1 (HMGB1), interleukin (IL)-33 and -25 that can initiate innate immune responses. These alarmins are recognized as activators of T2-immune responses characteristic for asthma, but recent evidence highlighted their role in non-T2 inflammation, airway remodeling and pulmonary fibrosis making them an attractive therapeutic target for chronic respiratory diseases (CRD).

**Areas covered:** In this review, firstly we discuss the role of TSLP, IL-33, IL-25 and HMGB1 in the pathogenesis of asthma, COPD, idiopathic pulmonary fibrosis and cystic fibrosis according to the published data. In the second part, we summarize the current evidence concerning the efficacy of the antialarmin therapies in CRD. Recent clinical trials showed that anti-TSLP and IL-33/R antibodies can improve severe asthma outcomes. Blocking the IL-33-mediated pathway decreased the exacerbation rates in COPD patients with more important benefit for former-smokers.

**Expert opinion:** Despite progress in the understanding of the alarmins' role in the pathogenesis of CRD, all their mechanisms of action are not yet identified. Blocking IL-33 and TSLP pathways offer an interesting option to treat severe asthma and COPD but future investigations are needed to established their place in the treatment strategies.

**Keywords:** Alarmins; biologics; chronic respiratory diseases; exacerbations; lung function.

**Case Reports**

Respirol Case Rep

- 
- 
- 

. 2023 Sep 20;11(10):e01224.

doi: 10.1002/rcr2.1224. eCollection 2023 Oct.

# Life-threatening bronchospasm induced by an angiotensin-converting enzyme inhibitor in a chronically ventilated patient: Diagnostic pitfalls and literature review

Esther-Lee Marcus[1], Amir Hush[1], Hisham Atrash[1], Roaia Shibli[1], Samuel N Heyman[2]

Affiliations expand

- PMID: 37744527

- PMCID: PMC10511829

- DOI: 10.1002/rcr2.1224

**Free PMC article**

**Abstract**

Cough- and asthma-like symptoms are common adverse reactions to angiotensin-converting enzyme inhibitors (ACEi). However, attributing these symptoms to the use of ACEi might be masked by clinical confounders. We report a 68-year-old female residing in a long-term acute-care facility for patients requiring prolonged invasive mechanical ventilation treated for years with ACEi. Daily reversible bouts of life-threatening severe bronchospasm gradually developed over 6 weeks and abruptly resolved following the cessation of ACEi treatment. The late appearance of bronchospasm and the unique clinical setup of chronic invasive ventilation in a patient with smoking-related chronic obstructive lung disease are among the principal confounders that delay the identification of the causative association between ACEi and respiratory compromise. Chronic positive pressure ventilation may also conceal small airway reactivity and obstruction, similar to auto-positive end-expiratory pressure (auto-PEEP). Conceivably, angiotensin receptor blockers should be preferred over ACEi in such patients.

**Keywords:** adverse drug reaction; angiotensin converting enzyme inhibitors; bronchospasm; chronic obstructive lung disease; mechanical ventilation.



# Conflict of interest statement

None declared.

- 24 references
- 1 figure

Respirol Case Rep

- 
- 
- 

. 2023 Sep 19;11(10):e01222.

doi: 10.1002/rcr2.1222. eCollection 2023 Oct.

# Immune checkpoint inhibitor-induced asthma and chronic obstructive pulmonary disease overlap in patient with adenocarcinoma

Yuki Hayakawa[1], Takako Kawaguchi[1], Kei Yamasaki[1], Miyu Endo[1], Masaya Komatsu[1], Yutaka Ishiguro[1], Yuichi Murata[1], Kazuhiro Yatera[1]

Affiliations expand

- PMID: 37736311

- PMCID: PMC10509402

- DOI: 10.1002/rcr2.1222

**Free PMC article**

## Abstract

A 67-year-old current smoker Japanese man, with no history of asthma, was diagnosed with lung adenocarcinoma. He received first-line chemotherapy with carboplatin, pemetrexed, ipilimumab, and nivolumab in July 20XX-1, and subsequently a maintenance therapy with nivolumab. In October 20XX, he became aware of wheezy dyspnoea, and chest computed tomography demonstrated worsening bronchial wall thickenings. Eosinophilia was noted, and a pulmonary function test showed obstructive dysfunction insufficiently responding to beta-agonists, with 130 mL increase of forced expiratory volume in one second and high fractional exhaled nitric oxide level (85 ppb). He was clinically diagnosed with asthma and chronic obstructive pulmonary disease overlap, secondary to immune checkpoint inhibitors (ICIs). The inhibition of binding between programmed cell death-protein-1 (PD-1), expressed on T cells, and programmed cell death-ligand-2 (PD-L2), expressed on tumour and dendritic cells, can induce airway

hyperresponsiveness. Physicians should be wary of asthmatic symptoms and chest image findings during ICIs therapy.

**Keywords:** adenocarcinoma; asthma; chronic obstructive pulmonary disease; immune checkpoint inhibitors.



## Conflict of interest statement

None declared.

- 5 references
- 2 figures

supplementary info

Publication typesexpand

full text links

Proceed to details

Cite

Share

24

EClinicalMedicine

- 
- 
- 

. 2023 Sep 9;64:102193.

doi: 10.1016/j.eclinm.2023.102193. eCollection 2023 Oct.

# Global, regional, and national incidence of six major immune-mediated

# inflammatory diseases: findings from the global burden of disease study 2019

GBD 2019 IMID Collaborators

Collaborators expand

- PMID: 37731935
- PMCID: PMC10507198
- DOI: 10.1016/j.eclinm.2023.102193

**Free PMC article**

## Abstract

**Background:** The causes for immune-mediated inflammatory diseases (IMIDs) are diverse and the incidence trends of IMIDs from specific causes are rarely studied. The study aims to investigate the pattern and trend of IMIDs from 1990 to 2019.

**Methods:** We collected detailed information on six major causes of IMIDs, including asthma, inflammatory bowel disease, multiple sclerosis, rheumatoid arthritis, psoriasis, and atopic dermatitis, between 1990 and 2019, derived from the Global Burden of Disease study in 2019. The average annual percent change (AAPC) in number of incidents and age standardized incidence rate (ASR) on IMIDs, by sex, age, region, and causes, were calculated to quantify the temporal trends.

**Findings:** In 2019, rheumatoid arthritis, atopic dermatitis, asthma, multiple sclerosis, psoriasis, inflammatory bowel disease accounted 1.59%, 36.17%, 54.71%, 0.09%, 6.84%, 0.60% of overall new IMIDs cases, respectively. The ASR of IMIDs showed substantial regional and global variation with the highest in High SDI region, High-income North America, and United States of America. Throughout human lifespan, the age distribution of incident cases from six IMIDs was quite different. Globally, incident cases of IMIDs increased with an AAPC of 0.68 and the ASR decreased with an AAPC of -0.34 from 1990 to 2019. The incident cases increased across six IMIDs, the ASR of rheumatoid arthritis increased (0.21, 95% CI 0.18, 0.25), while the ASR of asthma (AAPC = -0.41), inflammatory bowel disease (AAPC = -0.72), multiple sclerosis (AAPC = -0.26), psoriasis (AAPC = -0.77), and atopic dermatitis (AAPC = -0.15) decreased. The ASR of overall and six individual IMID increased with SDI at regional and global level. Countries with higher ASR in 1990 experienced a more rapid decrease in ASR.

**Interpretation:** The incidence patterns of IMIDs varied considerably across the world. Innovative prevention and integrative management strategy are urgently needed to mitigate the increasing ASR of rheumatoid arthritis and upsurging new cases of other five IMIDs, respectively.

**Funding:** The Global Burden of Disease Study is funded by the Bill and Melinda Gates Foundation. The project funded by Scientific Research Fund of Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital (2022QN38).

**Keywords:** Global burden of disease study; Immune-mediated inflammatory disease; Incidence; Trend.



# Conflict of interest statement

K Abuabara reports grants or contracts from Pfizer and Cosmetique Internacional SNC to their institution, University of California San Francisco; consulting fees from TARGET RWE; outside the submitted work. S Bhaskar reports leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid, with the Rotary Club or Sydney as Board Director and Chair of Youth, with Rotary District 9675 as Chair of Diversity, Equity and Inclusion, and with Global Hub Health Germany as Founding Member and Co-manager, all outside the submitted work. R Buchbinder reports grants from Australian National Health and Medical Research Council (NHMRC), Arthritis Australia, Cabrini Foundation, HCF Foundation, Australian Department of Health to their institution; royalties or licenses from UptoDate as personal payments for a chapter on plantar fasciitis; all outside the submitted work. A K Demetriades reports leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid, with European Association of Neurosurgical Societies (EANS) as President and with Global Neuro Foundation as Board Member, all outside the submitted work. I Filip and A Radfar report payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Avicenna Medical and Clinical Research Institute. T Fukumoto reports payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from AbbVie, Eli Lilly, Sanofi, Pfizer, Maruho, Novartis, Taiho, Sun Pharma, UCB, and Janssen Pharma, all outside the submitted work. C Herteliu reports a research grant from Romanian Ministry of Research Innovation and Digitalization, MCID, for project titled “Enhancing institutional performance through development of infrastructure and transdisciplinary research ecosystem within socio-economic domain–PERFECTIS,” project number ID-585-CTR-42-PFE-2021, outside the submitted work. N Ismail reports leadership or fiduciary role in other board, society, committee or advocacy group, unpaid, with the Malaysian Academy of Pharmacy as council member and bursar, outside the submitted work. K Krishan reports non-financial support from UGC Centre of Advanced Study, CAS II, Department of Anthropology, Panjab University, Chandigarh, India, outside the submitted work. V Shivarov reports a pending Bulgarian patent for Possible SARS-CoV-2 preimmune

epitopes; stock or stock options in ICON PLC through restricted stock units; other financial interests from PRAHS/ICON PLC through their salary; all outside the submitted work. C R Simpson reports research grants from MBIE (NZ), HRC (NZ), Ministry of Health (NZ), MRC (UK), HDRUK, and CSO (UK) to their institution, all outside the submitted work. J A Singh reports consulting fees from Crealta/Horizon, Medisys, Fidia, PK Med, Two Labs Inc., Adept Field Solutions, Clinical Care Options, Clearview Healthcare Partners, Putnam Associates, Focus Forward, Navigant Consulting, Spherix, MedIQ, Jupiter Life Science, UBM, Trio Health, Medscape, WebMD, Practice Point Communications, the National Institutes of Health, and the American College of Rheumatology all as personal payments; payment or honoraria for speakers' bureaus from Simply Speaking; support for attending meetings or travel from the steering committee of OMERACT; unpaid participation on a Data Safety Monitoring Board or Advisory Board with the US Food and Drug Administration Arthritis Advisory Committee; leadership or fiduciary role in board, society, committee or advocacy group, paid or unpaid, with OMERACT as a steering committee member, with the Veterans Affairs Rheumatology Field Advisory Committee as Chair (unpaid), and with the UAB Cochrane Musculoskeletal Group Satellite Center on Network Meta-analysis and editor and director (unpaid); stock or stock options in Atai Life Sciences, Kintara Therapeutics, Intelligent Biosolutions, Acumen Pharmaceutical, TPT Global Tech, Vaxart Pharmaceuticals, Atyu Biopharma, Adaptimmune Therapeutics, GeoVax Labs, Pieris Pharmaceuticals, Enzolytics Inc., Seres Therapeutics, Tonix Pharmaceuticals Holding Corp., and Charlotte's Web Holdings, Inc., and previously owned stock options in Amarin, Viking, and Moderna Pharmaceuticals; all outside the submitted work. M Zielińska reports other financial or non-financial interests as an employee of AstraZeneca, outside the submitted work. E Upadhyay reports a published patent for A system and method of reusable filters for anti-pollution mask, A system and method for electricity generation through crop stubble by using microbial fuel cells, A system for disposed personal protection equipment (PPE) into biofuel through pyrolysis and method, A novel herbal pharmaceutical aid for formulation of gel and method thereof, and reports leadship for Joint Secretary of Indian Meteorological Society, Jaipur Chapter, India, Member Secretary-DSTPURSE Program.

Proc Natl Acad Sci U S A

. 2023 Sep 26;120(39):e2302409120.

doi: 10.1073/pnas.2302409120. Epub 2023 Sep 18.

# Emergency department visits respond nonlinearly to wildfire smoke

Sam Heft-Neal[1], Carlos F Gould[2], Marissa L Childs[3], Mathew V Kiang[4], Kari C Nadeau[5], Mark Duggan[6 7 8], Eran Bendavid[9 10], Marshall Burke[1 2 8]

Affiliations expand

- PMID: 37722035

- PMCID: PMC10523589 (available on 2024-03-18)

- DOI: 10.1073/pnas.2302409120

**Abstract**

Air pollution negatively affects a range of health outcomes. Wildfire smoke is an increasingly important contributor to air pollution, yet wildfire smoke events are highly salient and could induce behavioral responses that alter health impacts. We combine geolocated data covering all emergency department (ED) visits to nonfederal hospitals in California from 2006 to 2017 with spatially resolved estimates of daily wildfire smoke PM[Formula: see text] concentrations and quantify how smoke events affect ED visits. Total ED visits respond nonlinearly to smoke concentrations. Relative to a day with no smoke, total visits increase by 1 to 1.5% in the week following low or moderate smoke days but decline by 6 to 9% following extreme smoke days. Reductions persist for at least a month. Declines at extreme levels are driven by diagnoses not thought to be acutely impacted by pollution, including accidental injuries and several nonurgent symptoms, and declines come disproportionately from less-insured populations. In contrast, health outcomes with the strongest physiological link to short-term air pollution increase dramatically in the week following an extreme smoke day: We estimate that ED visits for asthma, COPD, and cough all increase by 30 to 110%. Data from internet searches, vehicle traffic sensors, and park visits indicate behavioral changes on high smoke days consistent with declines in healthcare utilization. Because low and moderate smoke days vastly outweigh high smoke days, we estimate that smoke was responsible for an average of 3,010 (95% CI: 1,760-

4,380) additional ED visits per year 2006 to 2017. Given the increasing intensity of wildfire smoke events, behavioral mediation is likely to play a growing role in determining total smoke impacts.

**Keywords:** behavior; health; pollution; wildfire.

## Conflict of interest statement

The authors declare no competing interest.

- 50 references

supplementary info

MeSH termsexpand

full text links

Proceed to details

Cite

Share

26

Crit Care Nurs Q

- 
- 
- 

. 2023 Oct-Dec;46(4):426-434.

doi: 10.1097/CNQ.0000000000000478.

# Asthma in Pregnancy

Sheldon Rao[1], Sujith Modugula, Karen Gaviglia, Tariq Cheema, Tiffany Dumont, Marvin Balaan, Briana DiSilvio

Affiliations expand

- PMID: 37684738

- DOI: 10.1097/CNQ.0000000000000478

**Abstract**

Asthma is a common chronic respiratory condition that affects approximately 10% of adult women in the United States. Pregnancy can present unique challenges for women with asthma, as changes in the body can alter the severity and management of asthma-related respiratory symptoms. In this article, we review the current understanding of asthma during pregnancy, including the direct effects of the disease state on the pregnant woman and fetus, risk factors for poor control of disease, as well as current treatment recommendations.



## Conflict of interest statement

The authors report no conflicts of interests or sources of funding.

- 36 references

full text links

Proceed to details

Cite

Share

27

Data Brief

- 
- 
- 

. 2023 Jul 18;50:109422.

doi: 10.1016/j.dib.2023.109422. eCollection 2023 Oct.

# Asthma control conundrum in clinical practice - Data from a two-stage Delphi survey and literature review

Giorgio Walter Canonica[1], Antonio Spanevello[2], Luis Pérez de Llano[3], Christian Domingo Ribas[4], John D Blakey[5,6], Gabriel Garcia[7], Hiromasa Inoue[8], Margareth Dalcolmo[9], Dong Yang[10], Soniya Mokashi[11], Abhishek Kurne[12], Aman Kapil Butta[13]

Affiliations expand

- PMID: 37663766

- PMCID: PMC10470358

- DOI: 10.1016/j.dib.2023.109422

**Free PMC article**

## Abstract

Definitions and measures of asthma control used in clinical trials and practice often vary, as highlighted in the manuscript, "Is asthma control more than just an absence of symptoms? An expert consensus statement". Furthermore, the authors discussed differences between patients and healthcare professionals (HCPs) in terms of understanding and managing asthma. Given these disparities, there is a need for consensus regarding what constitutes well-controlled asthma and, especially, how best it can be measured and recorded. In the current work, we describe our data and provide more detail on the methodology from a two-stage Delphi survey and a structured literature review, which were designed to reach a consensus definition of asthma control and alleviate misalignments between patients and HCPs. Survey data were collected using a two-stage Delphi technique; a method used to collate expert opinions over a series of sequential questionnaires to reach a consensus. The collated Delphi survey data were compared with results from a comprehensive, structured literature review of 216 publications, to assess if there was a correlation between existing guidance and measures of asthma control used in clinical trials and standard clinical practice. In order to collate and interpret findings from the Delphi survey, responses from 82 panelists (73 HCPs and 9 authors) were qualitatively analyzed, quantitatively categorized, and presented as percentages or counts in Excel databases, which are detailed in the current work. Searches conducted using PubMed and Cochrane identified 664 manuscripts, and Embase was used to identify 89 congress abstracts. After applying a stringent screening method using predefined key words, the structured literature review consisted of 185 peer-reviewed manuscripts and 31 congress abstracts, and assessed existing guidance and measures of asthma control used in clinical trials. In this publication, we provide further insight into the predefined keywords, search strings, and strategy applied to identify manuscripts and congress abstracts for inclusion/exclusion, and detail methods for data extraction. Together, the data from the Delphi survey and structured literature review aimed to provide greater insights into challenges and approaches in achieving asthma control in clinical practice, with the potential for results to be used to guide a universally accepted definition and measure of asthma control that can be used

and understood by patients, HCPs, and researchers. Qualitative and quantitative methodology and analysis from the Delphi survey and literature review search strategy can potentially be used to identify disparities and explore expert opinion and relevant literature in other therapeutic areas to guide a consensus where disparities exist.

**Keywords:** Asthma communication; Asthma consensus; Asthma expert recommendation; Disparities in asthma control; Quantitative form; Screening questions; Standard definitions in asthma.



# Conflict of interest statement

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: A. Spanevello reports consulting fees from GSK; payment or honoraria from AstraZeneca, Chiesi, and GSK; and participation on a data safety monitoring board or advisory board for GSK. L. Pérez de Llano reports grants or contracts from AstraZeneca, Esteve, FAES Pharma, and Teva, consulting fees from AstraZeneca, GEBRO, Gilead, GSK, MSD, Novartis, and Sanofi; payment or honoraria from AstraZeneca, Chiesi, Esteve, GSK, LEO Pharma, MSD, Novartis, and Sanofi; support for attending meetings and/or travel from AstraZeneca, Chiesi, FAES Pharma, GSK, and Novartis; and participation on a data safety monitoring board or advisory board for AstraZeneca. C. Domingo Ribas has received funding for travel or speaker fees from ALK, Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, Esteve, Ferrer, GSK, Menarini, Novartis, Pfizer, and Stallergenes, and declares no specific conflicts of interest to report regarding this paper. J.D. Blakey reports grants or contracts from AstraZeneca, GSK, and Novartis; consulting fees from Boehringer Ingelheim, Chiesi, and GSK; payment or honoraria from AstraZeneca, Chiesi, and GSK; support for attending meetings and/or travel from AstraZeneca, Boehringer Ingelheim, and GSK; receipt of medical writing support from GSK and Teva; payment to their institution for advisory work from Asthma Australia; and unpaid advisory work from Asthma WA. H. Inoue declares research grants from Boehringer Ingelheim, payment or honoraria for lectures and advisory committees from AstraZeneca, Boehringer Ingelheim, GSK, Kyorin, Novartis, and Sanofi. G.W. Canonica declares no conflict of interest for the current paper, and reports having received research grants as well as being lecturer or having received advisory board fees from A.Menarini, Allergy Therapeutics, Anallergo, AstraZeneca, Chiesi, FAES Pharma, Firma, Genentech, GSK, Guidotti-Malesci, Hal Allergy, Innovacaremd, Novartis, OmPharma, RedMaple, Sanofi-Aventis, Sanofi-Genzyme, Stallergenes-Greer, ThermoFisher, Uriach Pharma, and Valeas. D. Yang, and M. Dalcolmo declare that they have no disclosures of interest. G. Garcia declares participation in advisory boards for AstraZeneca, Boehringer Ingelheim, GSK, Novartis, and Sanofi; participation in sponsored activities for AstraZeneca, Boehringer Ingelheim, GSK, Novartis, Sanofi, and Phoenix; principal investigator for AstraZeneca, Boehringer Ingelheim, Chiesi, Covance, GSK, Iqvia, Novartis, Parexel, PPD, Sanofi, and Zambon. S. Mokashi, A.

Kurne, and A. Butta were GSK employees at the time of study conduct and hold shares in GSK.

- 3 references

full text links

Proceed to details

Cite

Share

28

Biomed Pharmacother

- 
- 
- 

. 2023 Oct;166:115385.

doi: 10.1016/j.biopha.2023.115385. Epub 2023 Aug 30.

# The effect of anti-IL5 monoclonal antibodies on regulatory and effector T cells in severe eosinophilic asthma

Laura Bergantini[1], Tommaso Pianigiani[2], Miriana d'Alessandro[2], Sara Gangi[2], Behar Cekorja[2], Elena Bargagli[2], Paolo Cameli[2]

Affiliations expand

- PMID: 37651801

- DOI: 10.1016/j.biopha.2023.115385

**Free article**

**Abstract**

**Introduction:** Biological treatments have redesigned the clinical management of severe eosinophilic asthmatic (SA) patients. Despite emerging evidence supporting the role of

natural Killer (NK), and T regulatory cells (Treg) in the pathogenesis of asthma, no data is available on the effects of anti-IL5/IL5R therapies on these cell subsets.

**Methods:** We prospectively enrolled fourteen SA patients treated with benralizumab (n = 7) or mepolizumab (n = 7) and compared them with healthy controls (HC) (n = 11) and mild to moderate asthmatic (MM) patients (n = 9). Clinical parameters were collected at baseline (T0) and during follow-up. Cellular analysis, including the analysis of T/NK cell subsets, was determined through multicolor flow cytometry.

**Results:** At T0, SA patients showed higher percentages of CD4 TEM (33.3 ± 17.9 HC, 42.6 ± 16.6 MM and 66.1 ± 19.7 in SA; p < 0.0001) than HC and MM patients. With different timing, the two drugs induce a reduction of CD4 TEM ( 76 ± 19 T0; 43 ± 14 T1; 45 ± 23 T6; 62 ± 18 at T24; p < 0.0001 for mepolizumab and 55 ± 21 T0; 55 ± 22 T1; 43 ± 14 T6; 27 ± 12 at T24; p < 0.0001 for benralizumab) and an increase of Treg cells (1.2 ± 1.3 T0; 5.1 ± 2.5 T1; 6.3 ± 3.4 T6; 8.4 ± 4.6 at T24; p < 0.0001 for mepolizumab and 3.4 ± 1.7 T0; 1.9 ± 0.8 T1; 1.9 ± 1 T6; 5.1 ± 2.4 at T24; p < 0.0001 for benralizumab). The change of $CD56^{dim}$ $PD\text{-}1^{+}$ significantly correlated with FEV1% (r = - 0.32; p < 0.01), while Treg expressing PD-1 correlates with the use of oral steroids ( r = 0.36 p = 0.0008) and ACT score (r = 0.36 p = 0.0008) p < 0.001) CONCLUSIONS: Beyond the clinical improvement, anti-IL-5 treatment induces a rebalancing of Treg and T effector cells in patients with SA.

**Keywords:** Benralizumab; Immune checkpoints; Mepolizumab; Regulatory T cells; Severe asthma.



# Conflict of interest statement

Declaration of Competing Interest PC served as a speaker and consultant and advisory board member for Astra Zeneca, Sanofi, Novartis, and GSK. PC, EB, MdA, and LB are investigators for current research financed by AstraZeneca (grants paid to his institution). All other authors declare no conflict of interest.

**Review**

Curr Allergy Asthma Rep

- 
- 
- 

. 2023 Oct;23(10):555-566.

doi: 10.1007/s11882-023-01106-w. Epub 2023 Aug 30.

# Omalizumab Treatment in Uncontrolled Asthma and CRSwNP Patients, with Previous Endoscopic Sinus Surgery, to Improve Quality of Life and Endoscopic Outcomes: a Two-Year Real-Life Study

Juan Maza-Solano[1], Amparo Callejon-Leblic[1,2], Daniel Martin-Jimenez[3], Ramon Moreno-Luna[1], Jaime Gonzalez-Garcia[1], Alfonso Cuvillo[4], Serafin Sanchez-Gomez[1]

Affiliations expand

- PMID: 37644255

- DOI: 10.1007/s11882-023-01106-w

## Abstract

**Purpose of review:** Despite molecular underlying advances, limited and divergent data on monoclonal antibodies (mAb) therapy in chronic rhinosinusitis with nasal polyps (CRSwNP) make further analysis necessary. The objective of this study is to evaluate the effect of omalizumab as an adjunct to endoscopic sinus surgery (ESS) on the treatment of CRSwNP under real-life conditions.

**Recent findings:** Since the introduction of omalizumab, as the first biologic agent for the treatment of diseases such as severe allergic asthma, different studies have demonstrated an effect of omalizumab on CRSwNP, with significant improvements in sinonasal symptoms and endoscopic scores. The high efficacy derived from mAb therapy and the

need for ESS prior to mAb recommended by guidelines, has led to compare both therapeutic alternatives, finding discrepancies in their effect on quality of life (QoL) and complementary tests outcomes. Patients with moderate-to-severe asthma with clinical criteria for omalizumab indication, and coexistent CRSwNP disease, were selected for a non-randomized interventional retrospective study into four treatment subgroups. Measures were analyzed and compared between groups and over time at the baseline, 16 weeks and 1 and 2 years after treatment. Omalizumab treatment in patients with previous ESS exhibited an earlier and more pronounced improvement in QoL, symptoms scale and endoscopic findings (nasal polyp score and the bilateral modified Lund-Kennedy) as early from week 16, which improvement persisted for 2 years. A greater mean improvement of 33.4 ± 6.5 (95% CI: 20.3-46.4; $p < 0.001$) points in sinonasal outcome test 22 (SNOT-22) was associated with ESS at week 16, against omalizumab effect (17.8 ± 7.6 [95% CI: 2.6-33.0]; $p = 0.023$). At year 2, an improvement in SNOT-22 of 62.6 ± 8.9 (95% CI: 48.4-84.1; $p < 0.001$) points was exclusively associated with omalizumab. Clinical evidence of the effect of omalizumab added to ESS treatment is provided in this study in the short- and long-term.

**Keywords:** Allergic asthma; CRSwNP; Endoscopic sinus surgery; Monoclonal antibody; Omalizumab treatment.



- 51 references

supplementary info

Publication types, MeSH terms, Substancesexpand

full text links

Proceed to details

Cite

Share

30

**Review**

Allergy

. 2023 Oct;78(10):2581-2595.

doi: 10.1111/all.15855. Epub 2023 Aug 28.

# UCRAID (Ukrainian Citizen and refugee electronic support in Respiratory diseases, Allergy, Immunology and Dermatology) action plan

Jean Bousquet[1,2,3], Boleslaw Samolinski[4], Igor Kaidashev[5], Marcus Maurer[1,2], Nicolas Roche[6,7], Bernardo Sousa-Pinto[8,9], Andrii Kurchenko[10], Roman Stepanenko[11], Vladyslav Tsaryk[10], Ludger Klimek[12,13], Maria Teresa Ventura[14,15], Anna Bedbrook[3,16], Wienczyslawa Czarlewski[3,17], Yuliia Lysanets[5], Maciej Kupczyk[18], Łukasz Skolimowski[19], Marek Kulus[20], Stefano Del Giacco[21], Markus Ollert[22,23,24], Judith Garcia-Aymerich[25,26], Carlos Robalo Cordeiro[27], Arzu Yorgancioglu[28], Christoph Schlapbach[29], Rita Amaral[8,9], Cristina Bonaglia[30], Isabelle Bossé[31], Rosalba Buguicchio[32], Demetrios Christou[1,2], Galyna Fedoruk[10], Pietro Fontanesi[30], Bilun Gemicioglu[33], Antonio F M Giuliano[14,34], Paolo Lepore[35], Alla Nakonechna[36,37], Sophia Neisinger[1,2], Ana M Pereira[8,9], Aiste Ramanauskaite[1,2], Filip Raciborski[4], Brigita Sitkauskiene[38], Oksana Sokhatska[39], Viktor Stepanenko[11], Katarina Stevanovic[1,2], Orysya Syzon[40], Violeta Kvedariene[41,42], Govert de Vries[43], Michiel van Eerd[43], Arunas Valiulis[44,45], Joao A Fonseca[8,9], Josep M Anto[25,26,46], Tari Haahtela[47], Holger Schünemann[48], Torsten Zuberbier[1,2]

Affiliations expand

- PMID: 37641384

- DOI: 10.1111/all.15855

**Free article**

## Abstract

Eight million Ukrainians have taken refuge in the European Union. Many have asthma and/or allergic rhinitis and/or urticaria, and around 100,000 may have a severe disease. Cultural and language barriers are a major obstacle to appropriate management. Two widely available mHealth apps, MASK-air® (Mobile Airways Sentinel NetworK) for the management of rhinitis and asthma and CRUSE® (Chronic Urticaria Self Evaluation) for patients with chronic spontaneous urticaria, were updated to include Ukrainian versions that make the documented information available to treating physicians in their own language. The Ukrainian patients fill in the questionnaires and daily symptom-medication scores for asthma, rhinitis (MASK-air) or urticaria (CRUSE) in Ukrainian. Then, following the

GDPR, patients grant their physician access to the app by scanning a QR code displayed on the physician's computer enabling the physician to read the app contents in his/her own language. This service is available freely. It takes less than a minute to show patient data to the physician in the physician's web browser. UCRAID-developed by ARIA (Allergic Rhinitis and its Impact on Asthma) and UCARE (Urticaria Centers of Reference and Excellence)-is under the auspices of the Ukraine Ministry of Health as well as European (European Academy of Allergy and Clinical immunology, EAACI, European Respiratory Society, ERS, European Society of Dermatologic Research, ESDR) and national societies.

**Keywords:** Ukrainian refugees; asthma; mHealth; rhinitis; urticaria.



- 54 references

## supplementary info

Publication types, Grants and fundingexpand

## full text links

Proceed to details

Cite

Share

31

**Review**

Allergol Int

- 
- 
- 

. 2023 Oct;72(4):507-520.

doi: 10.1016/j.alit.2023.08.004. Epub 2023 Aug 24.

# Relationship between Aspergillus and asthma

Ritesh Agarwal[1], Valliappan Muthu[2], Inderpaul Singh Sehgal[2]

Affiliations expand

- PMID: 37633774

- DOI: 10.1016/j.alit.2023.08.004

**Abstract**

Fungal sensitization is highly prevalent in severe asthma. The relationship between fungus and asthma, especially Aspergillus fumigatus, has been the subject of extensive research. The ubiquitous presence of A. fumigatus, its thermotolerant nature, the respirable size of its conidia, and its ability to produce potent allergens are pivotal in worsening asthma control. Due to the diverse clinical manifestations of fungal asthma and the lack of specific biomarkers, its diagnosis remains intricate. Diagnosing fungal asthma requires carefully assessing the patient's clinical history, immunological tests, and imaging. Depending on the severity, patients with fungal asthma require personalized treatment plans, including inhaled corticosteroids and bronchodilators, and antifungal therapy. This review provides a comprehensive overview of the association between Aspergillus and asthma by reviewing the relevant literature and highlighting key findings. We discuss the diagnosis of various entities included in fungal asthma. We also debate whether newer definitions, including allergic fungal airway disease, offer any additional advantages over the existing ones. Finally, we provide the current treatment options for the individual entities, including A. fumigatus-associated asthma, severe asthma with fungal sensitization, and allergic bronchopulmonary mycoses.

**Keywords:** ABPA; Allergic bronchopulmonary mycosis; Bronchiectasis; Cystic fibrosis; Fungal asthma.



## supplementary info

Publication typesexpand

## full text links

Adv Ther

. 2023 Oct;40(10):4606-4625.

doi: 10.1007/s12325-023-02590-2. Epub 2023 Aug 17.

# Understanding the Clinical Implications of Individual Patient Characteristics and Treatment Choice on the Risk of Exacerbation in Asthma Patients with Moderate-Severe Symptoms

Dave Singh[1], Sean Oosterholt[2], Ian Pavord[3], Gabriel Garcia[4], Abhijith Pg[5], Oscar Della Pasqua[6,7]

Affiliations expand

- PMID: 37589831

- PMCID: PMC10499702

- DOI: 10.1007/s12325-023-02590-2

**Free PMC article**

## Abstract

**Introduction:** The assessment of future risk has become an important feature in the management of patients with asthma. However, the contribution of patient-specific characteristics and treatment choices to the risk of exacerbation is poorly understood. Here we evaluated the effect of interindividual baseline differences on the risk of exacerbation

and treatment performance in patients receiving regular maintenance doses of inhaled corticosteroids (ICS) or ICS/long-acting beta-agonists (LABA) combination therapy.

**Methods:** Exacerbations and changes to asthma symptoms 5-item Asthma Control Questionnaire (ACQ-5) were simulated over a 12-month period using a time-to-event and a longitudinal model developed from phase III/IV studies in patients with moderate-severe asthma (N = 16,282). Simulations were implemented to explore treatment performance across different scenarios, including randomised designs and real-world settings. Treatment options included regular dosing with ICS monotherapy [fluticasone propionate (FP)] and combination therapy [fluticasone propionate/salmeterol (FP/SAL) or budesonide/formoterol (BUD/FOR)]. Exacerbation rate was analysed using the log-rank test. The cumulative incidence of events was summarised stratified by treatment.

**Results:** Being a woman, smoker, having higher baseline ACQ-5 and body mass index (BMI) and lower forced expiratory volume in the first second ($FEV_1$) are associated with increased exacerbation risk ($p < 0.01$). This risk is bigger in winter because of the seasonal variation effect. Across the different scenarios, the use of FP/SAL resulted in a 10% lower annual incidence of exacerbations relative to FP or regular dosing BUD/FOR, independently of baseline characteristics. Similar differences in the annual incidence of exacerbations were also observed between treatments in obese patients (BMI ≥ 25-35 $kg/m^2$) ($p < 0.01$) and in patients who do not achieve symptom control on FP monotherapy.

**Conclusions:** Individual baseline characteristics and treatment choices affect future risk. Achieving comparable levels of symptom control whilst on treatment does not imply comparable risk reduction, as shown by the lower exacerbation rates in FP/SAL vs. BUD/FOR-treated patients. These factors should be considered as a basis for personalised clinical management of patients with moderate-severe asthma.

**Keywords:** ACQ-5; Asthma exacerbation; Clinical trial simulations; Fluticasone propionate; Future risk; ICS/LABA combination therapy; Salmeterol; Symptom control; Treatable traits.

# Plain language summary

The goal of this project was to demonstrate that individual baseline characteristics can affect the risk of exacerbation as well as the overall treatment response in patients receiving regular maintenance doses of inhaled corticosteroids, given as monotherapy or in combination with long-acting beta-agonists. Using computer simulations based on a drug–disease model previously developed from a large pool of patients with moderate–severe asthma symptoms (N = 16,282), we describe how demographic and clinical baseline patient characteristics at the time of treatment start correlate with the risk of exacerbation. Our results indicate that poor symptom control, limited lung function, obesity, smoking and sex are associated with significant increase in the incidence of asthma attacks. Such an effect is augmented in winter because of the contribution of seasonal variation. This analysis also allowed us to assess how different treatments modify or reduce the annual incidence of moderate to severe attacks. In addition, simulated scenarios showed that

combination therapy with fluticasone propionate/salmeterol results in 10% fewer asthma attacks relative to budesonide/formoterol combination therapy. Such a difference may be associated with corticosteroid-specific properties, which vary between inhaled corticosteroids. Consequently, even though comparable level of immediate relief and symptom control may be achieved whilst on treatment, these effects do not imply the same long-term reduction in the risk of exacerbation. These factors should be considered as a basis for personalised clinical management of patients with moderate–severe asthma.



# Conflict of interest statement

Ian Pavord has received honoraria for speaking at sponsored meetings from AstraZeneca, Boehringer Ingelheim, Aerocrine, Almirall, Novartis, Teva, Chiesi, Sanofi/Regeneron, Menarini and GSK, and payments for organising educational events from AstraZeneca, GSK, Sanofi/Regeneron and Teva; he has received honoraria for attending advisory panels with Genentech, Sanofi/Regeneron, AstraZeneca, Boehringer Ingelheim, GSK, Novartis, Teva, Merck, Circassia, Chiesi and Knopp and payments to support FDA approval meetings from GSK; he has received sponsorship to attend international scientific meetings from Boehringer Ingelheim, GSK, AstraZeneca, Teva and Chiesi; he has received a grant from Chiesi to support a phase 2 clinical trial in Oxford; he is co-patent holder of the rights to the Leicester Cough Questionnaire and has received payments for its use in clinical trials from Merck, Bayer and Insmed; and in 2014–2015 he was an expert witness for a patent dispute involving AstraZeneca and Teva; Dave Singh has received personal fees from Aerogen, AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, CSL Behring, Epiendo, Genentech, GSK, Glenmark, Gossamerbio, Kinaset, Menarini, Novartis, Pulmatrix, Sanofi, Synairgen, Teva, Theravance and Verona, and is supported by the National Institute for Health Research (NIHR) Manchester Biomedical Research Centre (BRC); Gabriel Garcia has participated in advisory boards for GSK, AstraZeneca, Sanofi, Novartis and Boehringer Ingelheim; he has received honoraria for speaking at sponsored meetings from GSK, Boehringer Ingelheim, AstraZeneca, Sanofi, Phoenix, and Novartis; and is a principal investigator in trials sponsored by GSK, Boehringer Ingelheim, AstraZeneca, Novartis, Sanofi, PPD, Zambon, Parexel, Covance, IQVIA, and Chiesi; Sean Oosterholt, Abhijith PG and Oscar Della Pasqua are GSK employees and hold stocks/shares in GSK.


- 45 references
- 7 figures


## supplementary info

Publication types, MeSH terms, Substancesexpand

## full text links

33

Pediatr Pulmonol

. 2023 Oct;58(10):2841-2845.

doi: 10.1002/ppul.26597. Epub 2023 Aug 17.

# Evaluation of the efficacy of asthma information videos ('Moving On Asthma') at improving knowledge in teenage children

Adam Gardiner[1], Moira Gibbons[2], Nicki Barker[2], Heather Elphick[2]

Affiliations expand

- PMID: 37589425

- DOI: 10.1002/ppul.26597

**Abstract**

**Introduction:** Asthma is a common inflammatory condition that can be life threatening. The National Review of Asthma Deaths (2014) recommended: Parents and children…should be educated about managing asthma. The aim of this study was to assess the efficacy of an educational video on asthma at improving knowledge in adolescent children.

**Methods:** A 3-min asthma education video was shown to young people aged 13-15 years in two contrasting schools. Knowledge of asthma was evaluated using a 6-question form completed at 3 timepoints: baseline (pre), immediately after intervention (post), and 1 week later (delayed). A total of 151 data sets from two schools were analysed.

**Results:** Knowledge was significantly improved immediately after watching the video for four out of six questions, indicating that the video was successful in effectively educating the children about asthma. There was no significant change to responses between immediately after watching the video and a week later, suggesting retention of the knowledge gained from viewing the intervention material.

**Conclusion:** The results suggest acquisition and retention of knowledge in young people after watching a video on asthma, providing evidence to support the use of digital, video-assisted, internet-based learning tools such as the 'Moving on Asthma' website as an aid to regular clinics for young people with asthma.

**Keywords:** asthma; children; education; knowledge; transition.



- 7 references

supplementary info

Grants and fundingexpand

full text links

Proceed to details

Cite

Share

34

ERJ Open Res

- 
- 
- 

. 2023 Sep 25;9(5):00208-2023.

doi: 10.1183/23120541.00208-2023. eCollection 2023 Sep.

# The association of vitamin K status with lung function and disease in a general population

Torkil Jespersen[1], Freja Bach Kampmann[1], Thomas Meinertz Dantoft[1], Niklas Rye Jørgensen[2,3], Line Lund Kårhus[1], Flemming Madsen[1], Allan Linneberg[1,3], Sanne Marie Thysen[1]

Affiliations expand

- PMID: 37588689

- PMCID: PMC10423920

- DOI: 10.1183/23120541.00208-2023

**Free PMC article**

**Abstract**

**Introduction:** Matrix Gla protein (MGP) is an inhibitor of lung tissue calcification. The plasma level of dephosphorylated-uncarboxylated MGP (dp-ucMGP) is a biomarker of vitamin K status. The present study assessed whether lower vitamin K status (reflected by higher dp-ucMGP) was associated with lung function and lung disease/symptoms.

**Methods:** A general population sample of 4092 individuals, aged 24 to 77 years, underwent a health examination including questionnaires, spirometry and measurements of plasma dp-ucMGP. Associations of dp-ucMGP with lung function and self-reported disease/symptoms were estimated using regression models adjusted for age, sex and height. Associations were expressed as β-estimates or odds ratios (ORs) per doubling in dp-ucMGP.

**Results:** Lower vitamin K status (higher dp-ucMGP) was associated with lower forced expiratory volume in 1 s ($FEV_1$) (98 mL; 95% CI: 54-141 mL) and lower forced vital capacity (FVC) (136 mL; 95% CI: 85-187 mL). Dp-ucMGP was not associated with the $FEV_1$/FVC ratio (0.0 percentage points higher than the expected value; 95% CI: -1.0-1.0). Furthermore, lower vitamin K status was associated with COPD (OR 2.24, 95% CI: 1.53-3.27), wheezing (OR 1.81, 95% CI: 1.44-2.28) and asthma (OR 1.44, 95% CI: 1.12-1.83).

**Conclusion:** Lower vitamin K status was associated with lower ventilatory capacity (lower $FEV_1$ and FVC), and with higher risk of self-reported asthma, COPD and wheezing. Vitamin K status was not associated with airflow obstruction ($FEV_1$/FVC ratio).



# Conflict of interest statement

Conflict of interest: F.B. Kampmann, A. Linneberg and S.M. Thysen have received an unrestricted grant and investigational products from Kappa Bioscience A/S for an

intervention trial (The InterVitaminK Trial; clinicatrials.gov identifier NCT05259046) using vitamin K supplements as the active intervention. Conflict of interest: The other authors declare no other conflicts of interest.

- 42 references
- 3 figures

full text links

Proceed to details

Cite

Share

35

**Review**

Allergy

. 2023 Oct;78(10):2606-2622.

doi: 10.1111/all.15836. Epub 2023 Aug 16.

# An EAACI review: Go green in health care and research. Practical suggestions for sustainability in clinical practice, laboratories, and scientific meetings

Isabella Pali-Schöll[1,2], Kerstin Hermuth-Kleinschmidt[3], Stephanie Dramburg[4], Ioana Agache[5], Hanna Mayerhofer[1,2], Erika Jensen-Jarolim[1,2], Anna Goshua[6], Kari C Nadeau[7]

Affiliations expand

- PMID: 37584433

- DOI: 10.1111/all.15836

**Abstract**

Health care professionals (HCPs) and researchers in the health care sector dedicate their professional life to maintaining and optimizing the health of their patients. To achieve this, significant amounts of resources are used and currently it is estimated that the health care sector contributes to more than 4% of net greenhouse gas (GHG) emissions. GHG emissions adversely impact planetary health and consequently human health, as the two are intricately linked. There are many factors of health care that contribute to these emissions. Hospitals and research labs also use high amounts of consumables which require large amounts of raw materials and energy to produce. They are further responsible for polluting the environment via disposal of plastics, drug products, and other chemicals. To maintain and develop state-of-the-art best practices and treatments, medical experts exchange and update their knowledge on methods and technologies in the respective fields at highly specialized scientific meetings. These meetings necessitate thousands of attendants traveling around the globe. Therefore, while the goal of HCPs is to care for the individual, current practices have an enormous (indirect) impact on the health of the patients by their negative environmental impacts. There is an urgent need for HCPs and researchers to mitigate these detrimental effects. The installation of a sustainability-manager at health care facilities and research organizations to implement sustainable practices while still providing quality health care is desirable. Increased use of telemedicine, virtual/hybrid conferences and green chemistry have recently been observed. The benefits of these practices need to be evaluated and implemented as appropriate. With this manuscript, we aim to increase the awareness about the negative impacts of the health care system (including health care research) on planetary and human health. We suggest some easy and highly impactful steps and encourage health care professionals and research scientists of all hierarchical levels to immediately implement them in their professional as well as private life to counteract the health care sector's detrimental effects on the environment.

**Keywords:** asthma; education; environment; lung diseases; prevention; sustainability.



- 126 references

supplementary info

Publication types, Grants and fundingexpand

full text links

**Editorial**

Am J Respir Crit Care Med

. 2023 Oct 1;208(7):745-746.

doi: 10.1164/rccm.202307-1255ED.

# CC16: A Treatable Trait in Asthma?

Chloe I Bloom[1], Ian M Adcock[1]

Affiliations expand

- PMID: 37582203

- DOI: 10.1164/rccm.202307-1255ED

***No abstract available***

## Comment on

- Circulating CC16 and Asthma: A Population-based, Multicohort Study from Early Childhood through Adult Life.
Voraphani N, Stern DA, Ledford JG, Spangenberg AL, Zhai J, Wright AL, Morgan WJ, Kraft M, Sherrill DL, Curtin JA, Murray CS, Custovic A, Kull I, Hallberg J, Bergström A, Herrera-Luis E, Halonen M, Martinez FD, Simpson A, Melén E, Guerra S.Am J Respir Crit Care Med. 2023 Oct 1;208(7):758-769. doi: 10.1164/rccm.202301-0041OC.PMID: 37523710

supplementary info

Publication typesexpand

full text links

Proceed to details

Cite

Share

37

**Review**

Brain Res Bull

. 2023 Oct 1;202:110727.

doi: 10.1016/j.brainresbull.2023.110727. Epub 2023 Aug 9.

# Brain structural and functional alterations related to anxiety in allergic asthma

Kolsoum Dehdar[1], Mohammad Reza Raoufy[2]

Affiliations expand

- PMID: 37562517

- DOI: 10.1016/j.brainresbull.2023.110727

**Free article**

## Abstract

Psychiatric disorders are common in patients with allergic asthma, and they can have a significant impact on their quality of life and disease control. Recent studies have suggested that there may be potential immune-brain communication mechanisms in asthma, which can activate inflammatory responses in different brain areas, leading to

structural and functional alterations and behavioral changes. However, the precise mechanisms underlying these alterations remain unclear. In this paper, we comprehensively review the relevant research on asthma-induced brain structural and functional alterations that lead to the initiation and promotion of anxiety. We summarize the possible pathways for peripheral inflammation to affect the brain's structure and function. Our review highlights the importance of addressing neuropsychiatric disorders in the clinical guidelines of asthma, to improve the quality of life of these patients. We suggest that a better understanding of the mechanisms underlying psychiatric comorbidities in asthma could lead to the development of more effective treatments for these patients.

**Keywords:** Allergen; Anxiety disorders; Asthma; Brain structural changes, Brain functional alterations.



# Conflict of interest statement

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

. 2023 Oct 1;23(5):364-369.

doi: 10.1097/ACI.0000000000000937. Epub 2023 Jul 25.

# Anaphylaxis due to antiallergic and antiasthmatic biologics

Fabiana Furci[1], Nicoletta Luxi[2], Gianenrico Senna[2,3], Gianluca Trifirò[4]

Affiliations expand

- PMID: 37555938

- DOI: 10.1097/ACI.0000000000000937

**Abstract**

**Purpose of review:** To provide a better understanding of the risk of anaphylaxis due to antiallergic and antiasthmatic biologics through an analysis of data reported in literature and in clinical trials, and by conducting a retrospective descriptive analysis of individual case safety reports on VigiBase, the WHO International Pharmacovigilance database.

**Recent findings:** Analysis of the data, as described, demonstrated safety of the antiallergic and antiasthmatic biologics with a low incidence of anaphylaxis.

**Summary:** Biologic therapies have revolutionized the treatment of many diseases, such as atopic dermatitis, nasal polyps, spontaneous chronic urticarial and severe asthma with a precise immunological action, in the sphere of precision medicine.Albeit these drugs are generally well tolerated, generating real-world evidence is crucial to re-evaluate clinically relevant adverse events, such as anaphylaxis, allowing to confirm their safety profile in particular in special populations such as paediatric patients.



- 39 references

## supplementary info

Publication types, MeSH terms, Substancesexpand

## full text links

Allergy

. 2023 Oct;78(10):2712-2723.

doi: 10.1111/all.15844. Epub 2023 Aug 7.

# Dupilumab-induced eosinophilia in patients with diffuse type 2 chronic rhinosinusitis

Fabio S Ryser[1,2], Ayla Yalamanoglu[3], Alan Valaperti[3], Catrin Brühlmann[4], Tina Mauthe[4], Stephan Traidl[5,6,7], Michael B Soyka[4], Urs C Steiner[1,8]

Affiliations expand

- PMID: 37548395

- DOI: 10.1111/all.15844

**Free article**

**Abstract**

**Background:** Dupilumab, a monoclonal anti-IL-4Rα antibody, is approved for several type 2 mediated inflammatory diseases like asthma, atopic dermatitis, and diffuse type 2 chronic rhinosinusitis (CRS). Clinical studies had reported a transient increase in blood eosinophils during dupilumab therapy. This study aimed to assess the impact of elevated blood eosinophils on clinical outcome and to investigate the cause of high blood eosinophil levels under dupilumab therapy.

**Methods:** Patients suffering from diffuse type 2 CRS treated with dupilumab were examined on days 0, 28, 90, and 180 after therapy start. Sino-Nasal-Outcome-Test Score (SNOT-22), Total Nasal Polyp Score (TNPS), and blood samples were collected. Cytokine

measurements and proteomics analysis were conducted. Flow cytometry analysis measured receptor expression on eosinophils.

**Results:** Sixty-eighty patients were included. Baseline eosinophilia ≥0.3G/L was observed in 63.2% of patients, and in 30.9% of patients, eosinophils increased by ≥0.5G/L under dupilumab. Subjects with eosinophilia ≥0.3G/L at baseline had the best SNOT-22 mean change compared to no eosinophilia. Eosinophil elevation during dupilumab therapy had no impact on clinical scores. The eosinophil adhesion molecule VCAM-1 decreased significantly during therapy in all patients. The chemokine receptor CXCR4 was significantly down- and IL-4 upregulated in subjects with eosinophil increase.

**Conclusion:** Our findings suggest that increased eosinophils in type 2 CRS are associated with a good clinical response to dupilumab. Patients with elevated IL-4 at baseline developed dupilumab-induced transient eosinophilia. We identified the downregulation of VCAM-1 and surface markers CD49d and CXCR4 on eosinophils as possible explanations of dupilumab-induced eosinophilia.

**Keywords:** Interleukin-4; VCAM-1; diffuse type 2 chronic rhinosinusitis; dupilumab; eosinophilia.



- 62 references

full text links

Proceed to details

Cite

Share

40

**Review**

Allergol Int

- 
- 
- 

. 2023 Oct;72(4):493-506.

doi: 10.1016/j.alit.2023.07.003. Epub 2023 Aug 4.

# Poorly controlled asthma - Easy wins and future prospects for addressing fungal allergy

David W Denning[1], Lorraine T Pfavayi[2]

Affiliations expand

- PMID: 37544851

- DOI: 10.1016/j.alit.2023.07.003

**Abstract**

Poorly controlled asthma is especially common in low resource countries. Aside from lack of access to, or poor technique with, inhaled beta-2 agonists and corticosteroids, the most problematic forms of asthma are frequently associated with both fungal allergy and exposure, especially in adults leading to more asthma exacerbations and worse asthma. The umbrella term 'fungal asthma' describes many disorders linked to fungal exposure and/or allergy to fungi. One fungal asthma endotype, ABPA, is usually marked by a very high IgE and its differential diagnosis is reviewed. Both ABPA and fungal bronchitis in bronchiectasis are marked by thick excess airway mucus production. Dermatophyte skin infection can worsen asthma and eradication of the skin infection improves asthma. Exposure to fungi in the workplace, home and schools, often in damp or water-damaged buildings worsens asthma, and remediation improves symptom control and reduces exacerbations. Antifungal therapy is beneficial for fungal asthma as demonstrated in nine of 13 randomised controlled studies, reducing symptoms, corticosteroid need and exacerbations while improving lung function. Other useful therapies include azithromycin and some biologics approved for the treatment of severe asthma. If all individuals with poorly controlled and severe asthma could be 'relieved' of their fungal allergy and infection through antifungal therapy without systemic corticosteroids, the health benefits would be enormous and relatively inexpensive, improving the long term health of over 20 million adults and many children. Antifungal therapy carries some toxicity, drug interactions and triazole resistance risks, and data are incomplete. Here we summarise what is known and what remains uncertain about this complex topic.

**Keywords:** Antifungal; Aspergillosis; Aspergillus; Bronchitis; IgE.

supplementary info

Publication typesexpand

full text links

Proceed to details

Cite

Share

41

**Review**

Respir Physiol Neurobiol

. 2023 Oct;316:104135.

doi: 10.1016/j.resp.2023.104135. Epub 2023 Aug 2.

# Window of opportunity for respiratory oscillometry: A review of recent research

Sabina Kostorz-Nosal[1], Dariusz Jastrzębski[2], Anna Błach[3], Szymon Skoczyński[2]

Affiliations expand

- PMID: 37536553

- DOI: 10.1016/j.resp.2023.104135

**Free article**

## Abstract

Oscillometry has been around for almost 70 years, but there are still many unknowns. The test is performed during tidal breathing and is therefore free from patient-dependent

factors that could influence the results. The Forced Oscillation Technique (FOT), which requires minimal patient cooperation, is gaining ground, particularly with elderly patients and children. In pulmonology, it is a valuable tool for assessing obstructive conditions (with a distinction between central and peripheral obstruction) and restrictive disorders (intrapulmonary and extrapulmonary). Its sensitivity allows the assessment of bronchodilator and bronchoconstrictor responses. Different lung diseases show different patterns of changes in FOT, especially studied in asthma and chronic obstructive pulmonary disease. Because of these differences, many studies have analysed the usefulness of this technique in different areas of medicine. In this paper, the authors would like to present the basics of oscillometry with the areas of its most recent clinical applications.

**Keywords:** Forced oscillation technique; Impulse oscillometry; Lung function; Spirometry.



# Conflict of interest statement

Declaration of Competing Interest There are no conflicts of interest to report for any authors.



Am J Respir Crit Care Med

. 2023 Oct 1;208(7):758-769.

doi: 10.1164/rccm.202301-0041OC.

# Circulating CC16 and Asthma: A Population-based, Multicohort Study from Early Childhood through Adult Life

Nipasiri Voraphani[1], Debra A Stern[1], Julie G Ledford[1], Amber L Spangenberg[1], Jing Zhai[1], Anne L Wright[1], Wayne J Morgan[1], Monica Kraft[1], Duane L Sherrill[1], John A Curtin[2,3], Clare S Murray[2,3], Adnan Custovic[4], Inger Kull[5,6], Jenny Hallberg[5,6], Anna Bergström[7], Esther Herrera-Luis[8], Marilyn Halonen[1], Fernando D Martinez[1], Angela Simpson[2,3], Erik Melén[5,6], Stefano Guerra[1]

Affiliations expand

- PMID: 37523710

- DOI: 10.1164/rccm.202301-0041OC

**Abstract**

**Rationale:** Club cell secretory protein (CC16) is an antiinflammatory protein highly expressed in the airways. CC16 deficiency has been associated with lung function deficits, but its role in asthma has not been established conclusively. **Objectives:** To determine *1*) the longitudinal association of circulating CC16 with the presence of active asthma from early childhood through adult life and *2*) whether CC16 in early childhood predicts the clinical course of childhood asthma into adult life. **Methods:** We assessed the association of circulating CC16 and asthma in three population-based birth cohorts: the Tucson Children's Respiratory Study (years 6-36; total participants, 814; total observations, 3,042), the Swedish Barn/Children, Allergy, Milieu, Stockholm, Epidemiological survey (years 8-24; total participants, 2,547; total observations, 3,438), and the UK Manchester Asthma and Allergy Study (years 5-18; total participants, 745; total observations, 1,626). Among 233 children who had asthma at the first survey in any of the cohorts, baseline CC16 was also tested for association with persistence of symptoms. **Measurements and Main Results:** After adjusting for covariates, CC16 deficits were associated with increased risk for the presence of asthma in all cohorts (meta-analyzed adjusted odds ratio per 1-SD CC16 decrease, 1.20; 95% confidence interval [CI], 1.12-1.28; $P < 0.0001$). The association was particularly strong for asthma with frequent symptoms (meta-analyzed adjusted relative risk ratio, 1.40; 95% CI, 1.24-1.57; $P < 0.0001$), was confirmed for both atopic and nonatopic asthma, and was independent of lung function impairment. After adjustment for known predictors of persistent asthma, children with asthma in the lowest CC16 tertile had a nearly fourfold increased risk for having frequent symptoms persisting into adult life compared with children with asthma in the other two CC16 tertiles (meta-analyzed adjusted odds ratio, 3.72; 95% CI, 1.78-7.76; $P < 0.0001$). **Conclusions:** Circulating CC16 deficits are associated with the presence of asthma with frequent symptoms from childhood through midadult life and predict the persistence of asthma symptoms into

adulthood. These findings support a possible protective role of CC16 in asthma and its potential use for risk stratification.

**Keywords:** CC16; asthma; birth cohorts.

## Comment in

- CC16: A Treatable Trait in Asthma?
  Bloom CI, Adcock IM.Am J Respir Crit Care Med. 2023 Oct 1;208(7):745-746. doi: 10.1164/rccm.202307-1255ED.PMID: 37582203 No abstract available.

supplementary info

Grants and fundingexpand

full text links

Proceed to details

Cite

Share

43

Rev Clin Esp (Barc)

. 2023 Oct;223(8):479-485.

doi: 10.1016/j.rceng.2023.07.006. Epub 2023 Jul 21.

# Impact of N-Acetylcysteine in the mortality of patients hospitalized with COVID-19: a retrospective cohort study

M A Galindo-Andúgar[1], Á Arias Arias[2], J Alfonso García Guerra[3], I Fernández Visier[4], J Manuel Fernández Ibáñez[5], A Bellido Maldonado[3]

Affiliations expand

- PMID: 37482215

- DOI: 10.1016/j.rceng.2023.07.006

**Abstract**

**Introduction and aim:** N-Acetylcysteine has been proposed for the treatment of COVID-19 thanks to its mucolytic, antioxidant and anti-inflammatory effects. Our aim is to evaluate its effect on patients admitted with COVID-19 in mortality terms.

**Material and methods:** Retrospective single-center cohort study. All patients admitted to our hospital for COVID-19 from March to April 2020 have been considered.

**Results:** A total of 378 patients were included, being 196 (51.9%) men, with an average age of 73.3±14.5 years. 52.6% (199) received treatment with N-Acetylcysteine. More than 70% presented coughs, fever, and/or dyspnea. The global hospital mortality was 26.7%. A multivariate analysis through logistic regression identified the age of patients [older than 80; OR: 8.4 (CI95%:3-23.4)], a moderate or severe radiologic affectation measured by the RALE score [OR:7.3 (CI95%:3.2-16.9)], the tobacco consumption [OR:2.8 (CI95%:1.3-6.1)] and previous arrhythmia [OR 2.8 (CI95%: 1.3-6.2)] as risk factor that were independently associated with mortality during the admission. The treatment with N-Acetylcysteine was identified as a protective factor [OR: 0.57 (CI95%: 0.31-0.99)]. Asthma also seems to have a certain protective factor although it was not statistically significant in our study [OR: 0.19 (CI95%: 0.03-1.06)].

**Conclusions:** Patients with COVID-19 treated with N-acetylcysteine have presented a lower mortality and a better evolution in this study. Future prospective studies or randomized clinical trials must confirm the impact of N-Acetylcysteine on COVID-19 patients.

**Keywords:** COVID-19; Hospital mortality; Mortalidad hospitalaria; N-Acetilcisteína; N-Acetylcysteine; SARS-CoV-2.



## supplementary info

MeSH terms, Substancesexpand

## full text links

Proceed to details

**Observational Study**

Respir Med

- 
- 
- 

. 2023 Oct;217:107365.

doi: 10.1016/j.rmed.2023.107365. Epub 2023 Jul 21.

# Asthma exacerbations in New Zealand 2010-2019: A national population-based study

Amy Hai Yan Chan[1], Andrew Tomlin[2], Kebede Beyene[3], Jeff Harrison[2]

Affiliations expand

- PMID: 37481169

- DOI: 10.1016/j.rmed.2023.107365

**Free article**

## Abstract

**Introduction:** Asthma is one of the most common long-term conditions in the world, with New Zealand (NZ) having one of the highest rates of asthma symptoms. Despite the significant burden of asthma in NZ, there is a lack of data on asthma exacerbation rates in NZ and how these have varied over time. This study is a national population-based study of asthma exacerbation rates in NZ between 2010 and 2019, and explores how these rates vary amongst different demographic groups.

**Methods:** A retrospective population-based observational cohort study covering the ten years 2010-2019 to determine asthma prevalence, and asthma exacerbation and hospitalisation rates, using de-identified data from five national healthcare datasets.

Exacerbations were defined based on hospital discharge diagnoses or oral corticosteroid dispensing.

**Results:** Total number of patients with asthma was 447,797 in 2010 to 512,627 in 2019, equating to approximately 10% of the population. Of these 19.4% experienced an exacerbation in 2010 (a population rate of 376.2 per 1000 patient-years); this exacerbation rate increased to 25.1% in 2019 (438.3 per 1000 patient-years). Exacerbations rates were consistently higher for females than males, and among Pacific peoples and Māori. In contrast, hospital admissions 25% lower in 2019 than 2010, decreasing from 1.4% to 0.9%, however over 50% of these admissions were in Māori and Pacific peoples.

**Conclusion:** Asthma exacerbation rates in NZ have increased over 2010-2019, however hospitalisation rates have decreased. This potentially suggests a move away from secondary to primary care management of exacerbations and provides important information for asthma care planning.

**Keywords:** Asthma; Descriptive; Epidemiology; Exacerbation; Hospitalisation; Population; Prevalence.



# Conflict of interest statement

Declaration of competing interest AC, KB and JH have received research funding from Health Research Council for work related to asthma. AC is also affiliated with Asthma UK Centre of Applied research, the recipient of the Auckland Medical Research Foundation Senior Research Fellowship and on the board of Asthma NZ. AC is a member of Respiratory Effectiveness Group and international member of the Pharmacy Respiratory Task Force. All other authors declare no relevant conflicts of interest.

**Review**

Curr Allergy Asthma Rep

.
. 2023 Oct;23(10):579-587.

doi: 10.1007/s11882-023-01103-z. Epub 2023 Jul 15.

# Occupational Rhinitis: An Update

Jose Zamora-Sifuentes[1], Jill A Poole[2]

Affiliations expand

- PMID: 37452992

- DOI: 10.1007/s11882-023-01103-z

**Abstract**

**Purpose of review:** Occupational rhinitis is an underdiagnosed disease with significant morbidity and implications in the workplace. Multiple factors associated with this disease continue to pose a challenge to investigators. This review aims to summarize recent literature in occupational rhinitis, including classifications, pathogenesis, diagnosis, and treatment, as well as the impact of occupational rhinitis on individuals. Additionally, it identifies areas in need of further research and investigation.

**Recent findings:** We highlight current research on the association between occupational rhinitis and occupational asthma and the role of immunotherapy in this disease. Discussion includes the impact of social trends on workers and the wider consequences of occupational rhinitis including decreased work productivity, absenteeism, and socioeconomic burden. Occupational rhinitis remains a challenging disease entity due to the numerous potential causative factors, reduced recognition, morbidity in asthma, and therapeutic limitations. Additional research is needed to better identify disease predictors and develop effective management strategies.

**Keywords:** Occupational asthma; Occupational disease; Occupational rhinitis; Work-related rhinitis.

- 52 references

supplementary info

Publication types, MeSH terms, Grants and fundingexpand

full text links

Proceed to details

Cite

Share

46

**Review**

Eur Respir Rev

. 2023 Jul 12;32(169):230036.

doi: 10.1183/16000617.0036-2023. Print 2023 Sep 30.

# Natural killer cells in the lung: potential role in asthma and virus-induced exacerbation?

Florian Lepretre[1], Delphine Gras[1], Pascal Chanez[1,2], Catherine Duez[3]

Affiliations expand

- PMID: 37437915

- PMCID: PMC10336552

- DOI: 10.1183/16000617.0036-2023

**Free PMC article**

**Abstract**

Asthma is a chronic inflammatory airway disorder whose pathophysiological and immunological mechanisms are not completely understood. Asthma exacerbations are mostly driven by respiratory viral infections and characterised by worsening of symptoms. Despite current therapies, asthma exacerbations can still be life-threatening. Natural killer (NK) cells are innate lymphoid cells well known for their antiviral activity and are present in the lung as circulating and resident cells. However, their functions in asthma and its exacerbations are still unclear. In this review, we will address NK cell activation and functions, which are particularly relevant for asthma and virus-induced asthma exacerbations. Then, the role of NK cells in the lungs at homeostasis in healthy individuals will be described, as well as their functions during pulmonary viral infections, with an emphasis on those associated with asthma exacerbations. Finally, we will discuss the involvement of NK cells in asthma and virus-induced exacerbations and examine the effect of asthma treatments on NK cells.



# Conflict of interest statement

Conflict of interest: C. Duez reports grants from Société Française d'allergologie and Fondation du Souffle outside the submitted work. Conflict of interest: P. Chanez reports grants, consultancy fees, lecture fees, travel support and advisory board participation from ALK, Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Menarini, Novartis and Sanofi-Aventis, outside the submitted work. All other authors have nothing to disclose.

- 146 references
- 2 figures

supplementary info

Publication types, MeSH terms, Supplementary conceptsexpand

full text links

Proceed to details

Cite

47

Respirology

- 
- 
- 

. 2023 Oct;28(10):942-953.

doi: 10.1111/resp.14553. Epub 2023 Jul 11.

# Supranormal lung function: Prevalence, associated factors and clinical manifestations across the lifespan

Caspar Schiffers[1], Rosa Faner[2,3,4], Alina Ofenheimer[1,5], Owat Sunanta[1], Patricia Puchhammer[1], Tobias Mraz[1,6], Marie-Kathrin Breyer[1,6], Otto Chris Burghuber[1,7], Sylvia Hartl[1,6,7], Alvar Agustí[2,3,4,8], Robab Breyer-Kohansal[1,6]

Affiliations expand

- PMID: 37434280

- DOI: 10.1111/resp.14553

**Abstract**

**Background and objective:** It is now well established that there are different life-long lung function trajectories in the general population, and that some are associated with better or worse health outcomes. Yet, the prevalence, clinical characteristics and risk factors of individuals with supranormal $FEV_1$ or FVC values (above the upper-limit of normal [ULN]) in different age-bins through the lifetime in the general population are poorly understood.

**Method:** To address these questions, we investigated the prevalence of supranormal $FEV_1$ and FVC values in the LEAD (Lung, hEart, sociAl and boDy) study, a general population cohort in Austria that includes participants from 6 to 82 years of age.

**Results:** We found that: (1) the prevalence of supranormal pre-bronchodilator $FEV_1$ and FVC values was 3.4% and 3.1%, respectively, and that these figures remained relatively stable through different age-bins except for participants >60 years., in whom they increased (5.0% and 4.2%, respectively). Approximately 50% of supranormal individuals had both increased $FEV_1$ and FVC values; (2) supranormal spirometric values were consistently accompanied by higher static lung volumes and lower specific airway resistance through

the lifespan, indicating better overall lung function; and (3) multivariate regression analysis identified that female sex, higher muscle mass (FFMI), less diabetes and fewer respiratory symptoms were consistently associated with supranormal $FEV_1$ and FVC values.

**Conclusion:** Supranormal $FEV_1$ and/or FVC values occur in about 3% of the general population in different age bins and are associated with better health markers.

**Keywords:** COPD; asthma; chronic obstructive pulmonary disease; diabetes; lung function trajectories; lung health; smoking; spirometry.



- 25 references

supplementary info

MeSH terms, Grants and fundingexpand

full text links

Proceed to details

Cite

Share

48

Arch Dis Child

- 
- 
- 

. 2023 Oct;108(10):839-845.

doi: 10.1136/archdischild-2022-325137. Epub 2023 Jul 10.

# Discharge criteria for inpatient paediatric asthma: a narrative systematic review

Aryanto Sudarmana[1], Joanna Lawrence[2,3,4], Neda So[5], Katherine Chen[5,3,4]

Affiliations expand

- PMID: 37429700

- DOI: 10.1136/archdischild-2022-325137

**Abstract**

**Introduction:** Criteria-led discharges (CLDs) and inpatient care pathways (ICPs) aim to standardise care and improve efficiency by allowing patients to be discharged on fulfilment of discharge criteria. This narrative systematic review aims to summarise the evidence for use of CLDs and discharge criteria in ICPs for paediatric inpatients with asthma, and summarise the evidence for each discharge criterion used.

**Methods:** Database search using keywords was performed using Medline, Embase and PubMed for studies published until 9 June 2022. Inclusion criteria included: paediatric patients <18 years old, admitted to hospital with asthma or wheeze and use of CLD, nurse-led discharge or ICP. Reviewers screened studies, extracted data and assessed study quality using the Quality Assessment with Diverse Studies tool. Results were tabulated. Meta-analysis was not performed due to heterogeneity of study designs and outcomes.

**Results:** Database search identified 2478 studies. 17 studies met the inclusion criteria. Common discharge criteria include bronchodilator frequency, oxygen saturation and respiratory assessment. Discharge criteria definitions varied between studies. Most definitions were associated with improvements in length of stay (LOS) without increasing re-presentation or readmission.

**Conclusion:** CLDs and ICPs in the care of paediatric inpatients with asthma are associated with improvements in LOS without increasing re-presentations or readmissions. Discharge criteria lack consensus and evidence base. Common criteria include bronchodilator frequency, oxygen saturations and respiratory assessment. This study was limited by a paucity of high-quality studies and exclusion of studies not published in English. Further research is necessary to identify optimal definitions for each discharge criterion.

**Keywords:** Child Health; Health Care Economics and Organizations; Paediatrics; Respiratory Medicine.



# Conflict of interest statement

Competing interests: None declared.

supplementary info

Publication types, MeSH terms, Substancesexpand

full text links

Proceed to details

Cite

Share

49

Respir Med

- 
- 
- 

. 2023 Oct;217:107341.

doi: 10.1016/j.rmed.2023.107341. Epub 2023 Jul 8.

# Effect of bronchial thermoplasty on static and dynamic lung compliance and resistance in patients with severe persistent asthma

Ahmet Baydur[1], Richard Barbers[2], Darren May[2]

Affiliations expand

- PMID: 37429559

- DOI: 10.1016/j.rmed.2023.107341

**Abstract**

**Rationale:** Bronchial thermoplasty (BT) reduces severity and frequency of bronchoconstriction and symptoms in severe, persistent asthmatics although it is usually not associated with change in spirometric variables. Other than spirometry. there are almost no data on changes in lung mechanics following BT.

**Objective:** To assess lung static and dynamic lung compliance (Cst,L and Cdyn,L, respectively) and static and dynamic lung resistance (Rst,L and Rdyn,L, respectively) before and after BT in severe asthmatics using the esophageal balloon technique.

**Methods:** Rdyn,L and Cdyn,L were measured at respiratory frequencies up to 145 breaths/min, using the esophageal balloon technique in 7 patients immediately before and 12-50 weeks after completing a series of 3 BT sessions.

**Results:** All patients experienced improved symptoms within a few weeks following completion of BT. Pre-BT, all patients exhibited frequency dependency of lung compliance, with mean Cdyn,L decreasing to 63% of Cst,L at maximum respiratory rates. Post-BT, Cst,L did not change significantly from pre-thermoplasty values, while Cdyn,L diminished to 62%% of Cst,L. In 4 of 7 patients, post-BT values of Cdyn,L were consistently higher than pre-BT over the range of respiratory rates. $R_L$ in 4 of 7 patients during quiet breathing and at higher respiratory frequencies decreased following BT.

**Conclusions:** Patients with severe persistent asthma exhibit increased resting lung resistance and frequency dependence of compliance, the magnitudes of which are ameliorated in some patients following bronchial thermoplasty and associated with variable change in frequency dependence of lung resistance. These findings are related to asthma severity and may be related to the heterogeneous and variable nature of airway smooth muscle modeling and its response to BT.

**Keywords:** Airway smooth muscle remodeling; Asthma; Bronchial thermoplasty; Esophageal balloon technique; Frequency dependence of compliance and resistance; Regional lung inhomogeneities.



# Conflict of interest statement

Declaration of competing interest None

50

Respir Med

- 
- 
- 

. 2023 Oct;217:107349.

doi: 10.1016/j.rmed.2023.107349. Epub 2023 Jul 7.

# Home-based pulmonary rehabilitation for adults with severe asthma exposed to psychosocial chronic stressors

Sarah Gephine[1], Stéphanie Fry[2], Emilie Margoline[2], Alice Gicquello[3], Cécile Chenivesse[4], Jean-Marie Grosbois[5]

Affiliations expand

- PMID: 37423480

- DOI: 10.1016/j.rmed.2023.107349

**Abstract**

**Objective:** To evaluate the effects of a home-based pulmonary rehabilitation (PR) programme on hyperventilation symptoms, anxiety and depressive symptoms, general fatigue, health-related quality of life (HRQoL) and exercise capacity in adults with severe asthma who have been exposed to psychosocial chronic stressors.

**Methods:** Data on 111 non-selected consecutive adults with severe asthma who enrolled in an 8-week home-based PR programme (weekly supervised 90-min session) was retrospectively analysed. Chronic stressors included physical, sexual and psychological violence and/or a traumatic experience related to an intensive care unit stay. Hyperventilation symptoms (Nijmegen questionnaire), Hospital Anxiety and Depression Scale, Fatigue Assessment Scale, COPD Assessment Test, Six-Minute Stepper Test and Timed-Up and Go test were assessed at baseline and after PR.

**Results:** At baseline, participants who have been exposed to chronic stressors (n = 48, 43.2%) were younger, more often female, more often treated for anxiety and depressive disorders, and had a higher score for anxiety symptoms, hyperventilation symptoms and a poorer HRQoL, compared to those who had not been exposed to chronic stressors (p <

0.05). All the study assessments were statistically improved after PR for both groups ($p < 0.001$). Anxiety and depressive symptoms, fatigue and health-related quality of life questionnaires were also clinically improved based on the minimal clinically important difference.

**Conclusion:** A large proportion of adults with severe asthma, mainly women, have been exposed to chronic stressors at the time of starting a PR programme, resulting in higher anxiety symptoms and hyperventilation symptoms. However, it did not prevent these individuals from benefiting from PR.

**Keywords:** Hyperventilation; Pulmonary rehabilitation; Severe asthma; Traumatic experience; Violence.



# Conflict of interest statement

Declaration of competing interest SG and EM has nothing to disclose. JMG reports personal fees and non-financial support unrelated to the submitted work from AstraZeneca, Boehringer Ingelheim, Chiesi, CSL Behring, GlaxoSmithKlein. AG reports personal fees and non-financial support unrelated to the submitted work from Sysmed, GlaxoSmithKlein, AstraZeneca, Sanofi, Thermo Ficher and Lowenstein. SF reports personal fees and non-financial support unrelated to the submitted work from AstraZeneca, Sanofi, GlaxoSmithKlein, Santelys, Vitalaire. CC reports personal fees and non-financial support unrelated to the submitted work from ALK-Abello, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKlein, MEDA Pharma, Medexact, Novartis, Pierre Fabre, Pfizer, Roche, Sanofi, Santélys, and TEVA.

. 2023 Oct;217:107348.

doi: 10.1016/j.rmed.2023.107348. Epub 2023 Jul 6.

# Severe asthma clinical remission after biologic treatment with anti-IL4/IL13: A real-life experience

Andrea Portacci[1], Ilaria Iorillo[2], Vitaliano Nicola Quaranta[3], Leonardo Maselli[4], Ernesto Lulaj[5], Enrico Buonamico[6], Silvano Dragonieri[7], Giovanna Elisiana Carpagnano[8]

Affiliations expand

- PMID: 37422023

- DOI: 10.1016/j.rmed.2023.107348

**Abstract**

**Introduction:** Dupilumab, a fully human anti-interleukin-4/interleukin-13 monoclonal antibody, has shown efficacy in many aspects of Type-2 severe asthma management. Currently, we lack real-life studies addressing the achievment of clinical remission in patients treated with this biologic.

**Materials and methods:** We performed a prospective study enrolling 18 patients with severe asthma treated with Dupilumab. We assessed main clinical, functional and biological severe asthma features at baseline (T0) and after a 1-year course of treatment (T12). Clinical remission was defined at T12 in patients without asthma exacerbations, no oral corticosteroid (OCS) use, ACT ≥ 20 and FEV1 improvement ≥ 100 ml from baseline.

**Results:** Among total population, 38.9% of patients achieved clinical remission at T12. Anti IL-4/IL-13 treatment significantly reduced asthma exacerbations and OCS use in the overall cohort, with a more pronounced ACT improvement in the remission group. Patients achieving clinical remission went through a step down of the inhalation therapy, suspending long-acting anti-muscarinics administration at T12.

**Conclusions:** Treatment with anti-IL4/IL13 can induce clinical remission in patients with T2 severe asthma.

**Keywords:** Dupilumab; Eosinophil; FeNO; Remission; Severe asthma.

## 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: Giovanna Elisiana Carpagnano reports a relationship with University of Bari that includes: speaking and lecture fees and travel reimbursement. Silvano Dragonieri reports a relationship with University of Bari that includes: speaking and lecture fees. Andrea Portacci reports a relationship with University of Bari that includes: board membership, speaking and lecture fees, and travel reimbursement. Enrico Buonamico reports a relationship with University of Bari that includes: speaking and lecture fees.



52

Respir Med

. 2023 Oct;217:107340.

doi: 10.1016/j.rmed.2023.107340. Epub 2023 Jul 7.

# Bronchial thermoplasty attenuates bronchodilator responsiveness

Cyndi Henry[1], Sabrina Biardel[1], Magali Boucher[1], Krystelle Godbout[1], Jamila Chakir[1], Andréanne Côté[1], Michel Laviolette[1], Ynuk Bossé[2]

Affiliations expand

- PMID: 37422022

- DOI: 10.1016/j.rmed.2023.107340

**Free article**

**Abstract**

**Introduction:** Bronchial thermoplasty is an effective intervention to improve respiratory symptoms and to reduce the rate of exacerbations in uncontrolled severe asthma. A reduction in airway smooth muscle is arguably the most widely discussed mechanisms accounting for these clinical benefits. Yet, this smooth muscle reduction should also translate into an impaired response to bronchodilator drugs. This study was designed to address this question.

**Methods:** Eight patients with clinical indication for thermoplasty were studied. They were uncontrolled severe asthmatics despite optimal environmental control, treatment of comorbidities, and the use of high-dose inhaled corticosteroids and long-acting $\beta_2$-agonists. Lung function measured by spirometry and respiratory mechanics measured by oscillometry were examined pre- and post-bronchodilator (salbutamol, 400 μg), both before and at least 1 year after thermoplasty.

**Results:** Consistent with previous studies, thermoplasty yielded no benefits in terms of baseline lung function and respiratory mechanics, despite improving symptoms based on two asthma questionnaires (ACQ-5 and ACT-5). The response to salbutamol was also not affected by thermoplasty based on spirometric readouts, including forced expiratory volume in 1 s ($FEV_1$), forced vital capacity (FVC), and $FEV_1$/FVC ratio. However, a significant interaction was observed between thermoplasty and salbutamol for two oscillometric readouts, namely reactance at 5 Hz ($X_{rs5}$) and reactance area (Ax), showing an attenuated response to salbutamol after thermoplasty.

**Conclusions:** Thermoplasty attenuates the response to a bronchodilator. We argue that this result is a physiological proof of therapeutic efficacy, consistent with the well-described effect of thermoplasty in reducing the amount of airway smooth muscle.

**Keywords:** Airway smooth muscle; Asthma drugs; Oscillometry; Reactance; Uncontrolled asthma.



# Conflict of interest statement

Declaration of competing interest YB's laboratory received funds from Boston Scientific Inc (25800$) to conduct this project. AC is funded partially by GlaxoSmithKline, and has

53

**Observational Study**

Pulm Pharmacol Ther

. 2023 Oct;82:102231.

doi: 10.1016/j.pupt.2023.102231. Epub 2023 Jul 4.

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

Paola Rogliani[1], Dejan Radovanovic[2], Josuel Ora[3], Nadia Starc[3], Stefano Verri[3], Elena Pistocchini[3], Luigino Calzetta[4]

Affiliations expand

- PMID: 37414133

- DOI: 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 ≥22 pulmonary centres in Italy and that enrols ≥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.



# Conflict of interest statement

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

**Review**

Pediatr Pulmonol

. 2023 Oct;58(10):2703-2718.

doi: 10.1002/ppul.26584. Epub 2023 Jul 5.

# Composite predictive models for asthma exacerbations or asthma deterioration in pediatric asthmatic patients: A systematic review of the literature

Carlos E Rodríguez-Martínez[1,2], Monica P Sossa-Briceño[3], Erick Forno[4]

Affiliations expand

- PMID: 37403820

- DOI: 10.1002/ppul.26584

**Abstract**

A variety of factors have shown to be useful in predicting which children are at high risk for future asthma exacerbations, some of them combined into composite predictive models. The objective of the present review was to systematically identify all the available published composite predictive models developed for predicting which children are at high risk for future asthma exacerbations or asthma deterioration. A systematic search of the literature was performed to identify studies in which a composite predictive model developed for predicting which children are at high risk for future asthma exacerbations or asthma deterioration was described. Methodological quality assessment was performed using accepted criteria for prediction rules and prognostic models. A total of 18 articles, describing a total of 17 composite predictive models were identified and included in the review. The number of predictors included in the models ranged from 2-149. Upon

analyzing the content of the models, use of healthcare services for asthma and prescribed or dispensed asthma medications were the most frequently used items (in 8/17, 47.0% of the models). Seven (41.2%) models fulfilled all the quality criteria considered in our evaluation. The identified models may help clinicians dealing with asthmatic children to identify which children are at a higher risk for future asthma exacerbations or asthma deterioration, therefore targeting and/or reinforcing specific interventions for these children in an attempt to prevent exacerbations or deterioration of the disease.

**Keywords:** asthma deterioration; asthma exacerbations; composite predictive models; prediction ability; validation.



- 34 references

supplementary info

Publication types, MeSH terms, Substancesexpand

full text links

Proceed to details

Cite

Share

55

Respir Med

. 2023 Oct;217:107334.

doi: 10.1016/j.rmed.2023.107334. Epub 2023 Jun 29.

# Efficacy of mometasone/indacaterol/glycopyrronium in patients with inadequately controlled asthma with respect to baseline

# eosinophil count: Post hoc analysis of IRIDIUM study

Konstantinos Kostikas[1], Jorge F Maspero[2], Kenneth R Chapman[3], Karen Mezzi[4], Xavier Jaumont[4], David Lawrence[4], Richard van Zyl-Smit[5]

Affiliations expand

- PMID: 37392789

- DOI: 10.1016/j.rmed.2023.107334

**Free article**

## Abstract

**Background:** Baseline characteristics could potentially guide asthma treatments. We evaluated whether baseline eosinophil levels affect the efficacy of mometasone/indacaterol/glycopyrronium (MF/IND/GLY) in patients with inadequately controlled asthma.

**Method:** In this post hoc analysis of IRIDIUM study, efficacy of high-dose MF/IND/GLY (160/150/50 µg, once-daily [o.d.]) versus high-dose MF/IND (320/150 µg o.d.) and high-dose fluticasone/salmeterol (FLU/SAL [500/50 µg, twice-daily [b.i.d.]); and efficacy of pooled MF/IND/GLY (160/150/50 µg and 80/150/50 µg) versus pooled MF/IND (320/150 µg and 160/150 µg) was evaluated in patient subgroups with baseline blood eosinophil count of <300 cells/µL or ≥300 cells/µL.

**Results:** Overall, 3065 patients were included. At Week 26, high-dose MF/IND/GLY showed improved trough $FEV_1$ versus high-dose MF/IND (Δ78mL [<300 cells/µL]; Δ54mL [≥300 cells/µL]) and FLU/SAL (Δ112mL [<300 cells/µL]; Δ98mL [≥300 cells/µL]). Similarly, pooled MF/IND/GLY also showed improved trough $FEV_1$ versus pooled MF/IND (Δ75mL [<300 cells/µL]; Δ68mL [≥300 cells/µL]). Over 52 weeks, high-dose MF/IND/GLY reduced the annualized rate of moderate or severe asthma exacerbations by 23% and 10%, severe exacerbations by 31% and 15%, and all exacerbation by 33% and 10% versus high-dose MF/IND for subgroups with <300 cells/µL and ≥300 cells/µL, respectively; and by 33% and 41%, 45% and 42%, 42% and 39% versus FLU/SAL, respectively. Similarly, pooled MF/IND/GLY reduced exacerbations by 22% and 8%, 21% and 7%, 27% and 8%, versus pooled MF/IND, for the respective subgroups.

**Conclusion:** MF/IND/GLY showed improvement in lung function and reduction in asthma exacerbations over MF/IND and FLU/SAL independent of baseline eosinophil levels, indicating that eosinophil levels did not affect the efficacy of MF/IND/GLY in patients with inadequately controlled asthma.

**Trial registration:** ClinicalTrials.gov, NCT02571777 (IRIDIUM).

**Keywords:** Eosinophil; Exacerbations; Glycopyrronium bromide; Indacaterol acetate; Lung function; Mometasone furoate.



# Conflict of interest statement

Declaration of competing interest Konstantinos Kostikas reports honoraria for presentations and consultancy fees from AstraZeneca, Boehringer Ingelheim, CSL Behring, Chiesi, ELPEN, GILEAD, GSK, Menarini, Novartis, Sanofi, Specialty Therapeutics, WebMD (paid to the University of Ioannina), is a member of the GOLD Assembly and was an employee of Novartis Pharma AG until October 31, 2018; his department received funding and grants from AstraZeneca, Boehringer Ingelheim, Chiesi, Innovis, ELPEN, GSK, Menarini, Novartis and NuvoAir (paid to the University of Ioannina). Jorge F. Maspero reports grants and personal fees from Novartis during the conduct of the study, grants and personal fees from Sanofi, and personal fees from AstraZeneca and ImmunoTek. Kenneth R. Chapman reports grants and personal fees from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Grifols, Novartis, Regeneron, Sanofi, and Takeda, grants from Vertex, and personal fees from CSL Behring, Inhibrx, and Kamada, all outside of the submitted work. Richard van Zyl-Smit reports personal fees from Aspen–GSK, AstraZeneca, Cipla, Merck Sharp & Dohme, Novartis, Pfizer, and Roche, Glenmark and Boehringer Ingelheim outside of the submitted work. Karen Mezzi, Xavier Jaumont are employees of Novartis. David Lawrence is an employee as well as share owner of Novartis.

. 2023 Oct;78(10):2774-2777.

doi: 10.1111/all.15785. Epub 2023 Jun 21.

# Epidemiology of sensitization to perennial aeroallergens in adults with severe asthma in Belgium. The BEIgE study

Florence Schleich[1], Eléonore Maury[2], Claus Bachert[3], Shane Hanon[4], Olivier Michel[5], Mieke Jansen[2], Sandra Gurdain[2], Jan Van Schoor[2]; Belgian IgE (BEIgE) Study Investigators

Collaborators, Affiliations expand

- PMID: 37340902

- DOI: 10.1111/all.15785

***No abstract available***

- 6 references

supplementary info

Publication types, Grants and fundingexpand

full text links

Proceed to details

Cite

Share

57

Addict Behav

. 2023 Oct;145:107777.

doi: 10.1016/j.addbeh.2023.107777. Epub 2023 Jun 12.

# Associations for subgroups of E-cigarette, cigarette, and cannabis use with asthma in a population sample of California adolescents

Rebecca J Williams[1], Thomas A Wills[2], Kelvin Choi[3], Ian Pagano[2]

Affiliations expand

- PMID: 37336095

- PMCID: PMC10330693 (available on 2024-10-01)

- DOI: 10.1016/j.addbeh.2023.107777

**Abstract**

Knowledge about the respiratory health consequences of adolescents' use of tobacco products with cannabis remains limited. We studied whether e-cigarettes, combustible cigarettes, and cannabis were independently associated with asthma in a population-based sample of 150,634 public high school students (10th and 12th graders), drawn in a two-stage design to be representative of the state of California in 2019-2020. Measures were obtained for use of e-cigarettes, combustible cigarettes, and cannabis; motives for use (three substances); method of use (for cannabis); ever being diagnosed with asthma; and having an asthma attack in past 12 months. Cross-classification indicated Nonuse for 64% of the sample; 15% Dual E-cigarette/Cannabis Use; 10% Exclusive Cannabis Use; 5% Exclusive E-cigarette Use; and 5% Triple Use. Multinomial logistic regression with a three-level criterion variable, controlling for age, sex, parental education, race/ethnicity, and three types of household use showed that compared with Nonuse, odds of Lifetime Asthma (vs. Never Had) was elevated for Triple Use (AOR = 1.14, CI 1.06-1.24), Dual E-cigarette/Cannabis Use (1.17, 1.12-1.23), Exclusive Cannabis Use (1.17, 1.11-1.23), and Exclusive E-cigarette Use (1.10, 1.02-1.18). Similar results were noted for Recent Asthma. Among persons who had used cannabis, 88% of the Triple group and 74% of the Dual E-cigarette/Cannabis group reported both smoking and vaping cannabis. Thus, co-occurrence of e-cigarette and cannabis use was a common pattern among adolescents in this study, and subgroups of cannabis and e-cigarette use showed similar associations with asthma. Preventive approaches should highlight the health implications of exclusive or combined e-cigarette and cannabis use.

**Keywords:** Asthma; Cannabis; E-cigarettes; Smoking; Substance use; Youth.



## Conflict of interest statement

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

supplementary info

Publication types, MeSH terms, Grants and fundingexpand

full text links

Proceed to details

Cite

Share

58

Allergy

. 2023 Oct;78(10):2669-2683.

doi: 10.1111/all.15772. Epub 2023 May 26.

# Dupilumab in the treatment of severe uncontrolled chronic rhinosinusitis with nasal polyps (CRSwNP): A multicentric observational Phase IV real-life study (DUPIREAL)

Eugenio De Corso[1], Ernesto Pasquini[2], Matteo Trimarchi[3], Ignazio La Mantia[4], Fabio Pagella[5], Giancarlo Ottaviano[6], Massimiliano Garzaro[7], Carlotta Pipolo[8], Sara Torretta[9], Veronica

Seccia[10], Elena Cantone[11], Andrea Ciofalo[12], Daniela Lucidi[13], Gian Luca Fadda[14], Pia Clara Pafundi[15], Stefano Settimi[16], Claudio Montuori[16], Francesca Anastasi[17], Giulio Pagliuca[18], Angelo Ghidini[19], Carlo Cavaliere[20], Marianna Maffei[21], Francesco Bussu[22], Stefania Gallo[23], Frank Rikki Mauritz Canevari[24], Gaetano Paludetti[16], Jacopo Galli[16]; Dupireal Italian Study Group

Collaborators, Affiliations expand

- PMID: 37203259

- DOI: 10.1111/all.15772

**Abstract**

**Background:** Chronic rhinosinusitis with nasal polyps (CRSwNP) is associated with significant morbidity and reduced health-related quality of life. Findings from clinical trials have demonstrated the effectiveness of dupilumab in CRSwNP, although real-world evidence is still limited.

**Methods:** This Phase IV real-life, observational, multicenter study assessed the effectiveness and safety of dupilumab in patients with severe uncontrolled CRSwNP (n = 648) over the first year of treatment. We collected data at baseline and after 1, 3, 6, 9, and 12 months of follow-up. We focused on nasal polyps score (NPS), symptoms, and olfactory function. We stratified outcomes by comorbidities, previous surgery, and adherence to intranasal corticosteroids, and examined the success rates based on current guidelines, as well as potential predictors of response at each timepoint.

**Results:** We observed a significant decrease in NPS from a median value of 6 (IQR 5-6) at baseline to 1.0 (IQR 0.0-2.0) at 12 months ($p < .001$), and a significant decrease in Sino-Nasal Outcomes Test-22 (SNOT-22) from a median score of 58 (IQR 49-70) at baseline to 11 (IQR 6-21; $p < .001$) at 12 months. Sniffin' Sticks scores showed a significant increase over 12 months ($p < .001$) compared to baseline. The results were unaffected by concomitant diseases, number of previous surgeries, and adherence to topical steroids, except for minor differences in rapidity of action. An excellent-moderate response was observed in 96.9% of patients at 12 months based on EPOS 2020 criteria.

**Conclusions:** Our findings from this large-scale real-life study support the effectiveness of dupilumab as an add-on therapy in patients with severe uncontrolled CRSwNP in reducing polyp size and improving the quality of life, severity of symptoms, nasal congestion, and smell.

**Keywords:** asthma; biologics; chronic rhinosinusitis with nasal polyps; dupilumab; smell.

- 31 references

full text links

Proceed to details

Cite

Share

59

Allergy

- 
- 
- 

. 2023 Oct;78(10):2659-2668.

doi: 10.1111/all.15771. Epub 2023 May 23.

# Sinus inflammation and chronic rhinosinusitis are associated with a diagnosis of new onset asthma in the following year

Brian S Schwartz[1,2], Jonathan S Pollak[1], Karen Bandeen-Roche[3], Annemarie G Hirsch[2], Ashton E Lehmann[4], Robert C Kern[5], Bruce K Tan[5], Atsushi Kato[6], Robert P Schleimer[5,6], Anju T Peters[6]

Affiliations expand

- PMID: 37195236

- DOI: 10.1111/all.15771

**Abstract**

**Background:** Chronic rhinosinusitis (CRS) and asthma commonly co-occur. No studies have leveraged large samples needed to formally address whether preexisting CRS is associated with new onset asthma over time.

**Methods:** We evaluated whether prevalent CRS [identified in two ways: validated text algorithm applied to sinus computerized tomography (CT) scan or two diagnoses] was associated with new onset adult asthma in the following year. We used electronic health record data from Geisinger from 2008 to 2019. For each year we removed persons with any evidence of asthma through the end of the year, then identified those with new diagnosis of asthma in the following year. Complementary log-log regression was used to adjust for confounding variables (e.g., sociodemographic, contact with the health system, comorbidities), and hazard ratios (HRs) and 95% confidence intervals (CI) were calculated.

**Results:** A total of 35,441 persons were diagnosed with new onset asthma and were compared to 890,956 persons who did not develop asthma. Persons with new onset asthma tended to be female (69.6%) and younger (mean [SD] age 45.9 [17.0] years). Both CRS definitions were associated (HR, 95% CI) with new onset asthma, with 2.21 (1.93, 2.54) and 1.48 (1.38, 1.59) for CRS based on sinus CT scan and two diagnoses, respectively. New onset asthma was uncommonly observed in persons with a history of sinus surgery.

**Conclusion:** Prevalent CRS identified with two complementary approaches was associated with a diagnosis of new onset asthma in the following year. The findings may have clinical implications for the prevention of asthma.

**Keywords:** asthma etiology; epidemiology; rhinosinusitis; risk factors.



- 38 references

supplementary info

Grants and fundingexpand

full text links

Proceed to details

Cite

Share

60

**Review**

Respir Care

. 2023 Oct;68(10):1430-1437.

doi: 10.4187/respcare.10913. Epub 2023 May 9.

# 2022 Year in Review: Pediatric Asthma

Joyce A Baker[1]

Affiliations expand

- PMID: 37160339

- PMCID: PMC10506641 (available on 2024-10-01)

- DOI: 10.4187/respcare.10913

**Abstract**

Asthma is the most common chronic disease in children. Asthma is a heterogeneous disease characterized by variable, reversible airway obstruction and hyper-responsive airways. There is a high economic burden due to a child having poorly controlled asthma with one or more asthma exacerbations resulting in an emergency department visit or hospitalization in a year. Publications on diagnosis, treatment, and management of pediatric asthma are ongoing with over 2,549 papers published from January-November 2022. The intent of this paper is to summarize 8 key topics that have prompted discussions with local, regional, and national asthma experts due to a shift in clinical practice or lessons learned from the recent pandemic that may have future application.

**Keywords:** COVID-19; asthma; pediatric; phenotypes; virus infections; wheezing.



## Conflict of interest statement

Ms Baker has disclosed no conflicts of interest.

## supplementary info

Publication types, MeSH termsexpand

Allergol Int

. 2023 Oct;72(4):557-563.

doi: 10.1016/j.alit.2023.03.007. Epub 2023 Apr 14.

# Dupilumab improves eosinophilic otitis media associated with eosinophilic chronic rhinosinusitis

Daiki Nakashima[1], Tsuguhisa Nakayama[2], Syunsuke Minagawa[3], Tetsuya Adachi[4], Chieko Mitsuyama[5], Yoko Shida[5], Tsuneya Nakajima[5], Shin-Ichi Haruna[6], Yoshinori Matsuwaki[7]

Affiliations expand

- PMID: 37061391

- DOI: 10.1016/j.alit.2023.03.007

**Free article**

## Abstract

**Background:** Eosinophilic otitis media (EOM) is a refractory condition associated with eosinophilic chronic rhinosinusitis and bronchial asthma. EOM is characterized by type-2 inflammation and is refractory to various treatments. We investigated the efficacy of dupilumab, interleukin-4 receptor alpha antagonist, for patients with EOM complicated by eosinophilic chronic rhinosinusitis (ECRS).

**Methods:** Between April 2017 and April 2022, we treated 124 patients with dupilumab for refractory CRS or bronchial asthma. Of these, 14 had EOM concurrently, and 10 of them who had been treated for >6 months were included in our study. We retrospectively evaluated the efficacy of dupilumab by the amount of systemic corticosteroid used, the frequency of exacerbations, severity score of EOM, computed tomography (CT) score of temporal bones, and pure tone audiometry. We also enrolled 8 EOM patients without dupilumab treatment as a control group.

**Results:** Dupilumab significantly improved the amount of systemic corticosteroid used and the frequency of exacerbation and compared with before dupilumab was used ($p = 0.01$ and $<0.01$, respectively). All patients could be weaned from systemic-corticosteroid therapy by 54 weeks of dupilumab use. The severity score of EOM and CT score for temporal bones were significantly lower than before the treatment ($p = 0.01$ and 0.01, respectively). Compared to the control group, the systemic corticosteroid used and severity scores were improved in the dupilumab group ($p = 0.02$ and $< 0.01$, respectively).

**Conclusions:** Dupilumab could be used to wean patients from systemic corticosteroids with the improvement of severity score in EOM associated with ECRS and bronchial asthma.

**Keywords:** Bronchial asthma; Corticosteroid; Dupilumab; Eosinophilic chronic rhinosinusitis; Eosinophilic otitis media.

. 2023 Oct;60(10):1800-1808.

doi: 10.1080/02770903.2023.2200844. Epub 2023 Apr 23.

# A narrative review on asthma and pest sensitization (cockroach, mouse and rat allergens): a social issue besides the medical problem

Gennaro Liccardi[1], Matteo Martini[2,3], Maria Beatrice Bilò[3,4], Manlio Milanese[5], Luigino Calzetta[6], Rossella Laitano[7], Paola Rogliani[1,7]

Affiliations expand

- PMID: 37042228

- DOI: 10.1080/02770903.2023.2200844

**Abstract**

**Objective:** Among animals defined as "pests", cockroaches and rodents (mouse and rat) represent the most common cause of airway allergic sensitization and bronchial asthma worldwide. Their frequency of sensitization has been widely assessed in US and other countries but poorly in Western Europe. This narrative review aims to provide a synthesis of data resulting in MEDLINE concerning allergic sensitization/asthma to pests as well as their related environmental/social risk factors, specifically in the European area.

**Data sources:** We performed a literature research in MEDLINE for clinical trials, randomized controlled trials, systematic reviews and meta-analyses.

**Study selections:** We selected studies to the following key words: allergic sensitization, allergic rhinitis, bronchial asthma, cockroach, hypersensitivity, integrated pest management, material hardship, medication compliance, mouse, pest, poverty, rat, rodents.

**Results:** Current evidence indicates that residence in poor and urban areas, exposure to outdoor/indoor pollutants and tobacco smoke, poverty, material hardship, poor-quality housing, differences in health care quality, medication compliance, health care access contribute to increased pest-related allergic sensitization and asthma morbidity.

**Conclusion:** Further research should be done on many aspects of pest allergy such as a better characterization of allergens and epidemiological aspects. Relevant social actions should be carried out against poverty, healthcare disparities, psycho-social stress, poor

compliance to therapy, with economic contributions to improve private and public living environments. Allergic sensitization to pests and pest-allergic respiratory diseases like asthma are "paradoxical" conditions, as they typically affect the poorest communities but can only be corrected by high-cost (diagnostic and preventive) interventions. We hope that progress can be made in this direction in the future.

**Keywords:** Allergic sensitization; allergic rhinitis; bronchial asthma; cockroach; hypersensitivity; integrated pest management; material hardship; medication compliance; mouse; pest; poverty; rat; rodents.



63

Med Sci Law

. 2023 Oct;63(4):334-336.

doi: 10.1177/00258024231169230. Epub 2023 Apr 11.

# Thunder storm mortality: Issues of medicolegal concern

Roger W Byard[1,2]

Affiliations expand

- PMID: 37041741

- DOI: 10.1177/00258024231169230

## Abstract

Thunderstorms refer to atmospheric disturbances that are associated with electrical discharges in the form of lightning, with acoustic effects from thunder. They involve the rapid upward movement of warm, moist air which then cools and condenses creating typical cumulonimbus clouds with precipitation. Thunderstorms range in severity but are usually associated with heavy rains, winds and sometimes sleet, hail and snow. If the intensity of a storm increases there may be tornadoes or cyclones. In cases with lightning strikes and minimal or no rain there is an associated risk for the development of quite devastating wild (bush) fires. Lightning strikes may also be associated with the development, or an exacerbation, of potentially lethal natural cardiac or respiratory diseases.

**Keywords:** Thunder storms; asthma; cyclones; death; lightning; wildfires.



## Review

Clin Chem Lab Med

. 2023 Mar 30;61(10):1679-1687.

doi: 10.1515/cclm-2022-1323. Print 2023 Sep 26.

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

Andrea Vianello[1], Gabriella Guarnieri[1], Alessia Achille[1], Federico Lionello[1], Sara Lococo[1], Martina Zaninotto[2], Marco Caminati[3], Gianenrico Senna[3]

Affiliations expand

- PMID: 36989607

- DOI: 10.1515/cclm-2022-1323

**Free article**

**Abstract**

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

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



- 75 references

supplementary info

Publication types, MeSH terms, Substancesexpand

full text links

J Asthma

. 2023 Oct;60(10):1869-1876.

doi: 10.1080/02770903.2023.2196563. Epub 2023 Apr 21.

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

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

Affiliations expand

- PMID: 36976568

- DOI: 10.1080/02770903.2023.2196563

**Abstract**

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

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

**Material and methods:** This is a registry-based multi-center cohort study evaluating data from adults with severe eosinophilic asthma included in the Dutch Register of Adult Patients with Severe Asthma for Optimal DIsease management (RAPSODI). Patients that

started with anti-IL-5/5Ra biologics and completed the work productivity and activity improvement questionnaire, were included. Study and patient characteristics were compared between the employed and unemployed patients. Work productivity and activity impairment are related to accompanying improvements in clinical outcomes.

**Results:** At baseline, 91 of 137 patients (66%) were employed which remained stable throughout the follow-up period. Patients in the working age category were younger and had significantly better asthma control ($p$ = 0.02). Mean overall work impairment due to health decreased significantly from 25.5% (SD2.6) to 17.6% (SD 2.8) during 12 months anti-IL-5/5Ra biologics treatment ($P$ = 0.010). There was a significant association between ACQ6 and overall work improvement after targeted therapy (β = 8.7, CI 2.1-15.4, $P$ = 0.01). The improvement of asthma control of 0.5 points on the asthma Control Questionnaire was associated with an overall work impairment of -9%.

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

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

# A hierarchical cluster analysis of the psycological impact of the COVID-19 pandemic on Italian severe asthma patients

G Guarnieri[1], L Chiurato[2], I Baiardini[3], M Caminati[4], G Senna[4,5], B Scarpa[2], A Vianello[1]

Affiliations expand

- PMID: 36951668

- DOI: 10.1080/02770903.2023.2188565

**Abstract**

**Introduction:** In the context of COVID-19 pandemic, a consistent medical concern raised among severe asthma patients, though the studies excluded an increased risk of severe disease as well as an increased susceptibility.The aim of the study was to apply the Psychological General Well-Being Index (PGWBI) questionnaire to severe asthmatics during the COVID-19 pandemic and to evaluate the data with a hierarchical cluster analysis.

**Methods:** 114 severe asthmatics were asked to respond anonymously to the PGWBI questionnaire. The patients underwent a lung functional test, fractional exhaled nitric oxide (FeNO) measurement, Asthma Control Test (ACT), and Asthma Control Questionnaire (ACQ6). A hierarchical cluster analysis was performed using an agglomerative approach and complete linkage to evaluate the results.

**Results:** The study population predominantly included female (60%), middle-aged patients, with normal lung function parameters, mild signs of airway, and satisfactory asthma control. The PGWBI score (82.46 ± 16.53) of the study population showed a good state of psychological well-being and was similar to that of a representative sample of healthy adult Italian subjects. Thus, Hierarchical cluster analysis identified 3 groups of patients: Cluster 1 (32%), Cluster 2 (64%), and Cluster 3 (4%). Whilst the Cluster 2 patients' PGWBI score fell within the normal range, the Cluster 1 patients had a significantly lower total score (68.57 ± 7.2; $p < 0.05$), suggesting moderate distress. The Cluster 3 patients presented a total score markedly low.

**Conclusion:** Although the majority of the severe asthma patients studied demonstrated good mental well-being during the COVID-19 pandemic, some did indeed show moderate to severe psychological distress.

**Keywords:** PGWBI; anti-Sars-Cov-2 vaccine; anxiety; biologic treatment.

**Meta-Analysis**

Thorax

. 2023 Oct;78(10):957-965.

doi: 10.1136/thorax-2022-219268. Epub 2023 Mar 22.

# Effect of obesity on airway and systemic inflammation in adults with asthma: a systematic review and meta-analysis

Hayley A Scott[1,2], Shawn Hm Ng[3], Rebecca F McLoughlin[4,5,6], Sarah R Valkenborghs[7,8], Parameswaran Nair[9], Alexandra C Brown[7,2], Olivia R Carroll[7,2], Jay C Horvat[7,2], Lisa G Wood[7,2]

Affiliations expand

- PMID: 36948588

- DOI: 10.1136/thorax-2022-219268

**Abstract**

**Background:** Obesity is associated with more severe asthma, however, the mechanisms responsible are poorly understood. Obesity is also associated with low-grade systemic inflammation; it is possible that this inflammation extends to the airways of adults with asthma, contributing to worse asthma outcomes. Accordingly, the aim of this review was to examine whether obesity is associated with increased airway and systemic inflammation and adipokines, in adults with asthma.

**Methods:** Medline, Embase, CINAHL, Scopus and Current Contents were searched till 11 August 2021. Studies reporting measures of airway inflammation, systemic inflammation and/or adipokines in obese versus non-obese adults with asthma were assessed. We conducted random effects meta-analyses. We assessed heterogeneity using the $I^2$ statistic and publication bias using funnel plots.

**Results:** We included 40 studies in the meta-analysis. Sputum neutrophils were 5% higher in obese versus non-obese asthmatics (mean difference (MD)=5.0%, 95% CI: 1.2 to 8.9, n=2297, p=0.01, $I^2$=42%). Blood neutrophil count was also higher in obesity. There was no difference in sputum %eosinophils; however, bronchial submucosal eosinophil count (standardised mean difference (SMD)=0.58, 95% CI=0.25 to 0.91, p<0.001, n=181, $I^2$=0%) and sputum interleukin 5 (IL-5) (SMD=0.46, 95% CI=0.17 to 0.75, p<0.002, n=198, $I^2$=0%) were higher in obesity. Conversely, fractional exhaled nitric oxide was 4.5 ppb lower in obesity (MD=-4.5 ppb, 95% CI=-7.1 ppb to -1.8 ppb, p<0.001, n=2601, $I^2$=40%). Blood C reactive protein, IL-6 and leptin were also higher in obesity.

**Conclusions:** Obese asthmatics have a different pattern of inflammation to non-obese asthmatics. Mechanistic studies examining the pattern of inflammation in obese asthmatics are warranted. Studies should also investigate the clinical relevance of this altered inflammatory response.

**Prospero registeration number:** CRD42021254525.

**Keywords:** asthma; neutrophil Biology; pulmonary eosinophilia.



# Conflict of interest statement

Competing interests: PN reports grants and personal fees from AZ, grants and personal fees from Teva, grants from Sanofi, personal fees from Equillium, grants from Foresee, personal fees from Arrowhead Pharma, grants from Cyclomedica, personal fees from GSK, outside the submitted work. LGW reports an Honorarium from Sanofi.

## supplementary info

Publication types, MeSH termsexpand

J Asthma

. 2023 Oct;60(10):1926-1934.

doi: 10.1080/02770903.2023.2191715. Epub 2023 Mar 30.

# Outcomes of children with life-threatening status asthmaticus requiring isoflurane therapy and extracorporeal life support

Sneha Kolli[1,2], Cydney Opolka[2], Adrianna Westbrook[1,3], Scott Gillespie[1,3], Carrie Mason[1], Brittany Truitt[1,2], Pradip Kamat[1,2], Anne Fitzpatrick[1,2], Jocelyn R Grunwell[1,2]

Affiliations expand

- PMID: 36927245

- PMCID: PMC10524452 (available on 2024-10-01)

- DOI: 10.1080/02770903.2023.2191715

**Abstract**

**Background:** Severe, refractory asthma is a life-threatening emergency that may be treated with isoflurane and extracorporeal life support. The objective of this study was to describe the clinical response to isoflurane and outcomes after discharge of children who received isoflurane and/or extracorporeal life-support for near-fatal asthma.

**Methods:** This was a retrospective descriptive study using electronic medical record data from two pediatric intensive care units within a single healthcare system in Atlanta, GA.

**Results:** Forty-five children received isoflurane, and 14 children received extracorporeal life support, 9 without a trial of isoflurane. Hypercarbia and acidosis improved within four hours of starting isoflurane. Four children died during the index admission for asthma. Twenty-seven percent had a change in Functional Status Score of three or more points from baseline to PICU discharge. Patients had median percent predicted FEV1 and FEV1/FVC ratios pre- and post-bronchodilator values below normal pediatric values.

**Conclusion:** Children who received isoflurane and/or ECLS had a high frequency of previous PICU admission and intubation. Improvement in ventilation and acidosis occurred within the first four hours of starting isoflurane. Children who required isoflurane or ECLS may develop long-lasting deficits in their functional status. Children with near-fatal asthma are a high-risk group and require improved follow-up in the year following PICU discharge.

**Keywords:** Isoflurane; extracorporeal life-support; functional status score; pediatric intensive care unit; pulmonary function tests; status asthmaticus.

# Conflict of interest statement

Author Disclosures: The authors have nothing to disclose.

doi: 10.1080/02770903.2023.2189947. Epub 2023 Mar 27.

# Redefining biomarkers in pediatric asthma: a commentary

Russell J Hopp[1], Mark C Wilson[1], M Asghar Pasha[2]

Affiliations expand

- PMID: 36894331

- DOI: 10.1080/02770903.2023.2189947

***No abstract available***

supplementary info

MeSH terms, Substancesexpand

full text links

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

1

Pediatr Rev

- 
- 
- 

. 2023 Oct 1;44(10):537-550.

doi: 10.1542/pir.2022-005618.

# Allergic Rhinitis

Barrie Cohen[1]

Affiliations expand

- PMID: 37777655

- DOI: 10.1542/pir.2022-005618

**Abstract**

Allergic rhinitis (AR) affects more than 400 million people worldwide, making it 1 of the most prevalent chronic diseases. Childhood AR is increasing, and almost half of patients with AR develop symptoms before age 6 years. Although a diagnosis of AR is associated with higher socioeconomic status, underserved and urban populations have more indoor aeroallergen sensitizations and are likely underdiagnosed with AR, further exacerbating health-care disparities. AR negatively impacts quality of life, school performance, and overall health outcomes. Untreated AR in children increases the risk for poor asthma control, increased asthma severity, and exacerbations. Many patients believe that they have seasonal allergies only but in reality have both perennial and seasonal AR, which may change the approach to allergen avoidance measures and treatment recommendations. Pharmacotherapy of AR has expanded, with many intranasal corticosteroids, intranasal antihistamines, and second-generation oral antihistamines approved for pediatric use. Allergen immunotherapy, including both subcutaneous and sublingual forms, are approved for children and are disease modifying, potentially reducing further allergen sensitization and progression to asthma. Many of the currently available biological therapies indicated for pediatric asthma and/or atopic diseases reduce AR symptoms as well. Children with moderate to severe or refractory AR or those with comorbidities should be referred to allergists for diagnostic testing and expanded management options, including immunotherapy and potential biological treatment.

. 2023 Sep 28;52(1):64.

doi: 10.1186/s40463-023-00668-z.

# The argument against the use of dupilumab in patients with limited polyp burden in chronic rhinosinusitis with nasal polyposis (CRSwNP)

Scott A Hardison[1,2], Brent A Senior[3,4]

Affiliations expand

- PMID: 37759322

- PMCID: PMC10537999

- DOI: 10.1186/s40463-023-00668-z

**Free PMC article**

## Abstract

Dupilumab and other biologics have revolutionized the management of recalcitrant polyps in patients with chronic rhinosinusitis with nasal polyposis (CRSwNP). Despite strong evidence for the efficacy of dupilumab in treating polyps, factors such as cost and uncertain efficacy over surgery have limited its use to patients who have failed the use of topical nasal steroids and initial surgical management. Likewise, the use of this drug is often directed towards patients with greater polyp burdens. Recent studies, however, have investigated the use of dupilumab and other biologics in expanded patient populations, including those with limited polyp burden. The overall trend in the literature suggests a future move towards the use of biologics as first-line therapy for all patients with CRSwNP. The arguments against widespread, routine use of dupilumab and biologics in all patients with CRSwNP are threefold. First, endoscopic sinus surgery has been found to provide similar symptomatic benefit to dupilumab in the treatment of these patient populations. The surgical improvement of patients' sinonasal anatomy offers a rapid elimination of sources of ongoing inflammation that contribute to long-term polyp formation and symptoms. Medical non-compliance in this specific patient population is known to be an issue, with surgery offering a much greater long-term prospect of symptomatic relief in non-compliant patients. The second concern revolves around the potential for side effects of dupilumab and other biologics. Initial studies have shown an acceptable safety profile,

but trials assessing the use of dupilumab for a separate indication revealed a higher rate of conjunctivitis. Long-term safety data is limited for biologics, and we must be prepared for the possibility of severe, unanticipated adverse events in the future. Our third and most profound concern is the significant cost of dupilumab. This medication is enormously expensive, and all current literature suggests that treatment would need to be life-long to remain effective. Studies comparing endoscopic sinus surgery to various biologics, including dupilumab, have shown comparable overall quality of life metrics with biologics, all while delivering considerably higher anticipated lifetime costs. As our knowledge progresses regarding the efficacy of dupilumab and other biologics in a variety of clinic situations, it is important to understand the context in which these advances are being made. While dupilumab and other biologics offer undeniable efficacy in the treatment of chronic rhinosinusitis with nasal polyposis which has failed to respond to standard therapies, we argue that biologics remain only a component of effective management in this patient population. Endoscopic sinus surgery and topical nasal steroids offer equal efficacy and substantially lower costs than biologics, and these factors should be considered when selecting treatment options for patients.

**Keywords:** Chronic rhinosinusitis; Endoscopic sinus surgery; Eosinophilic rhinitis; Nasal polyposis; Quality of life; Sinusitis.



# Conflict of interest statement

Dr Senior: Consultant for Styker, Neurent, and Lyra Therapeutics. Nothing to disclose for Dr. Hardison.

- 17 references

Hong Kong Med J

. 2023 Sep 26.

doi: 10.12809/hkmj2310696. Online ahead of print.

# Indications for house dust mite allergen-specific immunotherapy

C W M Leung[1], H C Chu[1], J C H Leung[2], T F Leung[3]

Affiliations expand

- PMID: 37749053

- DOI: 10.12809/hkmj2310696

**Free article**

***No abstract available***

**Keywords:** Asthma; Dermatitis, atopic; House dust mites; Immunotherapy; Rhinitis, allergic.

## Conflict of interest statement

The authors have no conflicts of interest to disclose.



**Review**

Allergy

- 
- 
- 

. 2023 Oct;78(10):2581-2595.

doi: 10.1111/all.15855. Epub 2023 Aug 28.

# UCRAID (Ukrainian Citizen and refugee electronic support in Respiratory diseases, Allergy, Immunology and Dermatology) action plan

Jean Bousquet[1,2,3], Boleslaw Samolinski[4], Igor Kaidashev[5], Marcus Maurer[1,2], Nicolas Roche[6,7], Bernardo Sousa-Pinto[8,9], Andrii Kurchenko[10], Roman Stepanenko[11], Vladyslav Tsaryk[10], Ludger Klimek[12,13], Maria Teresa Ventura[14,15], Anna Bedbrook[3,16], Wienczyslawa Czarlewski[3,17], Yuliia Lysanets[5], Maciej Kupczyk[18], Łukasz Skolimowski[19], Marek Kulus[20], Stefano Del Giacco[21], Markus Ollert[22,23,24], Judith Garcia-Aymerich[25,26], Carlos Robalo Cordeiro[27], Arzu Yorgancioglu[28], Christoph Schlapbach[29], Rita Amaral[8,9], Cristina Bonaglia[30], Isabelle Bossé[31], Rosalba Buquicchio[32], Demetrios Christou[1,2], Galyna Fedoruk[10], Pietro Fontanesi[30], Bilun Gemicioglu[33], Antonio F M Giuliano[14,34], Paolo Lepore[35], Alla Nakonechna[36,37], Sophia Neisinger[1,2], Ana M Pereira[8,9], Aiste Ramanauskaite[1,2], Filip Raciborski[4], Brigita Sitkauskiene[38], Oksana Sokhatska[39], Viktor Stepanenko[11], Katarina Stevanovic[1,2], Orysya Syzon[40], Violeta Kvedariene[41,42], Govert de Vries[43], Michiel van Eerd[43], Arunas Valiulis[44,45], Joao A Fonseca[8,9], Josep M Anto[25,26,46], Tari Haahtela[47], Holger Schünemann[48], Torsten Zuberbier[1,2]

Affiliations expand

- PMID: 37641384

- DOI: 10.1111/all.15855

**Free article**

## Abstract

Eight million Ukrainians have taken refuge in the European Union. Many have asthma and/or allergic rhinitis and/or urticaria, and around 100,000 may have a severe disease. Cultural and language barriers are a major obstacle to appropriate management. Two widely available mHealth apps, MASK-air® (Mobile Airways Sentinel NetworK) for the management of rhinitis and asthma and CRUSE® (Chronic Urticaria Self Evaluation) for patients with chronic spontaneous urticaria, were updated to include Ukrainian versions that make the documented information available to treating physicians in their own

language. The Ukrainian patients fill in the questionnaires and daily symptom-medication scores for asthma, rhinitis (MASK-air) or urticaria (CRUSE) in Ukrainian. Then, following the GDPR, patients grant their physician access to the app by scanning a QR code displayed on the physician's computer enabling the physician to read the app contents in his/her own language. This service is available freely. It takes less than a minute to show patient data to the physician in the physician's web browser. UCRAID-developed by ARIA (Allergic Rhinitis and its Impact on Asthma) and UCARE (Urticaria Centers of Reference and Excellence)-is under the auspices of the Ukraine Ministry of Health as well as European (European Academy of Allergy and Clinical immunology, EAACI, European Respiratory Society, ERS, European Society of Dermatologic Research, ESDR) and national societies.

**Keywords:** Ukrainian refugees; asthma; mHealth; rhinitis; urticaria.



- 54 references

supplementary info

Publication types, Grants and fundingexpand

full text links

Proceed to details

Cite

Share

5

**Controlled Clinical Trial**

Immunotherapy

-
-
-

. 2023 Oct;15(14):1171-1181.

doi: 10.2217/imt-2023-0051. Epub 2023 Aug 10.

# A novel dose-adjustment protocol for interrupted subcutaneous immunotherapy for allergic rhinitis

Xian Feng[1], Juan Liu[1]

Affiliations expand

- PMID: 37585664

- DOI: 10.2217/imt-2023-0051

**Abstract**

**Background:** This study aimed to develop a novel dose strategy for subcutaneous immunotherapy to reduce medical waste and financial burdens for patients who are required to restart subcutaneous immunotherapy. **Patients & methods:** A prospective, nonrandomized concurrent controlled trial was performed to assess the safety and advantages of the novel dose-adjustment protocol compared with the conventional one. 76 subjects were grouped to receive novel or conventional dose-adjustment protocols. **Results:** The injections, visits and time needed to reach the pre-established dose with the novel regimen were decreased. Furthermore, there were no differences in side reactions between the two groups. **Conclusion:** The novel protocol seemed safe and well tolerated, offering the advantages of time efficiency and reduced healthcare costs.

**Keywords:** allergic rhinitis; conventional immunotherapy; house dust mite; safety; subcutaneous immunotherapy.

## Plain language summary

A common sickness people can acquire from house dust mites is called allergic rhinitis. One way to treat it is with regular shots of a special medicine made from dust mite allergens. This is termed subcutaneous immunotherapy. Patients need to take these shots in their arm for about 3–5 years. Initially, the shot is given once a week for at least 15 weeks; then the frequency can be reduced to every 4–8 weeks. However, if a patient misses their scheduled shot, they may have to start getting weekly shots again. This can lead to a lot of medical waste and can be expensive for patients. Therefore we developed a new way to give these shots. In this study, patients who needed to start weekly shots again were administered this new treatment plan. The new plan significantly reduced the number of doctor's visits and shots. This new and improved treatment regimen is convenient and saves patients time and money. The side effects of this new treatment method were not higher compared with the traditional treatment. Therefore this new treatment method is

safe, cost-effective and patient-friendly. It also saves time and reduces both medical waste and financial costs.

## supplementary info

Publication types, MeSH terms, Substancesexpand

## full text links

Proceed to details

Cite

Share

6

**Review**

Curr Allergy Asthma Rep

. 2023 Oct;23(10):567-578.

doi: 10.1007/s11882-023-01104-y. Epub 2023 Aug 10.

# Management of Mechanical Nasal Obstruction Isolated or Associated to Upper Airway Inflammatory Diseases in Real Life: Use of both Subjective and Objective Criteria

Carla Merma-Linares[1,2,3,4], M Dolores Martinez[5,6], Miriam Gonzalez[5,6], Isam Alobid[7,8], Enric Figuerola[5,6], Joaquim Mullol[9,10,11]

Affiliations expand

- PMID: 37561310

- PMCID: PMC10506933

- DOI: 10.1007/s11882-023-01104-y

**Free PMC article**

**Abstract**

**Purpose of review:** Mechanical nasal obstruction (MNO) is a prevalent condition with a high impact on patient's quality-of-life (QoL) and socio-economic burden. The aim of this study was to determine the usefulness of both subjective and objective criteria in the appropriate management of MNO, either alone or associated to upper airway inflammatory diseases such as allergic rhinitis (AR) or chronic rhinosinusitis with nasal polyps (CRSwNP).

**Recent findings:** A long debate persists about the usefulness of subjective and objective methods for making decisions on the management of patients with nasal obstruction. Establishing standards and ranges of symptom scales and questionnaires is essential to measure the success of an intervention and its impact on QoL. To our knowledge this is the first real-life study to describe the management of MNO using both subjective and objective criteria in MNO isolated or associated to upper airway inflammatory diseases (AR or CRSwNP). Medical treatment (intranasal corticosteroids) has a minor but significant improvement in MNO subjective outcomes (NO, NOSE, and CQ7) with no changes in loss of smell and objective outcomes. After surgery, all MNO patients reported a significant improvement in both subjective and objective outcomes, this improvement being higher in CRSwNP. We concluded that in daily clinical practice, the therapeutic recommendation for MNO should be based on both subjective and objective outcomes, nasal corrective surgery being the treatment of choice in MNO, either isolated or associated to upper airway inflammatory diseases, AR or CRSwNP.

**Keywords:** Allergic Rhinitis; CRSwNP; Diagnostic Techniques; Nasal Obstruction; Nasal Surgical Procedures.



# Conflict of interest statement

The authors declare non-financial interests that are directly or indirectly related to the work submitted for publication.

- 34 references

- 3 figures

supplementary info

Publication types, MeSH termsexpand

full text links

Proceed to details

Cite

Share

7

**Review**

Curr Allergy Asthma Rep

. 2023 Oct;23(10):579-587.

doi: 10.1007/s11882-023-01103-z. Epub 2023 Jul 15.

# Occupational Rhinitis: An Update

Jose Zamora-Sifuentes[1], Jill A Poole[2]

Affiliations expand

- PMID: 37452992

- DOI: 10.1007/s11882-023-01103-z

**Abstract**

**Purpose of review:** Occupational rhinitis is an underdiagnosed disease with significant morbidity and implications in the workplace. Multiple factors associated with this disease continue to pose a challenge to investigators. This review aims to summarize recent literature in occupational rhinitis, including classifications, pathogenesis, diagnosis, and

treatment, as well as the impact of occupational rhinitis on individuals. Additionally, it identifies areas in need of further research and investigation.

**Recent findings:** We highlight current research on the association between occupational rhinitis and occupational asthma and the role of immunotherapy in this disease. Discussion includes the impact of social trends on workers and the wider consequences of occupational rhinitis including decreased work productivity, absenteeism, and socioeconomic burden. Occupational rhinitis remains a challenging disease entity due to the numerous potential causative factors, reduced recognition, morbidity in asthma, and therapeutic limitations. Additional research is needed to better identify disease predictors and develop effective management strategies.

**Keywords:** Occupational asthma; Occupational disease; Occupational rhinitis; Work-related rhinitis.



- 52 references

supplementary info

Publication types, MeSH terms, Grants and fundingexpand

full text links

Proceed to details

Cite

Share

8

**Review**

Immunotherapy

- 
- 
- 

. 2023 Oct;15(14):1105-1116.

doi: 10.2217/imt-2023-0026. Epub 2023 Jul 12.

# Mepolizumab in chronic rhinosinusitis with nasal polyposis

Xuandao Liu[1], Tze Choong Charn[2], De-Yun Wang[3]

Affiliations expand

- PMID: 37435679

- DOI: 10.2217/imt-2023-0026

**Abstract**

Chronic rhinosinusitis with nasal polyposis (CRSwNP) is a heterogeneous upper airway disease that is prevalent globally. Recent research into the molecular basis of the disease has led to the development of biologics as a new therapeutic option for severe and recalcitrant forms of CRSwNP. Mepolizumab is a monoclonal antibody targeting IL-5, one of the signature cytokines of the type 2 immune response and which plays an important role in the pathogenesis of CRSwNP. Here we present the latest evidence behind mepolizumab, examining disease pathophysiology and pharmacology, as well as data from clinical trials, real-life studies and meta-analyses. As we welcome this promising step forward into precision medicine, we discuss practical issues and future perspectives on mepolizumab and biologics for CRSwNP.

**Keywords:** biologics; chronic rhinosinusitis; mepolizumab; nasal polyps; type 2 inflammation; upper airway disease.

## Plain language summary

Mepolizumab is a new injectable drug developed to control difficult-to-treat cases of chronic rhinosinusitis with nasal polyposis (CRSwNP), an inflammatory disease of the nose that affects many people worldwide. It works by blocking the action of IL-5, an important protein in the body that regulates inflammation. One of the main effects of this protein is promoting the activity of eosinophils, a type of white blood cell. Eosinophils contribute to tissue damage when activated inappropriately. A recent large-scale study (SYNAPSE) on patients using this drug has been completed, reporting favorable results. In this article, we discuss the science behind the disease, the drug and data from patient studies. We conclude by discussing several future challenges and opportunities in the management of CRSwNP.

supplementary info

Publication types, MeSH terms, Substancesexpand

full text links

Proceed to details

Cite

Share

9

**Review**

Eur Arch Otorhinolaryngol

. 2023 Oct;280(10):4319-4325.

doi: 10.1007/s00405-023-08083-w. Epub 2023 Jul 6.

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

Qian Wang[1], Ruifang Zhu[1,2], Yan Ning[1], Yaoqing Feng[1], Yan Feng[1,2], Shifan Han[3,4]

Affiliations expand

- PMID: 37410146

- DOI: 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

## supplementary info

Publication types, MeSH termsexpand

## full text links

Proceed to details

Cite

Share

10

**Review**

Sci Total Environ

. 2023 Oct 1;893:164801.

doi: 10.1016/j.scitotenv.2023.164801. Epub 2023 Jun 14.

# Impact of environmental nitrogen pollution on pollen allergy: A scoping review

Paulien Verscheure[1], Olivier Honnay[2], Niko Speybroeck[3], Robin Daelemans[2], Nicolas Bruffaerts[4], Brecht Devleesschauwer[5], Tobias Ceulemans[6], Laura Van Gerven[7], Raf Aerts[8], Rik Schrijvers[9]

Affiliations expand

- PMID: 37321510

- DOI: 10.1016/j.scitotenv.2023.164801

**Free article**

## Abstract

The current rise in the prevalence of allergies to aeroallergens is incompletely understood and attributed to interactions with environmental changes and lifestyle changes. Environmental nitrogen pollution might be a potential driver of this increasing prevalence. While the ecological impact of excessive nitrogen pollution has been widely studied and is relatively well understood, its indirect effect on human allergies is not well documented. Nitrogen pollution can affect the environment in various ways, including air, soil, and water. We aim to provide a literature overview of the nitrogen-driven impact on plant communities, plant productivity, and pollen properties and how they lead to changes in allergy burden. We included original articles investigating the associations between nitrogen pollution, pollen, and allergy, published in international peer-reviewed journals between 2001 and 2022. Our scoping review found that the majority of studies focus on atmospheric nitrogen pollution and its impact on pollen and pollen allergens, causing allergy symptoms. These studies often examine the impact of multiple atmospheric pollutants and not just nitrogen, making it difficult to determine the specific impact of nitrogen pollution. There is some evidence that atmospheric nitrogen pollution affects pollen allergy by increasing atmospheric pollen levels, altering pollen structure, altering

allergen structure and release, and causing increased allergenic reactivity. Limited research has been conducted on the impact of soil and aqueous nitrogen pollution on pollen allergenic reactivity. Further research is needed to fill the current knowledge gap about the impact of nitrogen pollution on pollen and their related allergic disease burden.

**Keywords:** Allergic disease; Environmental pollution; Nitrogen; OneHealth; Planetary health; Pollen.



# Conflict of interest statement

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



Eur Arch Otorhinolaryngol

. 2023 Oct;280(10):4713-4714.

doi: 10.1007/s00405-023-08006-9. Epub 2023 Jun 5.

# Azelastine/fluticasone and allergic rhinitis in clinical practice

Desiderio Passali[1], Giulio Cesare Passali[2], Valerio Damiani[3], Giorgio Ciprandi[4]

Affiliations expand

- PMID: 37277684

- DOI: 10.1007/s00405-023-08006-9

***No abstract available***

## Comment on

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

- 5 references

. 2023 Oct;72(4):573-579.

doi: 10.1016/j.alit.2023.02.007. Epub 2023 Mar 12.

# Comparison of rush-subcutaneous and sublingual immunotherapy with house dust mite extract for pediatric allergic rhinitis: A prospective cohort study

Masaaki Hamada[1], Keigo Saeki[2], Ichiro Tanaka[3]

Affiliations expand

- PMID: 36918306

- DOI: 10.1016/j.alit.2023.02.007

**Free article**

**Abstract**

**Background:** We aimed to compare the effectiveness and safety of subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT) with standardized house dust mite (HDM) extract for allergic rhinitis.

**Methods:** Participants with allergic rhinitis selected their treatment between HDM SCIT or HDM SLIT, according to their wishes. We prospectively followed symptoms of allergic rhinitis using the allergic rhinitis symptom medication score (ARSMS), along with adverse reactions, during the dose escalation and maintenance phases for two years. We compared the outcomes between propensity score-matched groups to adjust the confounding factors.

**Results:** After propensity score matching, 88 patients in the HDM SCIT (n = 44) and HDM SLIT groups (n = 44) remained for analysis. The HDM SCIT group showed significantly earlier effectiveness than the HDM SLIT group (median time to decrease in ARSMS [≥2 points]: 5.5 vs. 18.0 months, $p < 0.001$). The incidence of systemic reactions was not significantly different between the two groups in the dose escalation phase (68.2% vs. 56.8%, $p = 0.379$). In the maintenance phase, the incidence of systemic reactions was higher in the HDM SCIT group than in the HDM SLIT group (18.2% vs. 0%, $p < 0.006$). All 44 patients in the HDM SCIT group completed two years of treatment, while nine patients in the HDM SLIT group discontinued treatment.

**Conclusions:** The HDM SCIT group showed an earlier onset of therapeutic effect and a lower discontinuation rate than the HDM SLIT group, although more severe systemic reactions were observed during the maintenance phase.

**Keywords:** Allergen immunotherapy; Allergic rhinitis; House dust mite; Subcutaneous immunotherapy; Sublingual immunotherapy.



13

**Case Reports**

Auris Nasus Larynx

. 2023 Oct;50(5):805-810.

doi: 10.1016/j.anl.2022.12.001. Epub 2022 Dec 27.

# Omalizumab is effective for a patient with pollen-food allergy syndrome who experienced intractable lip edema

Daiki Sakamoto[1], Satoko Hamada[2], Yoshiki Kobayashi[3], Masami Shimono[1], Akihiro Shimamura[1], Akira Kanda[3], Mikiya Asako[3], Hiroshi Iwai[1]

Affiliations expand

- PMID: 36581536

- DOI: 10.1016/j.anl.2022.12.001

**Abstract**

Pollen-food allergy syndrome (PFAS) is an immunoglobulin E (IgE)-mediated allergic reaction caused when patients with pollen allergy ingest food having cross-reactivity with pollen. To date, no effective treatment method for this has been established. Here we report the case of a patient with PFAS who experienced lip edema, causing difficulties in treatment. This report describes the case of a 12-year-old boy with perennial allergic rhinitis since the age of 8 years. After ingesting fresh fruits and raw vegetables at the age of 11 years, he started to experience lip edema repeatedly. Thus, the patient was referred to our department. Based on the results of serum antigen-specific IgE, prick-to-prick, and allergen component tests, he was diagnosed with PFAS. He has been instructed to avoid causative food. Furthermore, the treatment using an antihistamine and antileukotriene receptor antagonist was initiated for pollen allergy. Sublingual immunotherapy (SLIT) for Japanese cedar pollen was initiated because the patient experienced severe nasal allergy symptoms during the dispersal season of this pollen. These treatments alleviated the nasal symptoms; however, the lip edema persisted. Omalizumab administration improved the lip edema. The combination of SLIT and omalizumab may be an effective treatment option for patients with PFAS.

**Keywords:** Allergic rhinitis; Omalizumab; Pollen-food allergy syndrome (PFAS); Sublingual immunotherapy (SLIT).



# Conflict of interest statement

Declaration of Competing Interest The authors have no conflicts of interest to declare.

## supplementary info

Publication types, MeSH terms, Substancesexpand

## full text links

14

Ear Nose Throat J

. 2023 Oct;102(10):654-660.

doi: 10.1177/01455613211018576. Epub 2021 Jun 15.

# The Impact of Surgical Posterior Nasal Nerve Cryoablation on Symptoms and Disease-Specific Quality of Life in Patients With Chronic Rhinitis

Farrukh R Virani[1], Machelle D Wilson[2], Angela M Beliveau[1], Amarbir S Gill[1], E Bradley Strong[1], Toby O Steele[1,3]

Affiliations expand

- PMID: 34128402
- PMCID: PMC8958794 (available on 2024-10-01)
- DOI: 10.1177/01455613211018576

**Abstract**

**Objective:** Preliminary data have demonstrated long-term efficacy of posterior nasal nerve (PNN) cryoablation in reducing rhinitis symptoms for patients with allergic rhinitis (AR) and nonallergic rhinitis (NAR). We sought to evaluate the impact of procedural cryoablation of the PNN on quality of life (QOL) in patients with AR and NAR.

**Methods:** Adult patients undergoing PNN cryoablation for AR or NAR after appropriate medical therapy were included for analysis. Demographics, medical therapies, baseline rhinitis symptom (total nasal symptom score [TNSS]), and disease-specific QOL (mini-rhinoconjunctivitis quality of life questionnaire [mini-RQLQ]) were recorded. The Wilcoxon signed-rank test was used to test for significant changes in baseline test scores posttreatment. Absolute and relative improvement in outcomes was determined for each participant. Secondary outcomes were assessed with univariate and multivariate analyses.

**Results:** Fourteen patients were enrolled with a mean follow-up of 16.5 weeks. The TNSS and mini-RQLQ scores significantly improved after PNN cryoablation (median δs [interquartile range]: -4 [3] and -1.61 [1.08], respectively; both *P* = .0002). The minimal clinically important difference for the TNSS and mini-RQLQ was obtained in 92.9% of patients in each category. Relative mean percentage (%) improvement after PNN cryoablation in the TNSS and mini-RQLQ was 40.7% and 40.5% (standard deviation = 24.9 and 29.5, respectively), respectively, for all patients. Patients with NAR (n = 10) reported mean improvement of 41.3% (29.1) as measured by the TNSS and 49.6% (25.9) by mini-RQLQ. Patients with AR reported mean percentage improvement in TNSS and mini-RQLQ scores of 39.5% (12.1) and 24.6% (28.5), respectively. Patients who had been prescribed a nasal anticholinergic for management prior to PNN cryoablation had statistically significantly increased improvement in mini-RQLQ scores from pre- to post-procedure (*P* = .0387).

**Conclusion:** Surgical cryoablation of the PNN significantly improves both symptoms and disease-specific QOL in majority of patients with AR and NAR.

**Keywords:** allergic rhinitis; chronic rhinitis; cryoablation; mixed rhinitis; nonallergic rhinitis; posterior nasal nerve; quality of life.



# Chronic cough

1

Eur J Pediatr

- 
- 
- 

. 2023 Sep 30.

doi: 10.1007/s00431-023-05202-x. Online ahead of print.

# School children brief training to save foreign body airway obstruction

Santiago Martínez-Isasi[1,2,3,4], Aida Carballo-Fazanes[5,6,7,8], Cristina Jorge-Soto[1,2,3], Martín Otero-Agra[9,10], Felipe Fernández-Méndez[1,9,10], Roberto Barcala-Furelos[9], Verónica Izquierdo[2,4], María García-Martínez[11], Antonio Rodríguez-Núñez[1,2,3,4,12]

Affiliations expand

- PMID: 37777603

- DOI: 10.1007/s00431-023-05202-x

**Abstract**

Foreign body airway obstruction (FBAO) is a relatively common emergency and a potential cause of sudden death both in children and older people; bystander immediate action will determine the victim's outcome. Although many school children's basic life support (BLS) training programs have been implemented in recent years, references to specific training on FBAO are lacking. Therefore, the aim was to assess FBAO-solving knowledge acquisition in 10-13-year-old school children. A quasi-experimental non-controlled simulation study was carried out on 564 ten-to-thirteen-year-old children from 5 schools in Galicia (Spain). Participants received a 60-min training led by their physical education teachers (5 min theory, 15 min demonstration by the teacher, and 30 min hands-on training) on how to help to solve an FBAO event. After the training session, the school children's skills were assessed in a standardized adult's progressive FBAO simulation scenario. The assessment was carried out by proficient researchers utilizing a comprehensive checklist specifically designed to address the variables involved in resolving a FBAO event according with current international guidelines. The assessment of school children's acquired knowledge during the simulated mild FBAO revealed that 62.2% of participants successfully identified the event and promptly encouraged the simulated patient to cough actively. When the obstruction progressed, its severity was recognized by 86.2% and back blows were administered, followed by abdominal thrusts by 90.4%. When the simulated victim became unconscious, 77.1% of children identified the situation and immediately called the emergency medical service and 81.1% initiated chest compressions. No significant differences in performance were detected according to participants' age. Conclusion: A brief focused training contributes to prepare 10-13-year-old school children to perform the recommended FBAO steps in a standardized simulated patient. We consider that FBAO should be included in BLS training programs for school children. What is Known: • Kids Save Lives strategy states that school children should learn basic life support (BLS) skills because of their potential role as first responders. • This BLS training does not include content for resolving a foreign body airway obstruction (FBAO). What is New: • Following a 60-min theoretical-practical training led by physical education teachers, 10-13-year-old

school children are able to solve a simulated FBAO situation. • The inclusion of FBAO content in BLS training in schools should be considered.

**Keywords:** Airway obstruction; Basic life support; Kids save Lives; School; Teachers; Training.



- 37 references

supplementary info

Grants and fundingexpand

full text links

Proceed to details

Cite

Share

2

Laryngoscope

- 
- 
- 

. 2023 Sep 29.

doi: 10.1002/lary.31072. Online ahead of print.

# Efficacy of Botulinum A Injection to the Laryngeal Adductor Compartment for Treatment of Cough

Brett A Campbell[1,2], Victoria B Flormann[2], Roger B Davis[3,4], Pavan S Mallur[1,2]

Affiliations expand

- PMID: 37772912

- DOI: 10.1002/lary.31072

**Abstract**

**Objectives:** Studies examining electromyography (EMG)-guided laryngeal onobotulinumtoxinA (BTxA) injection for chronic cough reveal promising efficacy, however, are limited by small cohorts and absent quantifiable outcomes. It further remains unclear if pulmonary disease limits efficacy, or if vagal motor neuropathy prognosticates response. We hypothesize BTxA injection results in qualitative improvement in cough, decrease in Cough Severity Index (CSI), no change in Voice Handicap Index-10 (VHI-10), and complication rates comparable to historical data. We also examine the correlation of pulmonary comorbidities and vocal fold hypomobility with treatment efficacy.

**Study design:** Retrospective review.

**Methods:** Charts for patients receiving percutaneous adductor compartment BTxA injection for cough were reviewed for the binary outcome of patient-reported presence or absence of improvement. Generalized estimating equations regression models were used to analyze the change in CSI (ΔCSI) and the correlation of ΔCSI with qualitative outcomes. Multivariable analyses were used to examine correlation of vocal fold hypomobility and pulmonary disease with qualitative outcomes and ΔCSI.

**Results:** Forty-seven patients underwent 197 BTxA injections from June 2012 to June 2022. A statistical proportion of 0.698 (0.599-0.813, $p < 0.0001$) or 69.8% of injections resulted in subjective improvement. Mean ΔCSI was -2.12 (0.22-4.02, $p < 0.05$), indicating overall improvement. With and without subjective improvement, estimated ΔCSI was -4.43 and +2.68, respectively ($p < 0.0001$). VHI-10 did not change (0.69, $p = 0.483$). Neither pulmonary disease nor vocal fold hypomobility correlated with subjective improvement or ΔCSI. Dysphagia occurred following 15 (7.6%) injections with no aspiration pneumonia or hospitalization.

**Conclusions:** BTxA injection to the laryngeal adductors may effectively treat cough with limited risk for serious complications.

**Level of evidence:** 4 Laryngoscope, 2023.

**Keywords:** Botox; botulinum toxin; cough; laryngeal hypersensitivity; neurogenic; post-viral vagal neuropathy.



- 30 references

supplementary info

Grants and fundingexpand

3

ERJ Open Res

. 2023 Sep 25;9(5):00425-2023.

doi: 10.1183/23120541.00425-2023. eCollection 2023 Sep.

# Burden of refractory and unexplained chronic cough on patients' lives: a cohort study

Luis Puente-Maestu[1], Ignacio Dávila[2], Santiago Quirce[3], Astrid Crespo-Lessmann[4], Eva Martínez-Moragón[5], Javier Sola[6], María Luisa Nieto[7], Francisco Javier González-Barcala[8], Luis Cea-Calvo[9], Marta Sánchez-Jareño[9], Cristina Rivas-Pardinas[9], Christian Domingo[10]

Affiliations expand

- PMID: 37753282

- PMCID: PMC10518856

- DOI: 10.1183/23120541.00425-2023

**Free PMC article**

## Abstract

**Background:** Chronic cough (cough lasting for ≥8 weeks) can lead to significant impairment in quality of life (QoL). Using patient-reported outcomes, this cohort study

assessed the perceived impact of chronic cough on QoL and everyday life in patients from outpatient hospital clinics with refractory chronic cough (RCC) or unexplained chronic cough (UCC).

**Methods:** This was a multicentre, non-interventional survey study. Cough severity was assessed on a 0-100 mm Visual Analogue Scale (VAS). Frequency, intensity and disruptiveness of cough were assessed using an adaptation of the Cough Severity Diary. The impact of cough on QoL was assessed using the Leicester Cough Questionnaire (LCQ). The physical impact of cough and associated impact on everyday life activities were explored using purpose-designed questions.

**Results:** 191 patients responded to the survey; 121 (63.4%) had RCC and 149 were women (78.0%). Mean score on the cough severity VAS was 62.9 mm. Mean LCQ total score of 11.9 indicated reduced QoL. Cough impaired patients' everyday life, including the inability to speak fluently (58.0% of patients) and feeling tired/drained (46.6%). Women perceived poorer chronic cough-related QoL than men, as reflected by lower LCQ scores, and greater impairment of physical health, including cough-related stress urinary incontinence, and psychological health.

**Conclusions:** Patients with RCC/UCC experience a significant burden in their everyday life, including impaired QoL, and perceive a negative impact on physical and psychological health and everyday activities, affecting work, relationships and leisure activities. The impact appears to be greater in women than men for several of the aspects studied.



# Conflict of interest statement

Conflict of interest: S. Quirce has received advisory board and speaker's honoraria from ALK, Allergy Therapeutics, AstraZeneca, Chiesi, GlaxoSmithKline, Leti, Mundipharma, Novartis, Sanofi and Teva. Conflict of interest: I. Dávila has received consultant's honoraria from Allergy Therapeutics, AstraZeneca, MSD, GlaxoSmithKline, Novartis and Sanofi. Conflict of interest: E. Martínez-Moragón has received consultant and speaker's honoraria from AstraZeneca, Sanofi, GlaxoSmithKline, Bial and FAES. Conflict of interest: A. Crespo-Lessman has received consultant's honoraria from AstraZeneca, Sanofi and GlaxoSmithKline, and grants from AstraZeneca and GlaxoSmithKline. Conflict of interest: C. Domingo has received consultant and speaker's honoraria from MSD, Novartis, Boehringer, Sanofi, TEVA, AstraZeneca, ALK and Allergy Therapeutics. Conflict of interest: F.J. González-Barcala has received consulting fees and speaker's honoraria from ALK, AstraZeneca, Bial, Chiesi, GebroPharma, GlaxoSmithKline, Menarini, Novartis, Rovi, Roxall, Sanofi, Stallergenes-Greer and Teva, and is an associate editor of this journal. Conflict of interest: L. Cea-Calvo, M. Sánchez-Jareño and C. Rivas-Pardiñas are full-time employees of MSD Spain. Conflict of interest: The authors have no other financial or nonfinancial competing interests.

- 34 references
- 1 figure

full text links

Proceed to details

Cite

Share

4

ERJ Open Res

. 2023 Sep 25;9(5):00736-2022.

doi: 10.1183/23120541.00736-2022. eCollection 2023 Sep.

# Impulse oscillometry indices in relation to respiratory symptoms and spirometry in the Swedish Cardiopulmonary Bioimage Study

Björn Qvarnström[1], Gunnar Engström[2], Sophia Frantz[3], Xingwu Zhou[1,4], Suneela Zaigham[1,2], Johan Sundström[5], Christer Janson[4], Per Wollmer[3], Andrei Malinovschi[1]

Affiliations expand

- PMID: 37753278
- PMCID: PMC10518858
- DOI: 10.1183/23120541.00736-2022

**Free PMC article**

**Abstract**

**Background:** Impulse oscillometry (IOS) is sensitive in detecting lung function impairment. In small studies, impaired IOS relates better to respiratory symptoms than spirometry. We studied how IOS related to spirometry and respiratory symptoms in a large population of individuals (n=10 360) in a cross-sectional analysis.

**Methods:** Normal values for IOS and spirometry were defined in healthy, never-smoking individuals, aged 50-64 years, from the Swedish CArdioPulmonary bioImage Study (n=3664 for IOS and 3608 for spirometry). For IOS, abnormal values for resistance at 5 Hz ($R_5$) and at 20 Hz and area of reactance were defined using the 95th percentile. Abnormal reactance at 5 Hz for IOS and abnormal conventional spirometry indices (forced expiratory volume in 1 s ($FEV_1$), forced and slow vital capacity and their ratios) were defined using the 5th percentile.

**Results:** Abnormal IOS parameters were found in 16% of individuals and were associated with increased odds ratios for nearly all respiratory symptoms when adjusted for age, gender and smoking. In individuals with normal spirometry, abnormal IOS resistance was related to cough and dyspnoea, while abnormal reactance was related to wheeze. In these individuals, the combination of abnormal $R_5$ with abnormal reactance resulted in approximately two-fold higher likelihood for having cough, chronic bronchitis and dyspnoea, even when further adjusting for $FEV_1$, expressed as % predicted.

**Conclusions:** Abnormal IOS is related to increased respiratory burden in middle-aged individuals with normal spirometry, especially when resistance and reactance parameters are combined. The different relationships between respiratory symptoms and reactance and resistance warrant further research.



# Conflict of interest statement

Conflict of interest: J. Sundström reports stock or stock options in Anagram Kommunikation AB and Symptoms Europe AB, not related to the present work. Conflict of interest: P. Wollmer reports personal fees from Chiesi Pharmaceuticals outside the submitted work, has a patent for a device and method for pulmonary capacity measurements issued, not related to the present work. Conflict of interest: All other authors declare no conflicts of interest with regard to the present study.

- 47 references
- 2 figures

full text links

5

Laryngoscope

. 2023 Sep 26.

doi: 10.1002/lary.31061. Online ahead of print.

# The Role of Bilateral Superior Laryngeal Nerve Block in Managing Refractory Chronic Cough

Brooke A Quinton[1], William S Tierney[2], Michael S Benninger[2], Rebecca C Nelson[2], Victoria L Gau[2], Candace M Hrelec[2], Paul C Bryson[1,2]

Affiliations expand

- PMID: 37750560

- DOI: 10.1002/lary.31061

**Abstract**

**Objective(s):** The aim was to investigate the utilization and efficacy of bilateral superior laryngeal nerve block in patients with refractory chronic cough.

**Methods:** A retrospective chart review of 164 patients with refractory chronic cough who underwent bilateral SLN block at a single institution between November 2018 and September 2022 was performed. Demographics, comorbidities, and patient-reported outcomes including pre- and postinjection Leicester Cough Questionnaire (LCQ) scores were collected and analyzed.

**Results:** The cohort underwent an average of 2.97 bilateral injections (range 1-22), containing either corticosteroid and local anesthetic or corticosteroid alone. Notably, 116 of 164 of patients reported an average of 67.3% reduction in their symptoms, with the treatment effect lasting 7.60 weeks on average. The average pre- and postinjection LCQ scores were 9.70 and 13.82, respectively. A lower LCQ score represents a greater impairment of health status due to cough, and the minimum important change is 1.3 points between questionnaires. The average improvement on LCQ following bilateral SLN block was 4.11 points for this cohort.

**Conclusion:** The use of in-office bilateral SLN block is an effective treatment that can be used alone or in conjunction with oral medications for the treatment of refractory chronic cough.

**Level of evidence:** 4 Laryngoscope, 2023.

**Keywords:** laryngeal hypersensitivity; laryngology; refractory chronic cough; superior laryngeal nerve block.





6

Eur Respir Rev

. 2023 Sep 6;32(169):230034.

doi: 10.1183/16000617.0034-2023. Print 2023 Sep 30.

# The role of vaccination in COPD: influenza, SARS-CoV-2, pneumococcus, pertussis, RSV and varicella zoster virus

Susanne Simon[1], Oana Joean[1], Tobias Welte[2,3], Jessica Rademacher[1,3]

Affiliations expand

- PMID: 37673427
- PMCID: PMC10481333
- DOI: 10.1183/16000617.0034-2023

**Free PMC article**

**Abstract**

Exacerbations of COPD are associated with worsening of the airflow obstruction, hospitalisation, reduced quality of life, disease progression and death. At least 70% of COPD exacerbations are infectious in origin, with respiratory viruses identified in approximately 30% of cases. Despite long-standing recommendations to vaccinate patients with COPD, vaccination rates remain suboptimal in this population.*Streptococcus pneumoniae* is one of the leading morbidity and mortality causes of lower respiratory tract infections. The Food and Drug Administration recently approved pneumococcal conjugate vaccines that showed strong immunogenicity against all 20 included serotypes. Influenza is the second most common virus linked to severe acute exacerbations of COPD. The variable vaccine efficacy across virus subtypes and the impaired immune response are significant drawbacks in the influenza vaccination strategy. High-dose and adjuvant vaccines are new approaches to tackle these problems. Respiratory syncytial virus is another virus known to cause acute exacerbations of COPD. The vaccine candidate RSVPreF3 is the first authorised for the prevention of RSV in adults ≥60 years and might help to reduce acute exacerbations of COPD. The 2023 Global Initiative for Chronic Lung Disease report recommends zoster vaccination to protect against shingles for people with COPD over 50 years.



## Conflict of interest statement

Conflict of interest: T. Welte reports support for the present manuscript from German Ministry of Research and Education; grants or contracts from Bavaria Nordisk, outside the submitted work; payment or honoraria from Janssen, GSK, MSD and Pfizer, outside the submitted work; and is a current editorial board member for European Respiratory Review. J. Rademacher reports receiving payment or honoraria from GSK and MSD, outside the submitted work. The remaining authors have nothing to disclose.

## Comment in

- doi: 10.1183/16000617.0028-2023
- 146 references
- 1 figure

supplementary info

MeSH terms, Substancesexpand

full text links

Proceed to details

Cite

Share

7

Tuberc Respir Dis (Seoul)

. 2023 Oct;86(4):264-271.

doi: 10.4046/trd.2023.0036. Epub 2023 Aug 11.

# State of the Art for Refractory Cough: Multidisciplinary Approach

Anne E Vertigan[1 2 3]

Affiliations expand

- PMID: 37582675

- DOI: 10.4046/trd.2023.0036


**Free article**


## Abstract

Chronic cough is a common problem that can be refractory to medical treatment. Nonpharmaceutical management of chronic cough has an important role in well selected patients. This review article outlines the history of chronic cough management, current approaches to speech pathology management of the condition and new modalities of nonpharmaceutical treatment. There is a need for further research into nonpharmaceutical options with well described randomised control trials.



**Keywords:** Chronic Cough; Inducible Laryngeal Obstruction; Nonpharmaceutical; Speech Pathology; Vocal Cord Dysfunction.




**Review**


Respir Med

- 
- 
- 

. 2023 Oct;217:107336.

doi: 10.1016/j.rmed.2023.107336. Epub 2023 Jun 25.

# Potential applications of P2X3 receptor antagonists in the treatment of refractory cough

Baiyi Yi[1], Shengyuan Wang[1], Wanzhen Li[1], Xianghuai Xu[2], Li Yu[3]

Affiliations expand

- PMID: 37364722

- DOI: 10.1016/j.rmed.2023.107336

**Abstract**

Refractory chronic cough is defined as a clinical condition in which the cause of the cough remains unclear after comprehensive examination and treatment, or the cause is clear but symptomatic treatment is ineffective. Patients with refractory chronic cough experience a variety of physiological and psychological issues that significantly lower their quality of life and place a significant socio-economic burden on society. As a result, research both domestically and internationally has turned heavily toward these patients. Recently, several studies have identified P2X3 receptor antagonists for the treatment of refractory chronic cough, and this paper reviews the background, mechanism of action, evidence-based proof and application prospects of this class of drugs. KEY MESSAGE: There were plenty of studies about P2X3 receptor antagonists in the past, and in recent years this series of drugs are effective in refractory chronic cough. Although review articles summarizing have been published previously, most have focused on their chemical properties rather than their clinical aspects, with some omitting drugs that have been in clinical studies for nearly two years such as Eliapixant and Sivopixant. Focusing on four P2X3 receptor antagonists with proven efficacy in clinical studies, we analyzed the characteristics and disadvantages of each drug by comparing their clinical results of them and theoretically explained the common side effects of these drugs, as well as their potential for treating refractory chronic cough. This article can be used as a reference for the follow-up studies of P2X3 receptor antagonists in chronic cough. Additionally, it also has implications for the clinical focus of the drug and the approaches to relieve some side effects.

**Keywords:** Cough; Pharmacotherapy; Purinergic receptor P2X3; Quality of life.



## Conflict of interest statement

Declaration of competing interest The authors of the manuscript entitled “Potential applications of P2X3 receptor antagonists in the treatment of refractory cough”declare that they have no competing interests.

- Cited by 1 article

supplementary info

Publication typesexpand

full text links

Proceed to details

Cite

Share

9

**Review**

J Microbiol Biotechnol

. 2023 Sep 28;33(9):1111-1118.

doi: 10.4014/jmb.2301.01033. Epub 2023 Mar 30.

# Gut Microbiome as a Possible Cause of Occurrence and Therapeutic Target in Chronic Obstructive Pulmonary Disease

Eun Yeong Lim[1], Eun-Ji Song[1], Hee Soon Shin[1,2]

Affiliations expand

- PMID: 37164760

- DOI: 10.4014/jmb.2301.01033

**Free article**

**Abstract**

As a long-term condition that affects the airways and lungs, chronic obstructive pulmonary disease (COPD) is characterized by inflammation, emphysema, breathlessness, chronic cough, and sputum production. Currently, the bronchodilators and anti-inflammatory drugs prescribed for COPD are mostly off-target, warranting new disease management strategies. Accumulating research has revealed the gut-lung axis to be a bidirectional communication system. Cigarette smoke, a major exacerbating factor in COPD and lung inflammation, affects gut microbiota composition and diversity, causing gut microbiota dysbiosis, a condition that has recently been described in COPD patients and animal models. For this review, we focused on the gut-lung axis, which is influenced by gut microbial metabolites, bacterial translocation, and immune cell modulation. Further, we have summarized the findings of preclinical and clinical studies on the association between gut microbiota and COPD to provide a basis for using gut microbiota in therapeutic strategies against COPD. Our review also proposes that further research on probiotics, prebiotics, short-chain fatty acids, and fecal microbiota transplantation could assist therapeutic approaches targeting the gut microbiota to alleviate COPD.

**Keywords:** Gut microbiota; chronic obstructive pulmonary disease; fecal microbiota transplantation; prebiotics; probiotics; short-chain fatty acids.

doi: 10.1016/j.rmed.2023.107417. Online ahead of print.

# Multiple bacterial culture positivity reflects the severity and prognosis as bronchiectasis in Mycobacterium avium complex pulmonary disease

Masashi Ito[1], Koji Furuuchi[2], Keiji Fujiwara[2], Fumiya Watanabe[3], Tatsuya Kodama[2], Fumiko Uesugi[1], Yoshiaki Tanaka[1], Takashi Yoshiyama[1], Atsuyuki Kurashima[1], Ken Ohta[1], Kozo Morimoto[4]

Affiliations expand

- PMID: 37775085

- DOI: 10.1016/j.rmed.2023.107417

**Abstract**

**Background:** Bacterial coinfections are observed in 19-66% of patients with Mycobacterium avium complex pulmonary disease (MAC-PD) during the entire duration of the disease. The impact of bacterial coinfection at diagnosis on the clinical course of MAC-PD has not been reported.

**Methods:** Among 558 patients diagnosed with MAC-PD between January 2016 and December 2020, 218 patients who underwent sputum culture tests twice or more within one year before and after diagnosis were included. We compared the patient characteristics and disease courses between the patients who had the same bacterial species detected twice or more (bacterial culture positive group: BCP group) and those who never had bacteria cultured (bacterial culture negative group: BCN group).

**Results:** We included 70 patients in the BCP group and 74 in the BCN group. The radiological findings showed that BCP at diagnosis correlated with a high modified Reiff score. During the median follow-up period of 42 months, the patients in the BCP group were more likely to accomplish spontaneous sputum conversion of MAC. The treatment initiation rate for MAC-PD in the BCP group was lower than that in the BCN group (41.4% vs. 67.6%, P = 0.003). In contrast, the time to the first bronchiectasis exacerbation in the BCP group was shorter than that in the BCN group, and the frequency of bronchiectasis exacerbations was higher in the BCP group.

**Conclusions:** Patients with BCP at diagnosis are less likely to initiate treatment for MAC-PD and more likely to develop bronchiectasis exacerbation.

**Keywords:** Bronchiectasis; Mycobacterium avium complex; Nontuberculous mycobacteria; Pseudomonas aeruginosa; Staphylococcus aureus.



## Conflict of interest statement

Declaration of competing interest All authors declare that they have none interest.



2

Am J Respir Crit Care Med

- 
- 
- 

. 2023 Sep 28.

doi: 10.1164/rccm.202303-0499OC. Online ahead of print.

# Inflammatory Molecular Endotypes in Bronchiectasis: A European Multicenter Cohort Study

Hayoung Choi[1,2], Soorack Ryu[3], Holly R Keir[4], Yan Hui Giam[2], Alison J Dicker[5], Lidia Perea[6], Hollian Richardson[7], Jeffrey T J Huang[8], Erin Cant[7], Francesco Blasi[9,10], Jennifer Pollock[4], Michal Shteinberg[11,12], Simon Finch[13], Stefano Aliberti[14,15], Oriol Sibila[16], Amelia Shoemark[17,13], James D Chalmers[18]

Affiliations expand

- PMID: 37769155

- DOI: 10.1164/rccm.202303-0499OC

## Abstract

**Rationale:** Although inflammation and infection are key disease drivers in bronchiectasis, few studies have integrated host inflammatory and microbiome data to guide precision medicine.

**Objectives:** To identify clusters among bronchiectasis patients based on inflammatory markers and assess the association between inflammatory endotypes, microbiome characteristics, and exacerbation risk.

**Methods:** Stable bronchiectasis patients were enrolled at three European centers and cluster analysis was used to stratify the patients according to the levels of 33 sputum and serum inflammatory markers. Clusters were compared in terms of microbiome composition (16S rRNA sequencing) and exacerbation risk over 12 months follow-up.

**Measurements and main results:** 199 patients were enrolled (109 [54.8%] female, median age 69 years). Four clusters of patients were defined according to their inflammatory profiles: cluster 1 (milder neutrophilic inflammation), cluster 2 (mixed-neutrophilic and type 2), cluster 3 (most severe neutrophilic), and cluster 4 (mixed-epithelial and type 2). Lower microbiome diversity was associated with more severe inflammatory clusters ($P<0.001$), and beta-diversity analysis demonstrated distinct microbiome profiles associated with each inflammatory cluster ($P=0.001$). Proteobacteria and Pseudomonas at phylum and genus levels, respectively, were more enriched in clusters 2 and 3 than in clusters 1 and 4. Furthermore, patients in clusters 2 (rate ratio [RR] 1.49, 95% CI 1.16-1.92) and 3 (RR 1.61, 95% CI 1.12-2.32) were at higher risk of exacerbation over 12 months follow-up compared to cluster 1 even after adjustment for prior exacerbation history.

**Conclusion:** Bronchiectasis inflammatory endotypes are associated with distinct microbiome profiles and future exacerbation risk.

**Keywords:** biomarkers; bronchiectasis; cluster analysis; inflammation; microbiome.

. 2023 Sep 26;16(9):e255845.

doi: 10.1136/bcr-2023-255845.

# Simultaneous diagnosis of allergic bronchopulmonary aspergillosis and *Mycobacterium avium* complex lung disease

Naoki Takasaka[1], Kentaro Chida[2], Takeo Ishikawa[2], Kazuyoshi Kuwano[3]

Affiliations expand

- PMID: 37751982

- PMCID: PMC10533704

- DOI: 10.1136/bcr-2023-255845

**Free PMC article**

## Abstract

Allergic bronchopulmonary aspergillosis (ABPA) and *Mycobacterium avium* complex lung disease (MAC-LD) often coexist because bronchiectasis, caused by ABPA or MAC, might be an important predisposing factor for both conditions. Here, we describe a man with asthma symptoms who had centrilobular small nodules and mucoid impaction on chest CT. We diagnosed the patient with simultaneous ABPA and MAC-LD on the basis of bronchoscopy findings. Itraconazole monotherapy led to substantial clinical improvement, avoiding the adverse effects of systemic corticosteroids. Sputum culture conversion of MAC was achieved after switching from itraconazole monotherapy to combination therapy comprising clarithromycin, rifampicin and ethambutol. ABPA recurred but was controlled by reinitiation of itraconazole. Overall, corticosteroid management was avoided for 38 months. Itraconazole monotherapy may be selected as initial treatment for ABPA with chronic infection, including MAC.

**Keywords:** Asthma; Bronchitis; Infections; Pneumonia (infectious disease).

## Conflict of interest statement

Competing interests: None declared.

- 29 references
- 3 figures

full text links

Proceed to details

Cite

Share

4

JDR Clin Trans Res

. 2023 Sep 25;23800844231196884.

doi: 10.1177/23800844231196884. Online ahead of print.

# Periodontal Effects of the Reversible Dipeptidyl Peptidase 1 Inhibitor Brensocatib in Bronchiectasis

J C Gunsolley[1], J D Chalmers[2], O Sibila[3], C Fernandez[4], F A Scannapieco[5]

Affiliations expand

- PMID: 37746735

- DOI: 10.1177/23800844231196884

Free article


## Abstract

**Aims:** Brensocatib is a reversible inhibitor of dipeptidyl peptidase 1 (cathepsin C), in development to treat chronic non-cystic fibrosis bronchiectasis. The phase 2, randomized, placebo-controlled WILLOW trial (NCT03218917) was conducted to examine whether brensocatib reduced the incidence of pulmonary exacerbations. Brensocatib prolonged the time to the first exacerbation and led to fewer exacerbations than placebo. Because brensocatib potentially affects oral tissues due to its action on neutrophil-mediated inflammation, we analyzed periodontal outcomes in the trial participants.

**Materials and methods:** Patients with bronchiectasis were randomized 1:1:1 to receive once-daily oral brensocatib 10 or 25 mg or placebo. Periodontal status was monitored throughout the 24-week trial in a prespecified safety analysis. Periodontal pocket depth (PPD) at screening, week 8, and week 24 was evaluated. Gingival inflammation was evaluated by a combination of assessing bleeding upon probing and monitoring the Löe-Silness Gingival Index on 3 facial surfaces and the mid-lingual surface.

**Results:** At week 24, mean ± SE PPD reductions were similar across treatment groups: -0.07 ± 0.007, -0.06 ± 0.007, and -0.15 ± 0.007 mm with brensocatib 10 mg, brensocatib 25 mg, and placebo, respectively. The distribution of changes in PPD and the number of patients with multiple increased PPD sites were similar across treatment groups at weeks 8 and 24. The frequencies of gingival index values were generally similar across treatment groups at each assessment. An increase in index values 0-1 and a decrease in index values 2-3 over time and at the end of the study were observed in all groups, indicating improved oral health.

**Conclusions:** In patients with non-cystic fibrosis bronchiectasis, brensocatib 10 or 25 mg had an acceptable safety profile after 6 months' treatment, with no changes in periodontal status noted. Improvement in oral health at end of the study may be due to regular dental care during the trial and independent of brensocatib treatment.

**Knowledge transfer statement:** The results of this study suggest that 24 weeks of treatment with brensocatib does not affect periodontal disease progression. This information can be used by clinicians when considering treatment approaches for bronchiectasis and suggests that the use of brensocatib will not be limited by periodontal disease risks. Nevertheless, routine dental/periodontal care should be provided to patients irrespective of brensocatib treatment.



**Keywords:** clinical trial; elastase; immunology; inflammation mediators; neutrophils; pathogenesis.

Proceed to details

Cite

Share

5

**Review**

Eur Respir Rev

- 
- 
- 

. 2023 Aug 9;32(169):220253.

doi: 10.1183/16000617.0253-2022. Print 2023 Sep 30.

# Post-COVID-19 dyspnoea and pulmonary imaging: a systematic review and meta-analysis

Elizabeth Guinto[1], Firoozeh V Gerayeli[1], Rachel L Eddy[1,2], Hyun Lee[1,3], Stephen Milne[1,2,4], Don D Sin[5,2]

Affiliations expand

- PMID: 37558261

- PMCID: PMC10410398

- DOI: 10.1183/16000617.0253-2022

**Free PMC article**

## Abstract

**Background:** A proportion of coronavirus disease 2019 (COVID-19) survivors experience persistent dyspnoea without measurable impairments in lung function. We performed a

systematic review and meta-analysis to determine relationships between dyspnoea and imaging abnormalities over time in post-COVID-19 patients.

**Methods:** Using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, we analysed studies published prior to 15 September 2022 and indexed by Google Scholar, PubMed and LitCOVID which assessed chest imaging in adults ≥3 months after COVID-19. Demographic, chest imaging, spirometric and post-COVID-19 symptom data were extracted. The relationships between imaging abnormalities and dyspnoea, sex and age were determined using a random effects model and meta-regression.

**Results:** 47 studies were included in the meta-analysis (n=3557). The most prevalent computed tomography (CT) imaging abnormality was ground-glass opacities (GGOs) (44.9% (95% CI 37.0-52.9%) at any follow-up time-point). Occurrence of reticulations significantly decreased between early and late follow-up (p=0.01). The prevalence of imaging abnormalities was related to the proportion of patients with dyspnoea (p=0.012). The proportion of females was negatively correlated with the presence of reticulations (p=0.001), bronchiectasis (p=0.001) and consolidations (p=0.025). Age was positively correlated with imaging abnormalities across all modalities (p=0.002) and imaging abnormalities present only on CT (p=0.001) (GGOs (p=0.004) and reticulations (p=0.001)). Spirometric values improved during follow-up but remained within the normal range at all time-points.

**Conclusions:** Imaging abnormalities were common 3 months after COVID-19 and their occurrence was significantly related to the presence of dyspnoea. This suggests that CT imaging is a sensitive tool for detecting pulmonary abnormalities in patients with dyspnoea, even in the presence of normal spirometric measurements.



# Conflict of interest statement

Conflict of interest: R.L. Eddy receives personal consulting fees from VIDA Diagnostics Inc., and lecture honoraria from AstraZeneca, outside the submitted work. S. Milne reports grants from British Columbia Lung Association, CHEST Foundation, Genome British Columbia, Mitacs and Michael Smith Health Research BC, and financial support from Chiesi Australia, outside the submitted work. D.D. Sin has received an honorarium for speaking engagements for COPD from GSK, AstraZeneca and Boehringer Ingelheim, and chairs a DSMB for an NHLBI-sponsored clinical trial in COPD, outside the submitted work. E. Guinto, F.V. Gerayeli and H. Lee do not declare any conflicts of interest.

- 88 references
- 4 figures

**Review**

Allergol Int

- 
- 
- 

. 2023 Oct;72(4):493-506.

doi: 10.1016/j.alit.2023.07.003. Epub 2023 Aug 4.

# Poorly controlled asthma - Easy wins and future prospects for addressing fungal allergy

David W Denning[1], Lorraine T Pfavayi[2]

Affiliations expand

- PMID: 37544851

- DOI: 10.1016/j.alit.2023.07.003

**Abstract**

Poorly controlled asthma is especially common in low resource countries. Aside from lack of access to, or poor technique with, inhaled beta-2 agonists and corticosteroids, the most

problematic forms of asthma are frequently associated with both fungal allergy and exposure, especially in adults leading to more asthma exacerbations and worse asthma. The umbrella term 'fungal asthma' describes many disorders linked to fungal exposure and/or allergy to fungi. One fungal asthma endotype, ABPA, is usually marked by a very high IgE and its differential diagnosis is reviewed. Both ABPA and fungal bronchitis in bronchiectasis are marked by thick excess airway mucus production. Dermatophyte skin infection can worsen asthma and eradication of the skin infection improves asthma. Exposure to fungi in the workplace, home and schools, often in damp or water-damaged buildings worsens asthma, and remediation improves symptom control and reduces exacerbations. Antifungal therapy is beneficial for fungal asthma as demonstrated in nine of 13 randomised controlled studies, reducing symptoms, corticosteroid need and exacerbations while improving lung function. Other useful therapies include azithromycin and some biologics approved for the treatment of severe asthma. If all individuals with poorly controlled and severe asthma could be 'relieved' of their fungal allergy and infection through antifungal therapy without systemic corticosteroids, the health benefits would be enormous and relatively inexpensive, improving the long term health of over 20 million adults and many children. Antifungal therapy carries some toxicity, drug interactions and triazole resistance risks, and data are incomplete. Here we summarise what is known and what remains uncertain about this complex topic.

**Keywords:** Antifungal; Aspergillosis; Aspergillus; Bronchitis; IgE.

. 2023 Oct;217:107366.

doi: 10.1016/j.rmed.2023.107366. Epub 2023 Jul 20.

# Monotherapy: Key cause of macrolide-resistant Mycobacterium avium complex disease

Daniel Loewenstein[1], Lars van Balveren[1], Arthur Lemson[2], Nicolien Hanemaaijer[1], Wouter Hoefsloot[2], Jakko van Ingen[3]

Affiliations expand

- PMID: 37481170

- DOI: 10.1016/j.rmed.2023.107366

**Free article**

**Abstract**

**Background:** Macrolide-resistant Mycobacterium avium complex (MAC) disease is very difficult to cure. Macrolide-resistance emerges in patients and is largely preventable by appropriate screening and treatment practices.

**Methods:** Patients with macrolide-resistant MAC isolates between March 2019 and March 2022 were retrieved from the mycobacteriology reference laboratory database at Radboudumc, Nijmegen, the Netherlands. Clinical consultation reports were extracted from the database to assess the cause of macrolide resistance.

**Results:** Sixteen patients with macrolide-resistant MAC disease were included, from a total of 815 patients with MAC isolates (2%); Macrolide monotherapy in bronchiectasis or CF was the most frequent cause of development of macrolide-resistance MAC disease (n = 8; 50%). Short (n = 3; mean duration 9 months, range 6-12) or guideline non-compliant (n = 2) treatment regimens and patient non-adherence (n = 2) were other key causes of macrolide-resistance.

**Conclusions:** Macrolide monotherapy after inappropriate screening is the most frequent cause of macrolide-resistant Mycobacterium avium complex disease in the Netherlands. Educational efforts are needed to prevent this.



## Conflict of interest statement

Declaration of competing interest There is no conflict of interest.

## supplementary info

MeSH terms, Substancesexpand

## full text links

Proceed to details

Cite

Share

8

Ann Thorac Surg

- 
- 
- 

. 2023 Oct;116(4):694-701.

doi: 10.1016/j.athoracsur.2023.05.017. Epub 2023 Jun 2.

# Lobectomy for Suspected Lung Cancer Without Prior Diagnosis

Michael T Onwugbufor[1], Monica L Soni[2], Jarrod D Predina[1], Sheila Knoll[1], Yin P Hung[3], Douglas J Mathisen[1], Yolonda L Colson[1], Henning A Gaissert[4]

Affiliations expand

- PMID: 37271441

- DOI: 10.1016/j.athoracsur.2023.05.017

**Abstract**

**Background:** We describe use, patients, and outcome of diagnostic lobectomy for suspected lung cancer without pathologic confirmation.

**Methods:** A retrospective review of consecutive lobectomy or bilobectomy for suspected or confirmed primary pulmonary malignancy was conducted using our participant's sample of The Society of Thoracic Surgeons database. Surgeons performed lobectomy based on clinical diagnosis or confirmation on a biopsy specimen. Lung cancer confirmed by biopsy specimen was compared with cases clinically suspected. Univariate and multivariate analyses identified variables associated with lobectomy without biopsy specimen confirmation.

**Results:** Among 2651 lobectomies performed between 2006 and 2019 in 2617 patients, lung cancer was confirmed by preoperative biopsy specimen in 51.6% (1368 of 2651) or was clinically suspected before the operation in 48.4% (1283 of 2651). The intraoperative biopsy specimen in 585 of 1283 cases (45.6%) proved lung cancer before lobectomy, whereas lobectomy proceeded in 698 cases (54.4%) without a diagnosis. Final pathology proved lung cancer in 90% (628 of 698) without a diagnosis before lobectomy and nonmalignant disease in 10% (70 of 698). Nonneoplastic pathology included granulomas (30 of 70 [43%]), pneumonia (12 of 70 [17%]), bronchiectasis (7 of 70 [10%]), and other lesions (21 of 70 [30%]). Operative mortality was 0.94% (25 of 2651) for the cohort and 1.0% (7 of 698) for diagnostic lobectomy only. Multivariate analysis identified patient age, type of lobectomy (right middle lobe), and the intermediate study tercile as associated with diagnostic lobectomy.

**Conclusions:** Lobectomy for suspected lung cancer without diagnosis is common, represents practice variation, and infrequently (10% diagnostic, 2.6% all lobectomies) removes nonmalignant disease. Tissue confirmation before lobectomy is preferred, particularly when operative risk is increased. Diagnostic lobectomy is acceptable in carefully selected patients and lesions.



# Comment in

- Using the Ultimate Lung Biopsy.
  Rshaidat H, Okusanya OT.Ann Thorac Surg. 2023 Oct;116(4):701-702. doi: 10.1016/j.athoracsur.2023.05.043. Epub 2023 Jun 28.PMID: 37385431 No abstract available.

supplementary info

MeSH termsexpand

full text links

9

Pharmacoepidemiol Drug Saf

. 2023 Oct;32(10):1077-1082.

doi: 10.1002/pds.5638. Epub 2023 May 28.

# Validation of diagnostic coding for bronchiectasis in an electronic health record system in Hong Kong

Wang Chun Kwok[1], Terence Chi Chun Tam[1], Chor Wing Sing[2], Esther Wai Yin Chan[2], Ching-Lung Cheung[2]

Affiliations expand

- PMID: 37169360

- DOI: 10.1002/pds.5638

## Abstract

**Background and objective:** Electronic medical record (EMR) databases can facilitate epidemiology research in various diseases including bronchiectasis. Given the diagnostic challenges of bronchiectasis, the validity of the coding in EMR requires clarification. We aimed to assess the validity of International Classification of Diseases, 9th Revision (ICD-9) code algorithms for identifying bronchiectasis in the territory-wide electronic medical health record system of Clinical Data Analysis and Reporting System (CDARS) in Hong Kong.

**Materials and methods:** Adult patients who had the diagnosis of bronchiectasis input from Queen Mary Hospital in 2011-2020 were identified using the ICD-9 code of 494 by CDARS. All patients who had high resolution computed tomography (HRCT) were reviewed by respiratory specialists to confirm the presence of bronchiectasis on HRCT.

**Results:** A total of 19 617 patients who had the diagnostic code of bronchiectasis among all public hospitals in Hong Kong and 1866 in Queen Mary Hospital in the same period. Six hundred and forty-eight cases were randomly selected and validated using medical record and HRCT review by a respiratory specialist. The overall positive predictive value (PPV) was 92.7% (95% CI 90.7-94.7).

**Conclusions:** This was the first ICD-9 coding validation for bronchiectasis in Hong Kong CDARS. Our study demonstrated that using ICD-9 code of 494 was reliable to support utility of CDARS database for further clinical research on bronchiectasis.

**Keywords:** EHR; algorithms; bronchiectasis; electronic health record; validation.



- 34 references

supplementary info

MeSH termsexpand

full text links