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

1
Eur Heart J Qual Care Clin Outcomes

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. 2023 Aug 4;qcad046.

doi: 10.1093/ehjqcco/qcad046. Online ahead of print.

# High risk of rehospitalization within one year following a pulmonary embolism-Insights from the Danish nationwide registries from 2000-2020

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Affiliations expand

- PMID: 37541959

- DOI: 10.1093/ehjqcco/qcad046

# Abstract

**Aim:** To identify the absolute risk, causes and factors associated with rehospitalization within 1 year of discharge with a pulmonary embolism (PE).

**Methods and results:** Using the Danish nationwide registries, all patients admitted with a first-time PE between 2000 and 2020 and discharged alive were included. Subsequent hospitalizations were categorized and crude cumulative incidences, were used to estimate the absolute risk (AR) of any rehospitalization and specific causes of rehospitalizations. Risk factors for rehospitalization were investigated using cause specific Cox regression models.A total of 55 201 patients were identified. The median age of the study population was 70 years (inter quartile range: 59;79), and the most prevalent comorbidities were cancer (29.3%) and ischemic heart disease (12.7%). The 1-year AR of any rehospitalization after discharge with a PE was 48.6% (95% confidence interval (CI); 48.2%-48.8%). The most common cause for being rehospitalized was due to respiratory disease (1-year AR: 9.5% (95% CI: 9.3%-9.8%)), followed by cardiovascular disease (1-year AR: 6.3% (95% CI: 5.9%-6.5%)), cancer (1-year AR: 6.0% (95% CI: 5.8%-6.4%)), venous thromboembolism (1-year AR: 5.2% (95% CI: 5.0%-5.2%)), and symptom diagnoses (1-year AR: 5.2% (95%CI: 5.0%-5.4%)). Factors that were associated with an increased risk of rehospitalization were cancer, liver disease, chronic obstructive pulmonary disease, chronic kidney disease, and immobilization.

**Conclusion:** Patients with PE have a high risk of rehospitalization, with almost half of patients being rehospitalized within 1 year. Identification of high-risk patients may help target interventions aiming at reducing the risk of rehospitalization.



**Keywords:** Epidemiology; Rehospitalization; Risk; pulmonary embolism.

Ther Adv Chronic Dis

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doi: 10.1177/20406223231190480. eCollection 2023.

# Fractional nitric oxide measurement in exhaled air (FeNO): perspectives in the management of respiratory diseases

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Affiliations expand

- PMID: 37538344

- PMCID: PMC10395178

- DOI: 10.1177/20406223231190480

## Abstract

Exhaled nitric oxide (NO) production, upregulated by inflammatory cytokines and mediators in central and peripheral airways, can be easily and non-invasively detected in exhaled air in asthma and other respiratory conditions as a promising tool for disease monitoring. The American Thoracic Society and European Respiratory Society released recommendations that standardize the measurement of the fractional exhaled NO (FeNO). In asthma, increased FeNO reflects eosinophilic-mediated inflammatory pathways and, as a biomarker of T2 inflammation can be used to identify asthma T2 phenotype. In this setting its measurement has shown to be an important tool especially in the diagnostic process, in the assessment and evaluation of poor adherence or predicting positive response to inhaled corticosteroids treatment, in phenotyping severe asthma patients and as a biomarker to predict the response to biologic treatments. The discovery of the role of NO in the pathogenesis of different diseases affecting the airways and the possibility to estimate the predominant site of increased NO production has provided new insight on its

regulatory role in the airways, making it suitable for a potential extended use in clinical practice for different pulmonary diseases, even though its role remains less clear than in asthma. Monitoring FeNO in pulmonary obstructive lung diseases including chronic bronchitis and emphysema, interstitial lung diseases, obstructive sleep apnea and other pulmonary diseases is still under debate but has opened up a window to the role NO may play in the management of these diseases. The use of FeNO is reliable, cost effective and recommendable in both adults and children, and should be implemented in the management of patients with asthma and other respiratory conditions.

**Keywords:** asthma management; central and peripheral airways; fractional exhaled nitric oxide; respiratory diseases.



# Conflict of interest statement

Jaymin Morjaria has received honoraria for speaking and financial support to attend meetings/advisory boards from Wyeth, Chiesi, Pfizer, MSD, Boehringer Ingelheim, Teva, GSK/Allen & Hanburys, Napp, Almirall, AstraZeneca, Trudell, Cook Medical, Medela AG, Medtronics and Novartis. He has been an expert witness in a court case relating to the impact of smoking on illness severity, ITU admissions and mortality from Covid-19 in South Africa in 2020. The entire proceeds of the work were donated to multiple charities. Mario Malerba has received honoraria for speaking and financial support for attending meetings and/or serving on the advisory boards from Chiesi, Astra-Zeneca, GSK, Laboratori Guidotti, Boehringer Ingelheim, Vitalaire, Grifols, CLS Behring. All the authors have no other relevant affiliations of financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed. Jaymin Morjaria is also an Associate Editor of Therapeutic Advances in Chronic Disease; therefore, the peer-review process was managed by alternative members of the Board, and he had no involvement in the decision-making process. Beatrice Ragnoli and Mario Malerba are members of the Editorial Board of Therapeutic Advances in Chronic Disease and had no involvement in the peer review process.

- 133 references
- 3 figures

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

UNIMORE

Review

Adv Ther

. 2023 Aug 4.

doi: 10.1007/s12325-023-02609-8. Online ahead of print.

# 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

- DOI: 10.1007/s12325-023-02609-8

## 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.



- 138 references

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

Med Sci Sports Exerc

. 2023 Aug 2.

doi: 10.1249/MSS.0000000000003268. Online ahead of print.

# The Impact of Exercise Training and Supplemental Oxygen on Peripheral Muscles in COPD: A Randomized Controlled Trial

Daniel Neunhäuserer, Martin Hudelmaier[1], David Niederseer, Marco Vecchiato[2], Wolfgang Wirth[1], Eva Steidle-Kloc[1], Bernhard Kaiser[3], Bernd Lamprecht, Andrea Ermolao[2], Michael Studnicka[3], Josef Niebauer

Affiliations expand

- PMID: 37535316

- DOI: 10.1249/MSS.0000000000003268

## Abstract

**Objective:** Exercise training is a cornerstone of the treatment of COPD while the related inter-individual heterogeneity in skeletal muscle dysfunction and adaptations are not yet fully understood. We set out to investigate the effects of exercise training and supplemental oxygen on functional and structural peripheral muscle adaptation.

**Methods:** In this prospective, randomized, controlled, double-blind study, 28 patients with non-hypoxemic COPD (FEV1 45.92 ± 9.06%) performed six-weeks of combined endurance and strength training, three times a week while breathing either supplemental oxygen or medical air. The impact on exercise capacity, muscle strength and quadriceps femoris muscle cross-sectional area (CSA), was assessed by maximal cardiopulmonary exercise testing, ten-repetition maximum strength test of knee extension, and magnetic resonance imaging, respectively.

**Results:** After exercise training, patients demonstrated a significant increase of functional capacity, aerobic capacity, exercise tolerance, quadriceps muscle strength and bilateral CSA. Supplemental oxygen affected significantly the training impact on peak work rate

when compared to medical air (+0.20 ± 0.03 vs +0.12 ± 0.03 Watt/kg, p = 0.047); a significant increase in CSA (+3.9 ± 1.3 cm2, p = 0.013) was only observed in the training group using oxygen. Supplemental oxygen and exercise induced peripheral desaturation were identified as significant opposing determinants of muscle gain during this exercise training intervention, which led to different adaptations of CSA between the respective subgroups.

**Conclusions:** The heterogenous functional and structural muscle adaptations seem determined by supplemental oxygen and exercise induced hypoxia. Indeed, supplemental oxygen may facilitate muscular training adaptations, particularly in limb muscle dysfunction, thereby contributing to the enhanced training responses on maximal aerobic and functional capacity.



# Conflict of interest statement

Conflict of Interest and Funding Source: The Salzburg COPD Exercise and Oxygen (SCOPE) study was supported by an unconditional and unrestricted grant by Air Liquide. All authors declare hereby to have no conflicts of interest. The results of this study are presented clearly, honestly and without fabrication, falsification, or inappropriate data manipulation. The results of the present study do not constitute endorsement by the American College of Sports Medicine.



BMC Pulm Med

. 2023 Aug 2;23(1):281.

doi: 10.1186/s12890-023-02565-7.

# Idiopathic pulmonary fibrosis in the United States: time to diagnosis and treatment

Michelle B Herberts[1], Taylor T Teague[1], Viengneesee Thao[2], Lindsey R Sangaralingham[2], Henry J Henk[3], Kevin T Hovde[2], Timothy M Dempsey[1 4], Andrew H Limper[5 6]

Affiliations expand

- PMID: 37532984
- PMCID: PMC10398946
- DOI: 10.1186/s12890-023-02565-7

**Free PMC article**

## Abstract

**Objective:** Create a timeline of diagnosis and treatment for IPF in the US.

**Design, setting, and participants:** A retrospective analysis was performed in collaboration with the OptumLabs Data Warehouse using an administrative claims database of Medicare Fee for Service beneficiaries. Adults 50 and over with IPF were included (2014 to 2019).

**Exposure:** To focus on IPF, the following diagnoses were excluded: post-inflammatory fibrosis, hypersensitivity pneumonitis, rheumatoid arthritis, sarcoidosis, scleroderma, and connective tissue disease.

**Main outcomes and measures:** Data were collected from periods prior, during, and following initial clinical diagnosis of IPF. This included prior respiratory diagnoses, number of respiratory-related hospitalizations, anti-fibrotic and oxygen use, and survival.

**Results:** A total of 44,891 with IPF were identified. The most common diagnoses prior to diagnosis of IPF were upper respiratory infections (47%), acute bronchitis (13%), other respiratory disease (10%), chronic obstructive pulmonary disease and bronchiectasis (7%), and pneumonia (6%). The average time to a diagnosis of IPF was 2.7 years after initial respiratory diagnosis. Half of patients had two or more respiratory-related hospitalizations prior to IPF diagnosis. Also, 37% of patients were prescribed oxygen prior to diagnosis of IPF. These observations suggest delayed diagnosis. We also observed only 10.4% were

treated with anti-fibrotics. Overall survival declined each year after diagnosis with median survival of 2.80 years.

**Conclusions and relevance:** Our retrospective cohort demonstrates that IPF is often diagnosed late, usually preceded by other respiratory diagnoses and hospitalizations. Use of available therapies is low and outcomes remain poor.

**Keywords:** Diagnosis; Idiopathic pulmonary fibrosis; Mortality; Oxygen; Treatment.



# Conflict of interest statement

The authors declare no competing interests.

- 25 references
- 5 figures



Am J Respir Crit Care Med

- 
- 
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. 2023 Aug 2.

doi: 10.1164/rccm.202307-1302ED. Online ahead of print.

# Revisiting the Use of Antibiotics to Prevent COPD Exacerbation: Is Doxycycline the Answer?

Muhammad Adrish [1], Nicola A Hanania [2]

Affiliations expand

- PMID: 37531185

- DOI: 10.1164/rccm.202307-1302ED

*No abstract available*

**Keywords:** COPD; Doxycycline; exacerbation.



ERJ Open Res

. 2023 Jul 31;9(4):00158-2023.

doi: 10.1183/23120541.00158-2023. eCollection 2023 Jul.

# Healthcare costs and resource utilisation in bronchiectasis, asthma and COPD

Raffaella Ronco[1,2], Giovanni Franco[3], Matteo Monzio Compagnoni[1,2], Stefano Aliberti[4,5], Fabrizio Luppi[3], Giovani Corrao[1,2], Paola Faverio[3]

Affiliations expand

- PMID: 37529638

- PMCID: PMC10388176

- DOI: 10.1183/23120541.00158-2023

**Free PMC article**

# Abstract

**Direct healthcare costs for patients with asthma are less than half (-52%) and for patients with COPD are 41% higher if compared to those of patients with bronchiectasis. The leading expense items in bronchiectasis are hospitalisations and antibiotics.** https://bit.ly/3Iq8AUP.



# Conflict of interest statement

Conflict of interest: G. Corrao received research support from the European Community, the Italian Medicines Agency (AIFA), and the Italian Ministry of Education, Universities and Research. He took part in a variety of projects that were funded by pharmaceutical companies (Novartis, GSK, Roche, AMGEN and BMS). He also received honoraria as a member of the Advisory Board of Roche. S. Aliberti received consulting fees, honoraria for lectures, presentations or educational events and participation on a data safety monitoring board or advisory board from Insmed, Zambon, AstraZeneca, CLS Behring, Grifols, Fondazione Internazionale Menarini, MSD, Brahms, Physioassist SAS, GlaxoSmithKline Spa and Thermofisher Scientific. He also received royalties from McGraw-Hill. No other potential conflicts of interest were declared for the other authors.

- 11 references

Review

ERJ Open Res

. 2023 Jul 31;9(4):00102-2023.

doi: 10.1183/23120541.00102-2023. eCollection 2023 Jul.

# Efficacy of interventions to alter measures of fat-free mass in people with COPD: a systematic review and meta-analysis

Alex R Jenkins[1], Kaveh Gaynor-Sodeifi[1], Hayley Lewthwaite[1,2,3], Jaycie Triandafilou[1], Letícia F Belo[1,4], Mayron Faria de Oliveira[1,5], Dennis Jensen[1,6]

Affiliations expand

- PMID: 37529637

- PMCID: PMC10388177

- DOI: 10.1183/23120541.00102-2023

**Free PMC article**

## Abstract

**Introduction:** Low fat-free mass (FFM) is linked to poor health outcomes in COPD, including impaired exercise tolerance and premature death. The aim of this systematic review was to synthesise evidence on the effectiveness of interventions for increasing FFM in COPD.

**Methods:** Searches of electronic databases (MEDLINE, Cochrane Library, Embase, Web of Science, Scopus) and trial registers (ClinicalTrials.gov) were undertaken from inception to August 2022 for randomised studies of interventions assessing measures of FFM in COPD. The primary outcome was change in FFM (including derivatives). Secondary outcomes were adverse events, compliance and attrition.

**Results:** 99 studies (n=5138 people with COPD) of 11 intervention components, used alone or in combination, were included. Exercise training increased mid-thigh cross-sectional area (*k*=3, standardised mean difference (SMD) 1.04, 95% CI 0.02-2.06; p=0.04), but not FFM (*k*=4, SMD 0.03, 95% CI -0.18-0.24; p=0.75). Nutritional supplementation significantly increased FFM index (*k*=11, SMD 0.31, 95% CI 0.13-0.50; p<0.001), but not FFM (*k*=19, SMD 0.16, 95% CI -0.06-0.39; p=0.16). Combined exercise training and nutritional supplementation increased measures related to FFM in 67% of studies. Anabolic steroids increased FFM (*k*=4, SMD 0.98, 95% CI 0.24-1.72; p=0.009). Neuromuscular electrical stimulation increased measures related to FFM in 50% of studies. No interventions were more at risk of serious adverse events, low compliance or attrition.

**Discussion:** Exercise training and nutritional supplementation were not effective in isolation to increase FFM, but were for localised muscle and index measures, respectively. Combined, exercise and nutritional supplementation shows promise as a strategy to increase FFM in COPD. Anabolic steroids are efficacious for increasing FFM in COPD.



# Conflict of interest statement

Conflict of interest: All authors declare no conflicts of interest relating to the production of this manuscript.

- 144 references
- 4 figures

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

Editorial

ERJ Open Res

. 2023 Jul 31;9(4):00336-2023.

doi: 10.1183/23120541.00336-2023. eCollection 2023 Jul.

# Gaining muscle mass in COPD: a work in progress

Hamish J C McAuley[1], Matthew Maddocks[2]

Affiliations expand

- PMID: 37529635
- PMCID: PMC10388174
- DOI: 10.1183/23120541.00336-2023

**Free PMC article**

## Abstract

**Interventions to improve muscle mass in COPD remain limited to exercise and nutrition. As novel drugs show promise, there should be focus on identifying target subgroups of patients, strategies to combine interventions and optimise outcome measures.** https://bit.ly/3WI5Sjg.

## Conflict of interest statement

Conflict of interest: The authors have nothing to disclose.

- 15 references

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Healthc Technol Lett

. 2023 Jun 8;10(4):80-86.

doi: 10.1049/htl2.12048. eCollection 2023 Aug.

# Non-invasive ventilation treatment for patients with chronic obstructive pulmonary disease

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Affiliations expand

- PMID: 37529410

- PMCID: PMC10388227

- DOI: 10.1049/htl2.12048

**Free PMC article**


# Abstract


Chronic obstructive pulmonary disease (COPD) affects the lives of millions of patients worldwide. Patients with advanced COPD may require non-invasive ventilation (NIV) to support the resultant deficiencies of the respiratory system. The purpose of this study was to evaluate the effects of varying the continuous positive airway pressure (CPAP) and oxygen supplementation components of NIV on simulated COPD patients by using an established and detailed model of the human respiratory system. The model used in the study simulates features of advanced COPD including the effects on the changes in ventilation control, increases in respiratory dead space and airway resistance, and the acid-base shifts in the blood seen in these patients over time. The results of the study have been compared with and found to be in general agreement with available clinical data. Our results demonstrate that under non-emergency conditions, low levels of oxygen supplementation combined with low levels of CPAP therapy seem to improve hypoxemia and hypercapnia in the model, whereas prolonged high-level CPAP and moderate-to-high levels of oxygen supplementation do not. The authors conclude that such modelling may be useful to help guide beneficial interventions for COPD patients using NIV.



**Keywords:** decision support systems; lung; medical expert systems; oxygen; patient treatment; physiological models; ventilation.




# Conflict of interest statement

The authors declare no conflict of interest.

- 22 references
- 7 figures

Multicenter Study

JAMA

. 2023 Aug 1;330(5):442-453.

doi: 10.1001/jama.2023.11676.

# Longitudinal Follow-Up of Participants With Tobacco Exposure and Preserved Spirometry

William McKleroy[1,2], Tracie Shing[3], Wayne H Anderson[4], Mehrdad Arjomandi[1,5], Hira Anees Awan[6], Igor Barjaktarevic[7], R Graham Barr[8,9], Eugene R Bleecker[10,11], John Boscardin[12], Russell P Bowler[13], Russell G Buhr[7], Gerard J Criner[14], Alejandro P Comellas[15], Jeffrey L Curtis[16,17], Mark Dransfield[18], Claire M Doerschuk[4], Brett A Dolezal[7], M Bradley Drummond[4], MeiLan K Han[16], Nadia N Hansel[19], Kinsey Helton[3], Eric A Hoffman[6,15,20], Robert J Kaner[21], Richard E Kanner[22], Jerry A Krishnan[23], Stephen C Lazarus[1,24], Fernando J Martinez[21], Jill Ohar[25], Victor E Ortega[26], Robert Paine 3rd[22], Stephen P Peters[25], Joseph M Reinhardt[6], Stephen Rennard[27], Benjamin M Smith[8,28], Donald P Tashkin[7], David Couper[3], Christopher B Cooper[7,29], Prescott G Woodruff[1,24]

Affiliations expand

- PMID: 37526720

- PMCID: PMC10394572 (available on 2024-02-01)

- DOI: 10.1001/jama.2023.11676

## Abstract

**Importance:** People who smoked cigarettes may experience respiratory symptoms without spirometric airflow obstruction. These individuals are typically excluded from chronic obstructive pulmonary disease (COPD) trials and lack evidence-based therapies.

**Objective:** To define the natural history of persons with tobacco exposure and preserved spirometry (TEPS) and symptoms (symptomatic TEPS).

**Design, setting, and participants:** SPIROMICS II was an extension of SPIROMICS I, a multicenter study of persons aged 40 to 80 years who smoked cigarettes (>20 pack-years) with or without COPD and controls without tobacco exposure or airflow obstruction. Participants were enrolled in SPIROMICS I and II from November 10, 2010, through July 31, 2015, and followed up through July 31, 2021.

**Exposures:** Participants in SPIROMICS I underwent spirometry, 6-minute walk distance testing, assessment of respiratory symptoms, and computed tomography of the chest at yearly visits for 3 to 4 years. Participants in SPIROMICS II had 1 additional in-person visit 5 to 7 years after enrollment in SPIROMICS I. Respiratory symptoms were assessed with the COPD Assessment Test (range, 0 to 40; higher scores indicate more severe symptoms). Participants with symptomatic TEPS had normal spirometry (postbronchodilator ratio of forced expiratory volume in the first second [FEV1] to forced vital capacity >0.70) and COPD Assessment Test scores of 10 or greater. Participants with asymptomatic TEPS had normal spirometry and COPD Assessment Test scores of less than 10. Patient-reported respiratory symptoms and exacerbations were assessed every 4 months via phone calls.

**Main outcomes and measures:** The primary outcome was assessment for accelerated decline in lung function (FEV1) in participants with symptomatic TEPS vs asymptomatic TEPS. Secondary outcomes included development of COPD defined by spirometry, respiratory symptoms, rates of respiratory exacerbations, and progression of computed tomographic-defined airway wall thickening or emphysema.

**Results:** Of 1397 study participants, 226 had symptomatic TEPS (mean age, 60.1 [SD, 9.8] years; 134 were women [59%]) and 269 had asymptomatic TEPS (mean age, 63.1 [SD, 9.1] years; 134 were women [50%]). At a median follow-up of 5.76 years, the decline in FEV1 was -31.3 mL/y for participants with symptomatic TEPS vs -38.8 mL/y for those with asymptomatic TEPS (between-group difference, -7.5 mL/y [95% CI, -16.6 to 1.6 mL/y]). The cumulative incidence of COPD was 33.0% among participants with symptomatic TEPS vs 31.6% among those with asymptomatic TEPS (hazard ratio, 1.05 [95% CI, 0.76 to 1.46]). Participants with symptomatic TEPS had significantly more respiratory exacerbations than those with asymptomatic TEPS (0.23 vs 0.08 exacerbations per person-year, respectively; rate ratio, 2.38 [95% CI, 1.71 to 3.31], P < .001).

**Conclusions and relevance:** Participants with symptomatic TEPS did not have accelerated rates of decline in FEV1 or increased incidence of COPD vs those with asymptomatic TEPS, but participants with symptomatic TEPS did experience significantly more respiratory exacerbations over a median follow-up of 5.8 years.

# Conflict of interest statement

Conflict of Interest Disclosures: Dr Arjomandi reported receiving grants from the Flight Attendants Medical Research Institute, the California Tobacco-Related Disease Research Program, Genentech, and Guardant Health. Dr Barjaktarevic reported receiving grants from Theravance, Viatris, and Aerogen and receiving personal fees from Theravance, Viatris, GSK (formerly GlaxoSmithKline), AstraZeneca, Grifols, Takeda, Inhibrx, Sanofi, Verona Pharma, and Aerogen. Dr Buhr reported receiving personal fees from Viatris, Theravance Biopharma, Dynamed, and the American College of Physicians. Dr Comellas reported receiving personal fees from GSK, AstraZeneca, Eli Lilly, and Genentech and nonfinancial support from VIDA Diagnostics. Dr Curtis reported receiving personal fees from AstraZeneca, CSL Behring, Novartis, and Basel that were paid directly to his institution. Dr Dransfield reported receiving personal fees from GSK, AstraZeneca, Teva, Pulmonx, and Novartis. Dr Drummond reported receiving grants and personal fees from Midmark, Boehringer Ingelheim, and Teva and receiving personal fees from Verona, Becker Pharma, Chiesi, Optimum Patient Care, Polarean, GSK, and AstraZeneca. Dr Han reported receiving personal fees from GSK, AstraZeneca, Boehringer Ingelheim, Cipla, Chiesi, Pulmonx, Novartis, Teva, Verona, Merck, Mylan, Sanofi, DevPro, Aerogen, Polarian, Regeneron, UpToDate, and Altesa; receiving in-kind clinical trial support from Novartis; and receiving grants from Sunovion, Nuvaira, Sanofi, AstraZeneca, Boehringer Ingelheim, Gala Therapeutics, Biodesix, and the American Lung Association; serving on data and safety monitoring boards for Novartis and Medtronic; and having stock options in Meissa Vaccines and Altesa. Dr Hansel reported receiving grants from AstraZeneca and GSK. Dr Hoffman reported receiving personal fees from VIDA Diagnostics. Dr Kaner reported receiving grants from Boehringer Ingelheim, Bellerophon, CSL Behring, Genentech, Respivant, and Toray; receiving personal fees from Galapagos NV, Boehringer Ingelheim, Genentech, AstraZeneca; serving on data and safety monitoring boards for PureTech and Pliant; and receiving nonfinancial support from Boehringer Ingelheim and Genentech. Dr Krishnan reported receiving personal fees from GSK, AstraZeneca, BData, and the Research Triangle Institute and receiving grants from Sergey Brin Family Foundation, the Patient-Centered Outcomes Research Institute, and the American Lung Association. Dr Martinez reported receiving personal fees from Novartis, AstraZeneca, Boehringer Ingelheim, Chiesi, CSL Behring, GSK, Polarean, PulmonX, Sunovion, Teva, Theravance, Viatris, and UpToDate; receiving grants from Chiesi, Sanofi, Regeneron, AstraZeneca, and GSK; and serving on an adjudication board for Medtronic. Dr Ortega reported receiving personal fees from Regeneron and Sanofi for serving on independent data and safety monitoring committees. Dr Paine reported receiving personal fees from Partner Therapeutics. Dr Reinhardt reported receiving personal fees from VIDA Diagnostics, Desmarais, and Boehringer Ingelheim and owning stock in Desmarais. Dr Rennard reported receiving personal fees from Veroina Pharma, Boehringer Ingelheim, and Beyond Air; being the founder and co-owner of GreatPlainsBioetrix; having a patent pending for wearable diagnostic, which is owned by University of Nebraska; serving as medical director of the Translational Development Network for the Alpha 1 Foundation; and holding shares in AstraZeneca, which were received as part of his compensation while working for the company from 2015 to 2019. Dr

Smith reported receiving grants from the Canadian Lung Association and the Quebec Health Research Fund. Dr Tashkin reported receiving personal fees from Viatris and Theravance Biopharma. Dr Woodruff reported receiving personal fees from Amgen, Sanofi, and AstraZeneca. No other disclosures were reported.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

FULL TEXT LINKS



Clin Respir J

. 2023 Jul 31.

doi: 10.1111/crj.13678. Online ahead of print.

# Home noninvasive ventilation use in patients hospitalized with COPD

Spyridon Fortis[1,2], Yubo Gao[1,3], Kelby Rewerts[1], Mary Vaughan Sarrazin[1,3], Peter J Kaboli[1,3]

Affiliations expand

- PMID: 37525442

- DOI: 10.1111/crj.13678

## Abstract

**Introduction:** The study objective was to estimate the prevalence of chronic hypercapnic respiratory failure (CHRF) and home noninvasive ventilation (NIV) use in a high-risk population, individuals with a history of at least one COPD-related hospitalizations.

**Methods:** We retrospectively analyzed electronic medical record data of patients with at least one COPD-related hospitalization between October 1, 2011, and September 30, 2017, to the Iowa City VA Medical Center. We excluded individuals with no obstructive ventilatory defect.

**Results:** Of 186 patients, the overall prevalence of compensated hypercapnic respiratory failure (CompHRF), defined as $PaCO_2$ > 45 mmHg with a pH = 7.35-7.45, was 52.7%, while the overall prevalence of home NIV was 4.3%. The prevalence of CompHRF was 43.6% and home NIV was 1.8% in those with one COPD-related hospitalization. Among those with ≥4 COPD-related hospitalizations, the prevalence of CompHRF was 77.8% (14 of 18), and home NIV was 11.1% (2 of 18).

**Conclusion:** Approximately half of individuals with at least one COPD-related hospitalization have CompHRF, but only 8.2% of those use home NIV. Future studies should estimate CHRF rates and the degree of underutilization of home NIV in larger multicenter samples.

**Keywords:** COPD; hypercapnia; noninvasive ventilation.



- 12 references

SUPPLEMENTARY INFO

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NPJ Prim Care Respir Med

. 2023 Jul 31;33(1):28.

doi: 10.1038/s41533-023-00349-4.

# Gold 2023: Highlights for primary care

Alvar Agustí[1], Antoni Sisó-Almirall[2], Miguel Roman[3], Claus F Vogelmeier[4]; members of the Scientific Committee of GOLD (Appendix)

Collaborators, Affiliations expand

- PMID: 37524724

- PMCID: PMC10390461

- DOI: 10.1038/s41533-023-00349-4

**Free PMC article**

*No abstract available*

## Conflict of interest statement

The authors declare no competing interests.

- 89 references
- 5 figures

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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Am J Respir Crit Care Med

. 2023 Jul 31.

doi: 10.1164/rccm.202302-0207OC. Online ahead of print.

# Indoor Pollution and Lung Function Decline in Current and Former Smokers: SPIROMICS AIR

Nadia N Hansel[1], Han Woo[2], Kirsten Koehler[3], Amanda Gassett[4], Laura M Paulin[5], Neil Alexis[6], Nirupama Putcha[7,8], Wendy Lorizio[2], Ashraf Fawzy[9,10], Daniel Belz[11], Coralynn Sack[12], R Graham Barr[13], Fernando J Martinez[14], MeiLan K Han[15], Prescott Woodruff[16], Cheryl Pirozzi[17,18], Robert Paine Iii[19], Igor Barjaktarevic[20], Christopher B Cooper[21], Victor Ortega[22], Marina Zusman[23], Joel Kaufman[24]

Affiliations expand

- PMID: 37523421

- DOI: 10.1164/rccm.202302-0207OC

## Abstract

**Rationale:** Indoor pollutants have been associated with COPD morbidity, but it is unclear whether they contribute to disease progression.

**Objectives:** We aim to determine whether indoor particulate matter (PM) and nitrogen dioxide (NO2) are associated with lung function decline among current and former smokers.

**Methods:** Of the 2,382 subjects with a history of smoking in SPIROMICS AIR, 1,208 participants had complete information to estimate indoor PM and NO2, using individual-based prediction models, in relation to measured spirometry at two or more clinic visits. We used a 3-way interaction model between time, pollutant, and smoking status; and assessed the indoor pollutant-associated difference in FEV1 decline separately using generalized linear mixed model.

**Measurements and main results:** Participants had an average rate of FEV1 decline of 60.3 mL/year for those currently smoking compared to 35.2 mL/year for those who quit. The association of indoor PM with FEV1 decline differed by smoking status. Among former smokers, every 10 µg/m3 increase in estimated indoor PM was associated with an additional 10 mL/year decline in FEV1 (p=0.044). Among current smokers, FEV1 decline did not differ by indoor PM. The results of indoor NO2 suggest similar trends to PM2.5.

**Conclusions:** Former smokers with COPD, who lived in homes with high estimated PM have accelerated lung function loss and those in homes with low PM had lung function loss similar to normal aging. In-home PM exposure may contribute to variability in lung function decline in people who quit smoking and may be a modifiable exposure.

**Keywords:** COPD; indoor particulate matter; lung function decline.



Int J Biometeorol

. 2023 Jul 31.

doi: 10.1007/s00484-023-02504-5. Online ahead of print.

# 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.

Review

Respir Res

. 2023 Jul 31;24(1):194.

doi: 10.1186/s12931-023-02500-8.

# Use of thiols and implications for the use of inhaled corticosteroids in the presence of oxidative stress in COPD

Mario Cazzola[1], Clive P Page[2], Jadwiga A Wedzicha[3], Bartolome R Celli[4], Antonio Anzueto[5], Maria Gabriella Matera[6]

Affiliations expand

- PMID: 37517999

- PMCID: PMC10388561

- DOI: 10.1186/s12931-023-02500-8

**Free PMC article**

## Abstract

**Background:** Oxidative stress and persistent airway inflammation are thought to be important contributors to the development of chronic obstructive pulmonary disease (COPD). This review summarizes the evidence for targeting oxidative stress and inflammation in patients with COPD with mucolytic/antioxidant thiols and inhaled corticosteroids (ICS), either alone or in combination.

**Main body:** Oxidative stress is increased in COPD, particularly during acute exacerbations. It can be triggered by oxidant air pollutants and cigarette smoke and/or by endogenous reactive oxygen species (ROS) released from mitochondria and activated inflammatory, immune and epithelial cells in the airways, together with a reduction in endogenous antioxidants such as glutathione (GSH). Oxidative stress also drives chronic inflammation and disease progression in the airways by activating intracellular signalling pathways and the release of further inflammatory mediators. ICS are anti-inflammatory agents currently recommended for use with long-acting bronchodilators to prevent exacerbations in patients with moderate-to-severe COPD, especially those with eosinophilic airway inflammation. However, corticosteroids can also increase oxidative stress, which may in turn reduce corticosteroid sensitivity in patients by several mechanisms. Thiol-based agents such as erdosteine, N-acetyl L-cysteine (NAC) and S-carboxymethylcysteine (S-CMC) are mucolytic agents that also act as antioxidants. These agents may reduce oxidative stress directly through the free sulfhydryl groups, serving as a source of reducing equivalents and indirectly though intracellular GSH replenishment. Few studies have compared the effects of corticosteroids and thiol agents on oxidative stress, but there is some evidence for greater antioxidant effects when they are administered together. The current Global Initiative for Chronic Obstructive Lung Disease (GOLD) report supports treatment with antioxidants (erdosteine, NAC, S-CMC) in addition to standard-of-care therapy as they have been demonstrated to reduce COPD exacerbations. However, such studies have demonstrated that NAC and S-CMC reduced the exacerbation risk only in patients not treated with ICS, whereas erdosteine reduced COPD exacerbations irrespective of concomitant ICS use suggesting that erdosteine has additional pharmacological actions to ICS.

**Conclusions:** Further clinical trials of antioxidant agents with and without ICS are needed to better understand the place of thiol-based drugs in the treatment of patients with COPD.

**Keywords:** Antioxidant; Chronic obstructive pulmonary disease; Glutathione; Inflammation; Inhaled corticosteroids; Mucolytics; Oxidative stress; Thiol-based drugs.



# Conflict of interest statement

MC, CPP, JAW, BRC, and AA report personal fees from Edmond Pharma. The authors report no other conflicts of interest in this work.

- 106 references
- 4 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

Lancet Glob Health

. 2023 Aug;11(8):e1183-e1193.

doi: 10.1016/S2214-109X(23)00217-6.

# The global economic burden of chronic obstructive pulmonary disease for 204 countries and territories in 2020-50: a health-augmented macroeconomic modelling study

Simiao Chen[1], Michael Kuhn[2], Klaus Prettner[3], Fengyun Yu[4], Ting Yang[5], Till Bärnighausen[4], David E Bloom[6], Chen Wang[7]

Affiliations expand

- PMID: 37474226
- PMCID: PMC10369014
- DOI: 10.1016/S2214-109X(23)00217-6

**Free PMC article**

# Abstract

**Background:** Chronic obstructive pulmonary disease (COPD) is the third leading cause of death worldwide and imposes a substantial economic burden. Gaining a thorough understanding of the economic implications of COPD is an important prerequisite for sound, evidence-based policy making. We aimed to estimate the macroeconomic burden of COPD for each country and establish its distribution across world regions.

**Methods:** In this health-augmented macroeconomic modelling study we estimated the macroeconomic burden of COPD for 204 countries and territories over the period 2020-50. The model accounted for (1) the effect of COPD mortality and morbidity on labour supply, (2) age and sex specific differences in education and work experience among those affected by COPD, and (3) the impact of COPD treatment costs on physical capital accumulation. We obtained data from various public sources including the Global Burden of Disease Study 2019, the World Bank database, and the literature. The macroeconomic burden of COPD was assessed by comparing gross domestic product (GDP) between a scenario projecting disease prevalence based on current estimates and a counterfactual scenario with zero COPD prevalence from 2020 to 2050.

**Findings:** Our findings suggest that COPD will cost the world economy INT$4·326 trillion (uncertainty interval 3·327-5·516; at constant 2017 prices) in 2020-50. This economic effect is equivalent to a yearly tax of 0·111% (0·085-0·141) on global GDP. China and the USA face the largest economic burdens from COPD, accounting for INT$1·363 trillion (uncertainty interval 1·034-1·801) and INT$1·037 trillion (0·868-1·175), respectively.

**Interpretation:** The macroeconomic burden of COPD is large and unequally distributed across countries, world regions, and income levels. Our study stresses the urgent need to invest in global efforts to curb the health and economic burdens of COPD. Investments in effective interventions against COPD do not represent a burden but could instead provide substantial economic returns in the foreseeable future.



**Funding:** Alexander von Humboldt Foundation, National Natural Science Foundation of China, CAMS Innovation Fund for Medical Science, Chinese Academy of Engineering project, Chinese Academy of Medical Sciences and Peking Union Medical College project, and Horizon Europe.


**Translations:** For the Chinese and German translations of the abstract see Supplementary Materials section.



# Conflict of interest statement

Declaration of interests We declare no competing interests.

## Comment in

- COPD generates substantial cost for health systems.
  Agarwal D.Lancet Glob Health. 2023 Aug;11(8):e1138-e1139. doi: 10.1016/S2214-109X(23)00304-2.PMID: 37474208 No abstract available.

- 29 references
- 2 figures

SUPPLEMENTARY INFO

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Lancet Glob Health

. 2023 Aug;11(8):e1138-e1139.

doi: 10.1016/S2214-109X(23)00304-2.

# COPD generates substantial cost for health systems

Dhiraj Agarwal[1]

Affiliations expand

- PMID: 37474208

- DOI: 10.1016/S2214-109X(23)00304-2

**Free article**

*No abstract available*

# Conflict of interest statement

I declare no competing interests.

# Comment on

- The global economic burden of chronic obstructive pulmonary disease for 204 countries and territories in 2020-50: a health-augmented macroeconomic modelling study.
  Chen S, Kuhn M, Prettner K, Yu F, Yang T, Bärnighausen T, Bloom DE, Wang C.Lancet Glob Health. 2023 Aug;11(8):e1183-e1193. doi: 10.1016/S2214-109X(23)00217-6.PMID: 37474226 **Free PMC article.**



Eur Respir J

. 2023 Aug 3;62(2):2201374.

doi: 10.1183/13993003.01374-2022. Print 2023 Aug.

# Antiviral CD8+ T-cell immune responses are impaired by cigarette smoke and in COPD

Jie Chen[1,2,3,4], Xinyuan Wang[1,5,4], Adrian Schmalen[6,7], Sophia Haines[1], Martin Wolff[8], Huan Ma[8], Huabin Zhang[9], Mircea Gabriel Stoleriu[1,10,11], Johannes Nowak[1], Misako Nakayama[1], Marta Bueno[12], Judith Brands[12], Ana L Mora[12,13], Janet S Lee[14], Susanne Krauss-Etschmann[8], Anna Dmitrieva[15,16], Marion Frankenberger[1], Thomas P Hofer[17], Elfriede Noessner[17], Andreas Moosmann[18,19], Jürgen Behr[20], Katrin Milger[20], Cornelia A Deeg[6], Claudia A Staab-Weijnitz[1], Stefanie M Hauck[7], Heiko Adler[15,16], Torsten Goldmann[21], Karoline I Gaede[22], Jochen Behrends[23], Ilona E Kammerl[1,4], Silke Meiners[24,8,25,4]

Affiliations expand

- PMID: 37385655

- PMCID: PMC10397470

- DOI: 10.1183/13993003.01374-2022

**Free PMC article**

## Abstract

**Background:** Virus infections drive COPD exacerbations and progression. Antiviral immunity centres on the activation of virus-specific CD8+ T-cells by viral epitopes presented on major histocompatibility complex (MHC) class I molecules of infected cells. These epitopes are generated by the immunoproteasome, a specialised intracellular protein degradation machine, which is induced by antiviral cytokines in infected cells.

**Methods:** We analysed the effects of cigarette smoke on cytokine- and virus-mediated induction of the immunoproteasome *in vitro*, *ex vivo* and *in vivo* using RNA and Western blot analyses. CD8+ T-cell activation was determined in co-culture assays with cigarette smoke-exposed influenza A virus (IAV)-infected cells. Mass-spectrometry-based analysis of MHC class I-bound peptides uncovered the effects of cigarette smoke on inflammatory antigen presentation in lung cells. IAV-specific CD8+ T-cell numbers were determined in patients' peripheral blood using tetramer technology.

**Results:** Cigarette smoke impaired the induction of the immunoproteasome by cytokine signalling and viral infection in lung cells *in vitro*, *ex vivo* and *in vivo*. In addition, cigarette

smoke altered the peptide repertoire of antigens presented on MHC class I molecules under inflammatory conditions. Importantly, MHC class I-mediated activation of IAV-specific $CD8^+$ T-cells was dampened by cigarette smoke. COPD patients exhibited reduced numbers of circulating IAV-specific $CD8^+$ T-cells compared to healthy controls and asthmatics.

**Conclusion:** Our data indicate that cigarette smoke interferes with MHC class I antigen generation and presentation and thereby contributes to impaired activation of $CD8^+$ T-cells upon virus infection. This adds important mechanistic insight on how cigarette smoke mediates increased susceptibility of smokers and COPD patients to viral infections.



# Conflict of interest statement

Conflict of Interest: H. Ma reports support for the present manuscript from the German Center for Lung Research (DZL). M. Nakayama reports overseas grant from Uehara Memorial Foundation (Japan) and overseas grant from Shiga university of Medical Science, outside the submitted work. A.L. Mora reports support for the present manuscript from NIH (NIH U01 HL1455550-01 and NIH NHLBI R01 HL149825). J.S. Lee reports participation on clinical adjudication committee with Janssen R&D, outside the submitted work. S. Krauss-Etschmann reports support for the present manuscript from the German Center for Lung Research. K. Milger reports consulting fees and lecture honoraria from AstraZeneca, GSK, Janssen, Novartis and Sanofi, outside the submitted work. C.A. Staab-Weijnitz reports support for the present manuscript from Helmholtz Association, German Center for Lung Research (DZL) and Deutsche Forschungsgemeinschaft (DFG) within the Research Training Group GRK2338. K.I. Gaede reports support for the present manuscript from Research Center Borstel – Leibniz Lung Center – BioMaterialBank North, Airway Research Center North, German Center for Lung Research (DZL), PopGen 2.0 Network (P2N). K.I. Gaede also holds a leadership role as member of the Board of Directors of the TMF (www.tmf-ev.de), outside the submitted work. I.E. Kammerl reports support for the present manuscript from ERS (Short Term Fellowship). All other authors have no potential conflicts of interest to declare.

# Comment in

- Blunted adaptive immune responses and acute exacerbations of COPD: breaking the code.
  Bracke KR, Polverino F.Eur Respir J. 2023 Aug 3;62(2):2301030. doi: 10.1183/13993003.01030-2023. Print 2023 Aug.PMID: 37536726 No abstract available.

- 60 references
- 7 figures

Int Angiol

. 2023 Aug;42(4):318-326.

doi: 10.23736/S0392-9590.23.05058-7. Epub 2023 Jun 28.

# Preoperative factors affecting long-term mortality in patients survived to ruptured abdominal aortic aneurysm repair

Nicola Troisi[1], Giacomo Isernia[2], Giulia Bertagna[3], Daniele Adami[3], Luigi Baccani[2], Gianbattista Parlani[2], Raffaella Berchiolli[3], Gioele Simonte[2]

Affiliations expand

- PMID: 37377398

- DOI: 10.23736/S0392-9590.23.05058-7

## Abstract

**Background:** Aim of this study was to retrospectively evaluate preoperative factors affecting long-term mortality in patients survived to surgical repair for ruptured abdominal aortic aneurysms (rAAAs).

**Methods:** From January 2007 to December 2021, 444 patients have been treated for symptomatic or ruptured aortoiliac aneurysms in two tertiary referral centers. Only 405 with diagnosis of rAAA at computed tomography were included in the present study. Initial outcome measures were assessed during at 30 and 90 days post-treatment. Estimated 10-year survival of patients survived after 90 days from the index procedure was evaluated with Kaplan-Meier Test. Uni- and multivariate analyses of the preoperative factors affecting 10-year survival in survivor patients was performed by means of log-rank and multivariate Cox regression analysis.

**Results:** Among included patients, 94 (23.3%) underwent endovascular aortic repair (EVAR) and 311 (76.8%) open surgical repair (OSR). Intraoperative death occurred in 29 patients (7.2%). At 30 days, overall death rate was 24.2% (98/405 cases). Hemorrhagic shock (HR 15.5, 95% CI 3.5 to 41.1, P<0.001) was an independent predictor for 30-day mortality. The overall rate of 90-day mortality was 32.6%. In survivors estimated survival rates at 1, 5, and 10 years were 84.2%, 58.2%, and 33.3%, respectively. Type of treatment (OSR vs. EVAR) did not affect long-term freedom from AAA-related death (HR 0.6, P=0.42). In survivor patients, multivariate analysis confirmed the association between late mortality and female sex (HR 4.7, 95% CI 3.8 to 5.9, P=0.03), age >80 years (HR 28.5, 95% CI 25.1 to 32.3, P<0.001), and chronic obstructive pulmonary disease (HR 5.2, 95% CI 4.3 to 6.3, P=0.02).

**Conclusions:** Late freedom from AAA-related death was not affected by the type of treatment (EVAR vs. OSR) in patients undergoing urgent repair for rAAA. In survivors, female gender, elderly age, and chronic obstructive pulmonary disease negatively affected long-term survival.



Am J Physiol Lung Cell Mol Physiol

. 2023 Aug 1;325(2):L233-L243.

doi: 10.1152/ajplung.00083.2023. Epub 2023 Jun 27.

# Tobacco smoking is associated with combined pulmonary fibrosis and emphysema and worse outcomes in interstitial lung disease

Dylan Douglas[1], Layne Keating[1], Rachel Strykowski[1], Cathryn T Lee[1], Nicole Garcia[1], Kavitha Selvan[1], Neha Kaushik[2], Iazsmin Bauer Ventura[1], Renea Jablonski[1], Rekha Vij[1], Jonathan H Chung[3], Shashi Bellam[2], Mary E Strek[1], Ayodeji Adegunsoye[1,4]

Affiliations expand

- PMID: 37366539
- PMCID: PMC10396279 (available on 2024-08-01)
- DOI: 10.1152/ajplung.00083.2023

## Abstract

Tobacco smoking is an established cause of pulmonary disease whose contribution to interstitial lung disease (ILD) is incompletely characterized. We hypothesized that compared with nonsmokers, subjects who smoked tobacco would differ in their clinical phenotype and have greater mortality. We performed a retrospective cohort study of tobacco smoking in ILD. We evaluated demographic and clinical characteristics, time to clinically meaningful lung function decline (LFD), and mortality in patients stratified by tobacco smoking status (ever vs. never) within a tertiary center ILD registry (2006-2021) and replicated mortality outcomes across four nontertiary medical centers. Data were analyzed by two-sided *t* tests, Poisson generalized linear models, and Cox proportional hazard models adjusted for age, sex, forced vital capacity (FVC), diffusion capacity of the lung for carbon monoxide (DLCO), ILD subtype, antifibrotic therapy, and hospital center. Of 1,163 study participants, 651 were tobacco smokers. Smokers were more likely to be older, male, have idiopathic pulmonary fibrosis (IPF), coronary artery disease, CT honeycombing and emphysema, higher FVC, and lower DLCO than nonsmokers ($P < 0.01$). Time to LFD in smokers was shorter (19.7 ± 20 mo vs. 24.8 ± 29 mo; $P = 0.038$) and survival time was decreased [10.75 (10.08-11.50) yr vs. 20 (18.67-21.25) yr; adjusted mortality HR = 1.50, 95%CI 1.17-1.92; $P < 0.0001$] compared with nonsmokers. Smokers had 12% greater odds of death for every additional 10 pack yr of smoking ($P < 0.0001$). Mortality outcomes remained consistent in the nontertiary cohort (HR = 1.51, 95%CI = 1.03-2.23; $P = 0.036$).

Tobacco smokers with ILD have a distinct clinical phenotype strongly associated with the syndrome of combined PF and emphysema, shorter time to LFD, and decreased survival. Smoking prevention may improve ILD outcomes.**NEW & NOTEWORTHY** Smoking in ILD is associated with combined pulmonary fibrosis and emphysema and worse clinical outcomes.

**Keywords:** interstitial lung disease; mortality; pulmonary fibrosis; smoking; tobacco.

# Conflict of interest statement

M.E.S. served on an advisory committee for Fibrogen; served as a consultant for, served as a speaker for, and received research support from Boehringer Ingelheim; and received research support from Galapagos and Novartis. A.A. received consultancy fees from Roche and Inogen, speaking and advisory board fees from Boehringer Ingelheim, grant funding from the CHEST foundation, and is supported by a career development award from the National Institutes of Health (NHLBI K23HL146942). None of the other authors has any conflicts of interest, financial or otherwise, to disclose.



Review

Curr Opin Allergy Clin Immunol

. 2023 Aug 1;23(4):309-318.

doi: 10.1097/ACI.0000000000000920. Epub 2023 Jun 20.

# COPD and biologic treatment: state of the art

Sebastian Ferri[1], Giovanni Paoletti[1,2], Corrado Pelaia[3], Enrico Heffler[1,2], Giorgio Walter Canonica[1,2], Francesca Puggioni[1]

Affiliations expand

- PMID: 37357768

- DOI: 10.1097/ACI.0000000000000920

## Abstract

**Purpose of review:** Chronic Obstructive Pulmonary Disease (COPD) is a common, heterogeneous disease associated with abnormal inflammatory response of the lung to noxious particles and gases. The progression of disease leads to respiratory failure, disability and premature death. Although recent progress in reducing the global burden of many chronic disease, such as heart disease and cancer, mortality and morbidity due to COPD continue to increase despite of cigarette smoking worldwide policy. Additionally, diagnostic and therapeutic options have not changed in decades. While patients affected by other respiratory disease may benefit with a personalized precision medicine, thanks to the new biological treatment, to date, there is no biological treatment available for COPD. COPD is generally a neutrophils-predominant disease but approximately 40% of patients with COPD had also an eosinophilic airway inflammation.

**Recent findings:** different Phase III trials have been recently performed to evaluate the efficacy and safety of several biological treatments, mostly against eosinophilic inflammation and, to date, some of this trial, still ongoing have promising results.

**Summary:** This review resumes the rationale, the attempts of biological treatment in COPD and latest promising results.



- 76 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

Comment

Lancet Respir Med

. 2023 Aug;11(8):e73.

doi: 10.1016/S2213-2600(23)00185-6. Epub 2023 Jun 21.

# Addressing the origins and health effects of small lungs

Magnus Ekström[1], Helena Backman[2], David Mannino[3]

Affiliations expand

- PMID: 37354918

- DOI: 10.1016/S2213-2600(23)00185-6

*No abstract available*

## Conflict of interest statement

ME is supported by an unrestricted grant from the Swedish Research Council (2019-02081), outside of the submitted work. ME discloses personal fees from AstraZeneca, outside of the submitted work. HB discloses personal fees from AstraZeneca, GSK, and Boehringer Ingelheim, outside of the submitted work. DM is a former employee and current shareholder of GSK, and a consultant to AstraZeneca and the COPD Foundation; he is also an expert witness for Schlesinger Law Offices.

# Comment in

- Addressing the origins and health effects of small lungs - Authors' reply.
  Burney P, Knox-Brown B, Amaral AFS.Lancet Respir Med. 2023 Aug;11(8):e74. doi: 10.1016/S2213-2600(23)00219-9. Epub 2023 Jun 21.PMID: 37354917 No abstract available.

# Comment on

- Small lung syndrome: the need to reclassify chronic lung disease.
  Burney P, Knox-Brown B, Amaral AFS.Lancet Respir Med. 2023 May;11(5):405-406. doi: 10.1016/S2213-2600(23)00091-7. Epub 2023 Mar 29.PMID: 37003282 No abstract available.



Editorial

Am J Respir Crit Care Med

. 2023 Aug 1;208(3):220-222.

doi: 10.1164/rccm.202306-0978ED.

# Leveraging Omics to Predict Chronic Obstructive Pulmonary Disease Exacerbations: The "Immunome"

Francesca Polverino[1], Ravi Kalhan[2]

Affiliations expand

- PMID: 37352489
- PMCID: PMC10395726
- DOI: 10.1164/rccm.202306-0978ED

**Free PMC article**

*No abstract available*

## Comment on

- Blood Gene Expression and Immune Cell Subtypes Associated with Chronic Obstructive Pulmonary Disease Exacerbations.
  Ryu MH, Yun JH, Morrow JD, Saferali A, Castaldi P, Chase R, Stav M, Xu Z, Barjaktarevic I, Han M, Labaki W, Huang YJ, Christenson S, O'Neal W, Bowler R, Sin DD, Freeman CM, Curtis JL, Hersh CP.Am J Respir Crit Care Med. 2023 Aug 1;208(3):247-255. doi: 10.1164/rccm.202301-0085OC.PMID: 37286295

- 14 references
- 1 figure

Ann Am Thorac Soc

. 2023 Aug;20(8):1124-1135.

doi: 10.1513/AnnalsATS.202210-857OC.

# Systemic Markers of Lung Function and Forced Expiratory Volume in 1 Second Decline across Diverse Cohorts

Debby Ngo[1,2], Katherine A Pratte[3], Claudia Flexeder[4,5,6], Hans Petersen[7], Hong Dang[8], Yanlin Ma[9], Michelle J Keyes[1], Yan Gao[10,6], Shuliang Deng[1], Bennet D Peterson[1], Laurie A Farrell[1], Victoria M Bhambhani[1], Cesar Palacios[1], Juweria Quadir[1], Lucas Gillenwater[3], Hanfei Xu[11], Claire Emson[12], Christian Gieger[4,13], Karsten Suhre[14], Johannes Graumann[15], Deepti Jain[16], Matthew P Conomos[16], Russell P Tracy[17], Xiuqing Guo[18], Yongmei Liu[19], W Craig Johnson[16], Elaine Cornell[17], Peter Durda[17], Kent D Taylor[18], George J Papanicolaou[20], Stephen S Rich[9], Jerome I Rotter[18], Steven I Rennard[21], Jeffrey L Curtis[22], Prescott G Woodruff[21], Alejandro P Comellas[23], Edwin K Silverman[24], James D Crapo[3], Martin G Larson[11,25], Ramachandran S Vasan[25,26,27], Thomas J Wang[28,29], Adolfo Correa[30,10], Mario Sims[30,10], James G Wilson[1,30], Robert E Gerszten[1,31], George T O'Connor[25,32], R Graham Barr[33,34], David Couper[8], Josée Dupuis[11], Ani Manichaikul[9], Wanda K O'Neal[8], Yohannes Tesfaigzi[7,35], Holger Schulz[4,5], Russell P Bowler[3]

Affiliations expand

- PMID: 37351609

- DOI: 10.1513/AnnalsATS.202210-857OC

## Abstract

**Rationale:** Chronic obstructive pulmonary disease (COPD) is a complex disease characterized by airway obstruction and accelerated lung function decline. Our understanding of systemic protein biomarkers associated with COPD remains incomplete. **Objectives:** To determine what proteins and pathways are associated with impaired pulmonary function in a diverse population. **Methods:** We studied 6,722

participants across six cohort studies with both aptamer-based proteomic and spirometry data (4,566 predominantly White participants in a discovery analysis and 2,156 African American cohort participants in a validation). In linear regression models, we examined protein associations with baseline forced expiratory volume in 1 second ($FEV_1$) and $FEV_1$/forced vital capacity (FVC). In linear mixed effects models, we investigated the associations of baseline protein levels with rate of $FEV_1$ decline (ml/yr) in 2,777 participants with up to 7 years of follow-up spirometry. **Results:** We identified 254 proteins associated with $FEV_1$ in our discovery analyses, with 80 proteins validated in the Jackson Heart Study. Novel validated protein associations include kallistatin serine protease inhibitor, growth differentiation factor 2, and tumor necrosis factor-like weak inducer of apoptosis (discovery $\beta = 0.0561$, $Q = 4.05 \times 10^{-10}$; $\beta = 0.0421$, $Q = 1.12 \times 10^{-3}$; and $\beta = 0.0358$, $Q = 1.67 \times 10^{-3}$, respectively). In longitudinal analyses within cohorts with follow-up spirometry, we identified 15 proteins associated with $FEV_1$ decline ($Q < 0.05$), including elafin leukocyte elastase inhibitor and mucin-associated TFF2 (trefoil factor 2; $\beta = -4.3$ ml/yr, $Q = 0.049$; $\beta = -6.1$ ml/yr, $Q = 0.032$, respectively). Pathways and processes highlighted by our study include aberrant extracellular matrix remodeling, enhanced innate immune response, dysregulation of angiogenesis, and coagulation. **Conclusions:** In this study, we identify and validate novel biomarkers and pathways associated with lung function traits in a racially diverse population. In addition, we identify novel protein markers associated with $FEV_1$ decline. Several protein findings are supported by previously reported genetic signals, highlighting the plausibility of certain biologic pathways. These novel proteins might represent markers for risk stratification, as well as novel molecular targets for treatment of COPD.

**Keywords:** airflow obstruction; biomarkers; proteomics.

# Comment in

- Multiomics and Multiancestry Approaches: Key Steps to Untangling the Web of Chronic Obstructive Pulmonary Disease Pathogenesis.
  Radder JE, Bon J.Ann Am Thorac Soc. 2023 Aug;20(8):1101-1102. doi: 10.1513/AnnalsATS.202304-311ED.PMID: 37526482 No abstract available.

Eur Respir J

. 2023 Aug 3;62(2):2300538.

doi: 10.1183/13993003.00538-2023. Print 2023 Aug.

# Real-world comparative effectiveness of three single-inhaler dual bronchodilators for the treatment of COPD

Jiaying Li[1,2], Sophie Dell'Aniello[1], Pierre Ernst[1,2,3], Samy Suissa[4,2,3]

Affiliations expand

- PMID: 37343975

- DOI: 10.1183/13993003.00538-2023

## Abstract

**Background:** Single-inhaler dual bronchodilators are now recommended as initial treatment of COPD for patients with multiple exacerbations or with moderate or severe dyspnoea. It is unclear whether there are differences in effectiveness among commonly used dual bronchodilators.

**Methods:** We identified a cohort of COPD patients, aged ≥40 years, treated during 2017-2020, from the UK Clinical Practice Research Datalink, a real-world practice setting. Inhaled corticosteroid-naïve patients initiating vilanterol-umeclidinium (VIL-UME) were compared with those initiating olodaterol-tiotropium (OLO-TIO) or indacaterol-glycopyrronium (IND-GLY) dual bronchodilators primarily on the incidence of moderate and severe COPD exacerbation over 1 year, and corresponding hazard ratios (HRs), after adjustment by propensity score weighting.

**Results:** The cohort included 15 224 initiators of VIL-UME, 5536 initiators of OLO-TIO and 5059 initiators of IND-GLY. The HR of a moderate or severe exacerbation with VIL-UME was 0.91 (95% CI 0.85-0.97) compared with OLO-TIO and 0.96 (95% CI 0.89-1.03) compared with IND-GLY. The risk of severe exacerbation was not different for VIL-UME when compared with OLO-TIO (HR 1.04, 95% CI 0.86-1.26) and IND-GLY (HR 1.05, 95% CI 0.86-1.28). All-cause mortality was lower with VIL-UME compared with IND-GLY (HR 0.82, 95% CI 0.68-0.98), but not compared with OLO-TIO (HR 0.87, 95% CI 0.72-1.04).

**Conclusion:** In a real-world setting of COPD treatment, the three dual bronchodilator combinations were similarly effective on the risk of a severe exacerbation of COPD. However, the VIL-UME and IND-GLY combinations may confer slightly superior effectiveness than OLO-TIO on the risk of moderate or severe exacerbation. The potential lower mortality with VIL-UME warrants further investigation.



# Conflict of interest statement

Conflict of interest: J. Li, S. Dell'Aniello and P. Ernst have no conflicts of interest to disclose. S. Suissa has attended scientific advisory committee meetings or received speaking fees from AstraZeneca, Atara, Boehringer Ingelheim, Bristol-Myers-Squibb, Merck, Novartis, Panalgo, Pfizer and Seqirus.



Sleep Med

. 2023 Aug;108:55-60.

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# The use of continuous positive airway pressure in COPD–OSA overlap syndrome: A systematic review

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Affiliations expand

- PMID: 37336060

- DOI: 10.1016/j.sleep.2023.05.025

## Abstract

**Background:** The co-occurrence of obstructive sleep apnea (OSA) and chronic obstructive pulmonary disease (COPD), known as COPD-OSA overlap syndrome, increases morbidity and mortality. The effectiveness of continuous positive airway pressure (CPAP) therapy, a commonly used treatment for OSA, in this patient population remains uncertain. Therefore, we conducted a systematic review to evaluate the efficacy of CPAP therapy in improving clinical outcomes.

**Methods:** We conducted a comprehensive systematic review to identify studies that evaluated the impact of CPAP therapy on COPD exacerbation, hospitalization, and mortality in patients with COPD-OSA overlap syndrome. We followed the Preferred Reporting Items for Systematic Review and Meta-Analysis Statement and assessed the quality of each study using the Newcastle-Ottawa quality scale.

**Results:** From the initial 3184 articles identified, we reviewed 365 and included five in the systematic review. Our findings revealed that CPAP therapy improved clinical outcomes, including COPD exacerbation, COPD related hospitalization, and mortality in patients with COPD-OSA overlap syndrome. However, the definition of COPD and OSA varied across studies, and the definition of CPAP usage was not consistent.

**Conclusion:** Our systematic review suggests that CPAP therapy is effective in improving outcomes in patients with COPD-OSA overlap syndrome. Nonetheless, further research is required to establish the efficacy of CPAP therapy by standardizing the definition of COPD, OSA, and CPAP usage.

**Keywords:** COPD-OSA Overlap syndrome; Clinical outcome; Continuous positive airway pressure; Systemic review.

## 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 termsexpand

FULL TEXT LINKS


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28

Respirology

. 2023 Aug;28(8):767-774.

doi: 10.1111/resp.14531. Epub 2023 Jun 13.

# Heparan sulphate in infectious and non-infectious exacerbations of COPD

Eleni Papakonstantinou[1,2], Maria-Elpida Christopoulou[2], Meropi Karakioulaki[1], Leticia Grize[1], Michael Tamm[1], Daiana Stolz[1,2]

Affiliations expand

- PMID: 37311657

- DOI: 10.1111/resp.14531

**Free article**


# Abstract


**Background and objective:** Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) are associated with worsening health outcomes and effective treatment of each episode is essential. In this study, we aimed to investigate if plasma levels of heparan sulphate (HS) are associated with the aetiology of AECOPD.

**Methods:** COPD patients (N = 1189), GOLD grade II-IV, from a discovery cohort (N = 638) and from a validation cohort (N = 551), were included in the study. HS and heparanase (HSPE-1) were measured longitudinally in plasma at stable state, at AECOPD and at 4 weeks follow-up.

**Results:** Plasma HS was higher in patients with COPD as compared with non-COPD controls and was significantly increased at AECOPD as compared to stable state ($p < 0.001$) in the discovery and in the validation cohorts. Four distinct exacerbation groups were classified based on aetiology (no-infection/bacterial-infection/viral-infection/bacterial and viral coinfection) in the validation cohort. The fold-increase of HS from stable state to AECOPD was associated with the aetiology of exacerbation and was higher in cases with bacterial and viral coinfections. HSPE-1 was also significantly increased at AECOPD, however, there was no association of HSPE-1 levels with the aetiology of these events. The probability of having an infection at AECOPD was raised as HS levels increased from stable state to AECOPD. This probability was higher for bacterial infections than viral infections.

**Conclusion:** The results of our study indicate that circulating levels of HS are increased at AECOPD and this increase may be associated with the aetiology of these events.



**Keywords:** COPD; COPD exacerbations; airway remodelling; bacterial infections; heparan sulphate; inflammation; viral infections.




- 31 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

Am J Cardiol

. 2023 Aug 1;200:72-74.

doi: 10.1016/j.amjcard.2023.04.044. Epub 2023 Jun 9.

# Outcomes After Isolated Aortic Valve Replacements in Patients With Chronic Obstructive Pulmonary Disease

Shashank Shekhar[1], Roop Kaw[2], Shivabalan Kathavarayan Ramu[1], Adam Pampori[1], Toshiaki Isogai[1], Amar Krishnaswamy[1], Rishi Puri[1], Grant Reed[1], Serge C Harb[1], James Yun[3], Samir R Kapadia[4]

Affiliations expand

- PMID: 37302283

- DOI: 10.1016/j.amjcard.2023.04.044

*No abstract available*

## Conflict of interest statement

Declaration of Competing Interest The authors have no conflicts of interest to declare.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

J Psychiatr Res

. 2023 Aug;164:8-14.

doi: 10.1016/j.jpsychires.2023.05.061. Epub 2023 Jun 3.

# Clinical characterization of patients with bipolar disorder and a history of asthma: An exploratory study

Francisco Romo-Nava[1], Thomas Blom[2], Alfredo B Cuellar-Barboza[3], Francisco J Barrera[4], Alessandro Miola[5], Nicole N Mori[2], Miguel L Prieto[6], Marin Veldic[5], Balwinder Singh[5], Manuel Gardea-Resendez[3], Nicolas A Nunez[5], Aysegul Ozerdem[5], Joanna M Biernacka[7], Mark A Frye[5], Susan L McElroy[2]

Affiliations expand

- PMID: 37290273

- DOI: 10.1016/j.jpsychires.2023.05.061

## Abstract

**Introduction:** Bipolar disorder (BD) and asthma are leading causes of morbidity in the US and frequently co-occur.

**Objectives:** We evaluated the clinical features and comorbidities of patients with BD and a history of asthma.

**Methods:** In a cross-sectional analysis from the Mayo Clinic Bipolar Biobank, we explored the clinical characteristics of the BD and an asthma phenotype and fitted a multivariable regression model to identify risk factors for asthma.

**Results:** A total of 721 individuals with BD were included. From these, 140 (19%) had a history of asthma. In a multivariable model only sex and evening chronotype were significant predictors of asthma with the odds ratios and 95% confidence intervals being 1.65 (1.00, 2.72; p=0.05) and 1.99 (1.25, 3.17; p < 0.01), respectively. Individuals with asthma had higher odds of having other medical comorbidities after adjusting for age, sex, and site including hypertension (OR = 2.29 (95% CI 1.42, 3.71); p < 0.01), fibromyalgia (2.29 (1.16, 4.51); p=0.02), obstructive sleep apnea (2.03 (1.18, 3.50); p=0.01), migraine (1.98 (1.31, 3.00); p < 0.01), osteoarthritis (2.08 (1.20, 3.61); p < 0.01), and COPD (2.80 (1.14, 6.84); p=0.02). Finally, individuals currently on lithium were less likely to have a history of asthma (0.48 (0.32, 0.71); p < 0.01).

**Conclusion:** A history of asthma is common among patients with BD and is associated with being female and having an evening chronotype, as well as with increased odds of having other medical comorbidities. A lower likelihood of a history of asthma among those currently on lithium is an intriguing finding with potential clinical implications that warrants further study.

**Keywords:** Asthma; Bipolar disorder; Chronotype; Comorbid; Fibromyalgia; Hypertension; Lithium; Migraine; Osteoarthritis; Sleep apnea.



# Conflict of interest statement

Declaration of competing interest Dr. Romo-Nava receives grant support from the National Institute of Mental Health K23 Award (K23MH120503) and from a 2017 NARSAD Young Investigator Award from the Brain and Behavior Research Foundation; has a U.S. Patent and Trademark Office patent # 10,857,356; receives consultant fees from Otsuka Pharmaceutical and has received non-financial research support from Soterix Medical. Dr. Cuellar-Barboza has received lecture and consultant fees from Asofarma and Exeltis. Dr. Prieto served on an advisory board for Janssen, receives grant support from ANID FONDECYT Regular 1181365, FONDEF ID19I10116 and Basal Funding for Scientific and Technological Center of Excellence, IMPACT, #FB210024. Dr. Nunez research was supported by National Institute of General Medical Sciences of the National Institutes of Health under award number T32 GM008685. Dr. Frye has received grant support from Assurex Health and Mayo Foundation, has received CME travel support and honoraria from Carnot Laboratories and American Physician Institute, and has financial interest/stockownership/royalties with Chymia LLC. Dr. Alessandro Miola has no conflict of interest to declare. Dr. McElroy is or has been a consultant to or member of the scientific advisory boards of F. Hoffmann-La Roche Ltd. Idorsia, Myriad, Novo Nordisk, Otsuka, Sipnose, Sunovion and Takeda. She is or has been a principal or co-investigator on studies

sponsored by Brainsway, Idorsia, Janssen, Marriott Foundation, Myriad, National Institute of Mental Health, Novo Nordisk, Otsuka, and Sunovion. She is also an inventor on United States Patent No. 6,323,236 B2, Use of Sulfamate Derivatives for Treating Impulse Control Disorders, and along with the patent's assignee, University of Cincinnati, Cincinnati, Ohio, has received payments from Johnson & Johnson, which has exclusive rights under the patent. All other co-authors declare no competing interests for the work presented.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS



Am J Respir Crit Care Med

. 2023 Aug 1;208(3):247-255.

doi: 10.1164/rccm.202301-0085OC.

# Blood Gene Expression and Immune Cell Subtypes Associated with Chronic Obstructive Pulmonary Disease Exacerbations

Min Hyung Ryu[1,2], Jeong H Yun[1,3,2], Jarrett D Morrow[1,2], Aabida Saferali[1,2], Peter Castaldi[1,2], Robert Chase[1], Meryl Stav[1], Zhonghui Xu[1], Igor Barjaktarevic[4], MeiLan Han[5], Wassim Labaki[5], Yvonne J Huang[5,6], Stephanie Christenson[7], Wanda O'Neal[8], Russell Bowler[9], Don D Sin[10,11], Christine M Freeman[5,12], Jeffrey L Curtis[5,13], Craig P Hersh[1,3,2]

Affiliations expand

- PMID: 37286295

- PMCID: PMC10395718 (available on 2024-08-01)

- DOI: 10.1164/rccm.202301-0085OC


# Abstract


**Rationale:** Acute exacerbations of chronic obstructive pulmonary disease (AE-COPDs) are associated with a significant disease burden. Blood immune phenotyping may improve our understanding of a COPD endotype at increased risk of exacerbations. **Objective:** To determine the relationship between the transcriptome of circulating leukocytes and COPD exacerbations. **Methods:** Blood RNA sequencing data ($n$ = 3,618) from the COPDGene (Genetic Epidemiology of COPD) study were analyzed. Blood microarray data ($n$ = 646) from the ECLIPSE (Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints) study were used for validation. We tested the association between blood gene expression and AE-COPDs. We imputed the abundance of leukocyte subtypes and tested their association with prospective AE-COPDs. Flow cytometry was performed on blood in SPIROMICS (Subpopulations and Intermediate Outcomes in COPD Study) ($n$ = 127), and activation markers for T cells were tested for association with prospective AE-COPDs. **Measurements and Main Results:** Exacerbations were reported 4,030 and 2,368 times during follow-up in COPDGene (5.3 ± 1.7 yr) and ECLIPSE (3 yr), respectively. We identified 890, 675, and 3,217 genes associated with a history of AE-COPDs, persistent exacerbations (at least one exacerbation per year), and prospective exacerbation rate, respectively. In COPDGene, the number of prospective exacerbations in patients with COPD (Global Initiative for Chronic Obstructive Lung Disease stage $\geqslant$2) was negatively associated with circulating $CD8^+$ T cells, $CD4^+$ T cells, and resting natural killer cells. The negative association with naive $CD4^+$ T cells was replicated in ECLIPSE. In the flow-cytometry study, an increase in CTLA4 on $CD4^+$ T cells was positively associated with AE-COPDs. **Conclusions:** Individuals with COPD with lower circulating lymphocyte counts, particularly decreased $CD4^+$ T cells, are more susceptible to AE-COPDs, including persistent exacerbations.



**Keywords:** COPD exacerbation; RNA sequencing; chronic obstructive pulmonary disease; circulating leukocytes; immune phenotyping.


# Comment in

- Leveraging Omics to Predict Chronic Obstructive Pulmonary Disease Exacerbations: The "Immunome".

Polverino F, Kalhan R.Am J Respir Crit Care Med. 2023 Aug 1;208(3):220-222. doi: 10.1164/rccm.202306-0978ED.PMID: 37352489 **Free PMC article.** No abstract available.

- Cited by 1 article

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

FULL TEXT LINKS


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32

Respir Med

. 2023 Aug-Sep;215:107297.

doi: 10.1016/j.rmed.2023.107297. Epub 2023 May 27.

# Bacterial load and related innate immune response in the bronchi of rapid decliners with chronic obstructive pulmonary disease

Silvestro Ennio D'Anna[1], Francesca Dossena[2], Isabella Gnemmi[2], Paola Brun[3], Antonio Spanevello[4], Vitina Carriero[5], Francesca Bertolini[5], Mauro Maniscalco[6], Fabio Lm Ricciardolo[5], Bruno Balbi[2], Antonino Di Stefano[2]

Affiliations expand

- PMID: 37245650

- DOI: 10.1016/j.rmed.2023.107297

# Abstract

**Background:** Characterization of COPD patients with rapid lung functional decline is of interest for prognostic and therapeutic reasons. We recently reported an impaired humoral immune response in rapid decliners.

**Objective:** To determine the microbiota associated to markers of innate immune host response in COPD patients with rapid lung functional decline.

**Methods:** In COPD patients monitored for at least 3 years (mean ± SD: 5.8 ± 3 years) for lung functional decline, the microbiota and related markers of immune response was measured in bronchial biopsies of patients with different lung functional decline (rate of FEV1% lung functional decline: no decline FEV1%, ≤20 ml/year n = 21, slow decline FEV1%, >20 ≤ 70 ml/year, n = 14 and rapid decline FEV1%, >70 ml/year, n = 15) using qPCR for microbiota and immunohistochemistry for cell-receptors and inflammatory markers.

**Main results:** Pseudomonas aeruginosa and Streptococcus pneumoniae were increased in rapid decliners vs slow decliners, S. pneumoniae was also increased compared to non decliners. In all patients, S. pneumoniae (copies/ml) positively correlated with pack-years consumption, lung function decline, TLR4, NOD1, NOD2 scored in bronchial epithelium and NOD1/$mm^2$ in lamina propria.

**Conclusion:** These data show an imbalance of microbiota components in rapid decliners which is associated to the expression of the related cell-receptors in all COPD patients. These findings may help in the prognostic stratification and treatment of patients.

**Keywords:** Airway inflammation; COPD; Chronic diseases; Microbiota; Outcome; Prevention; Rehabilitation; Viruses.



# Conflict of interest statement

Declaration of competing interest All the Authors disclose any commercial interest that they may have in the subject of study and the source of any financial or material support.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

Respir Med

. 2023 Aug-Sep;215:107298.

doi: 10.1016/j.rmed.2023.107298. Epub 2023 May 26.

# Degradation of neuromuscular junction contributes to muscle weakness but not physical compromise in chronic obstructive pulmonary disease patients taking lipids-lowering medications

Rizwan Qaisar [1], Asima Karim [2], Tahir Muhammad [3], Shaea A Alkahtani [4], Hossam Kamli [5], Firdos Ahmad [6]

Affiliations expand

- PMID: 37245649

- DOI: 10.1016/j.rmed.2023.107298

## Abstract

**Objectives:** The relevant data about the effects and the associated mechanisms of statins on muscle strength and physical capacity is inconsistent. We investigated the potential contribution of neuromuscular junction (NMJ) degradation to muscle weakness and

physical compromise in patients with chronic obstructive pulmonary disease (COPD) on statins.

**Method:** We recruited male COPD patients (age range = 63-75 years, n = 150) as nonusers (n = 71) and users of statin medications (n = 79) along with age-matched controls (n = 76). The COPD patients were evaluated at baseline and one year later. The data about handgrip strength (HGS), body composition, short physical performance battery (SPPB), and plasma c-terminal agrin fragment-22 (CAF22) as a marker of NMJ disintegration was collected at two time points.

**Results:** We observed lower HGS, SPPB scores, and higher CAF22 levels in all COPD patients than controls, irrespective of the treatment status (all $p < 0.05$). Statins further reduced HGS and elevated CAF22 in COPD patients (both $p < 0.05$). The decline in SPPB was relatively modest in statin users (≈3.7%, $p = 0.032$) than in nonusers (≈8.7%, $p = 0.002$). The elevated plasma CAF22 exhibited robust negative correlations with a reduction in HGS but not with SPPB in COPD patients taking statins. We also found a reduction in markers of inflammation and no increase in oxidative stress markers following statin use in COPD patients.

**Conclusion:** Altogether, statin-induced NMJ degradation exacerbates muscle decline but does not contribute to physical compromise in COPD patients.

**Keywords:** C-terminal agrin-fragment 22; Chronic obstructive pulmonary disease; Handgrip strength; Neuromuscular junction; Short physical performance battery; Statins.



# Conflict of interest statement

Declaration of competing interest The authors declare that they have no conflict of interest.

J Clin Nurs

. 2023 Aug;32(15-16):5093-5102.

doi: 10.1111/jocn.16771. Epub 2023 May 27.

# Physical activity trajectories and their determinants in patients with chronic obstructive pulmonary disease: A cohort study

Ran An[1], Shifang Zhang[1], Xiuxiu Huang[1], Yue Lan[1], Ting Cao[1], Qiaoqin Wan[1]

Affiliations expand

- PMID: 37243430

- DOI: 10.1111/jocn.16771

## Abstract

**Aims and objectives:** The aim was to identify latent trajectories in physical activity (PA) and their determinants in adults with chronic obstructive pulmonary disease (COPD) based on the socio-ecological model.

**Background:** PA has been linked to poor long-term outcomes in patients with COPD. However, few studies have explored their PA trajectories and their predictors.

**Design:** Cohort study.

**Methods:** We used data from a national cohort and included 215 participants. PA was quantified using a short PA questionnaire, and group-based trajectory modelling was used to explore the PA trajectories. Multinomial logistic regression was conducted to identify the predictors of PA trajectories. Generalised linear mixed models were used to elucidate

the associations between predictors and PA during follow-up. A STROBE checklist was used to guide the reporting of this study.

**Results:** Three PA trajectory patterns were identified among 215 COPD participants with an average age of 60.51 ± 8.87: stable inactive group (66.7%), sharp decline group (25.7%) and stable active group (7.5%). The logistic regression showed that age, sex, income, peak expiratory flow, upper limb capacity, depressive symptoms, the frequency of contact with children were PA predictors. Upper limb capacity weakness and depressive symptoms were found to be associated with a sharp decline in PA during follow-up.

**Conclusions:** This study revealed three PA trajectories among patients with COPD. In addition to strengthening the physical functions and mental health of patients, support from the family, community and society also play a crucial role in promoting PA of patients with COPD.

**Relevance to clinical practice:** It is essential to identify distinct PA trajectories in patients with COPD to develop future interventions that promote PA.

**No patient or public contribution:** A national cohort study was used and no patients or the public were involved in the design and implementation of this study.

**Keywords:** COPD; physical activity; socio-ecological model; trajectory.



- 44 references

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

FULL TEXT LINKS


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Infect Dis (Lond)

-

. 2023 Aug;55(8):533-542.

doi: 10.1080/23744235.2023.2217904. Epub 2023 May 26.

# Airflow obstruction and chronic obstructive pulmonary disease are common in pulmonary tuberculosis even without sequelae findings on chest X-ray

Hye Jung Park[1], Min Kwang Byun[1], Jaeuk Lee[1], Chi Young Kim[1], Sojung Shin[2,3], Youlim Kim[2,3], Chin Kook Rhee[4], Ki Suck Jung[5], Kwang Ha Yoo[2,3]

Affiliations expand

- PMID: 37243367

- DOI: 10.1080/23744235.2023.2217904

## Abstract

**Purpose:** Pulmonary tuberculosis (TB) is a well-known risk factor for airflow obstruction and chronic obstructive pulmonary disease (COPD). The prognosis of TB without sequelae on chest X-ray (CXR) remains uncertain.

**Methods:** We used the 2008-2009 Korea National Health and Nutrition Examination Survey (KNHANES) data and 2007-2012 KNHANES-matched Health Insurance Review and Assessment Service cohort data. Airflow obstruction was assessed using a pulmonary function test. COPD was defined using diagnostic codes and the use of COPD medication for 3-year. We classified subjects into three groups based on TB history and sequelae on CXR.

**Results:** In 4911 subjects, the CXR(-) (no TB sequelae on CXR) post-TB group ($n$ = 134) showed similar characteristics and normal lung function compared to that of the control group ($n$ = 4,405), while the CXR(+) (TB sequelae on CXR) post-TB group ($n$ = 372) showed different characteristics and reduced lung function. The prevalence of airflow obstruction was 9.3%, 13.4%, and 26.6% in control, CXR(-) post-TB, and CXR(+) post-TB groups, respectively. COPD was more common in the post-TB with CXR(+) (6.5%) or without CXR (-

) (4.5%) groups, than in the control group (1.8%). Compared to the CXR(-) post-TB group, the control group showed a lower risk for airflow obstruction (OR, 0.774; $p$ = .008). The CXR(+) post-TB group showed a higher risk for airflow obstruction (OR, 1.456; $p$ = .011). The Control group also showed a lower risk for the development of COPD than the CXR(-) post-TB group (OR, 0.496; $p$ = .011).

**Conclusions:** We need to educate TB patients that airway obstruction and COPD can easily develop, even if TB sequelae are not observed on CXR.

**Keywords:** COPD; Pulmonary tuberculosis; airflow obstruction.



Life Sci Alliance

. 2023 May 25;6(8):e202201853.

doi: 10.26508/lsa.202201853. Print 2023 Aug.

# Modeling fibrotic alveolar transitional cells with pluripotent stem cell–derived alveolar organoids

Victoria Ptasinski[1,2,3,4], Susan J Monkley[5], Karolina Öst[1], Markus Tammia[1], Hani N Alsafadi[2,3,4], Catherine Overed-Sayer[6], Petra Hazon[1], Darcy E Wagner[2,3,4], Lynne A Murray[7]

Affiliations expand

- PMID: 37230801
- PMCID: PMC10213712
- DOI: 10.26508/lsa.202201853


**Free PMC article**

# Abstract


Repeated injury of the lung epithelium is proposed to be the main driver of idiopathic pulmonary fibrosis (IPF). However, available therapies do not specifically target the epithelium and human models of fibrotic epithelial damage with suitability for drug discovery are lacking. We developed a model of the aberrant epithelial reprogramming observed in IPF using alveolar organoids derived from human-induced pluripotent stem cells stimulated with a cocktail of pro-fibrotic and inflammatory cytokines. Deconvolution of RNA-seq data of alveolar organoids indicated that the fibrosis cocktail rapidly increased the proportion of transitional cell types including the *KRT5*$^{-}$*/KRT17*$^{+}$ aberrant basaloid phenotype recently identified in the lungs of IPF patients. We found that epithelial reprogramming and extracellular matrix (ECM) production persisted after removal of the fibrosis cocktail. We evaluated the effect of the two clinically approved compounds for IPF, nintedanib and pirfenidone, and found that they reduced the expression of ECM and pro-fibrotic mediators but did not completely reverse epithelial reprogramming. Thus, our system recapitulates key aspects of IPF and is a promising system for drug discovery.




# Conflict of interest statement

AstraZeneca funded this study and participated in the study design, data collection, data analysis and data interpretation. V Ptasinski, SJ Monkley, K Öst, M Tammia, C Overed-Sayer, P Hazon, and LA Murray were full-time employees at AstraZeneca at the time of the study and may own shares in AstraZeneca.


- 75 references
- 24 figures


SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

Respir Med

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doi: 10.1016/j.rmed.2023.107265. Epub 2023 May 22.

# The minimal important difference of the constant work rate cycle test in severe COPD

Marieke C van der Molen[1], Dirk-Jan Slebos[2], Sonja W S Augustijn[3], Huib A M Kerstjens[2], Jorine E Hartman[2]

Affiliations expand

- PMID: 37224889

- DOI: 10.1016/j.rmed.2023.107265

**Free article**

## Abstract

**Background:** The Constant Work Rate Cycle Test (CWRT) is a commonly used and sensitive test to detect treatment success in patients with Chronic Obstructive Pulmonary Disease (COPD). Earlier, the Minimal Important Difference (MID) of the CWRT was estimated at 101 s (or 34%) change from baseline based on one well executed study.

However, this study was performed in a population of patients with mild-to-moderate COPD, and we have learned that MIDs might be quite different in patients with severe COPD. Therefore, we aimed to establish the MID of the CWRT in patients with severe COPD.

**Methods:** We included 141 patients with severe COPD, who underwent either pulmonary rehabilitation, bronchoscopic lung volume reduction with endobronchial valves, or a sham bronchoscopy as a control group. CWRT workload was set at 75% of the peak work capacity, as determined by an incremental cycle test. We used the change in 6-min walking test (6-MWT), forced expiratory volume in 1s ($FEV_1$), residual volume (RV), and St. George's Respiratory Questionnaire (SGRQ) total score as anchors to calculate the MID.

**Results:** All anchors had an association of ≥0.41 with change in CWRT. The MID estimates for the different anchors were: 6-MWT 278 s (95%), $FEV_1$ 273 s (90%), RV 240 s (84%), and SGRQ 208 s (71%). The average of these four MID estimates resulted in an MID of 250 s (or 85%).

**Conclusion:** We established the MID for CWRT at 250 s (or 85%) change from baseline in patients with severe COPD.



# Conflict of interest statement

Declaration of competing interest There is no conflict of interest.

Neurol Ther

. 2023 Aug;12(4):1051-1068.

doi: 10.1007/s40120-023-00493-6. Epub 2023 May 24.

# Comparison Between Burden of Care Partners of Individuals with Alzheimer's Disease Versus Individuals with Other Chronic Diseases

Murat Demirbas[1], Julie H Hahn-Pedersen[2], Henrik L Jørgensen[3,4]

Affiliations expand

- PMID: 37222859

- PMCID: PMC10310688

- DOI: 10.1007/s40120-023-00493-6

**Free PMC article**

## Abstract

**Background:** Caregiving in Alzheimer's disease (AD) is often provided by informal care partners, who spend more hours per week on average than care partners of individuals with conditions other than AD. However, the burden of care in partners of individuals with AD has not been systematically compared to that of other chronic diseases.

**Objective:** The current study therefore aims to compare the care partner burden of AD to that of other chronic diseases through a systematic literature review.

**Methods:** Data was collected from journal articles published in the last 10 years, using two unique search strings in PubMed and analysed using pre-defined patient-reported outcome measures (PROMs) including the EQ-5D-5L, GAD-7, GHQ-12, PHQ-9, WPAI and the ZBI. The data was grouped according to the included PROMs and the diseases studied.

The number of participants in the studies reporting burden of caregiving in AD was adjusted to reflect the number of participants in studies reporting care partner burden in other chronic diseases.

**Results:** All results in this study are reported as a mean value and standard deviation (SD). The ZBI measurement was the most frequently used PROM to collect care partner burden (15 studies) and showed a moderate burden (mean 36.80, SD 18.35) on care partners of individuals with AD, higher than most of the other included diseases except for those characterized by psychiatric symptoms (mean scores 55.92 and 59.11). Other PROMs such as PHQ-9 (six studies) and GHQ-12 (four studies) showed a greater burden on care partners of individuals with other chronic diseases such as heart failure, haematopoietic cell transplantations, cancer and depression compared to AD. Likewise, GAD-7 and EQ-5D-5L measurements showed a lesser burden on care partners of individuals with AD compared to care partners of individuals with anxiety, cancer, asthma and chronic obstructive pulmonary disease. The current study suggests that care partners of individuals with AD experience a moderate burden, but with some variations depending on the PROMs used.

**Conclusion:** The results of this study were mixed with some PROMs indicating a greater burden for care partners of individuals with AD versus other chronic diseases, and other PROMs showing a greater burden for care partners of individuals with other chronic diseases. Psychiatric disorders imposed a greater burden on care partners compared to AD, while somatic diseases in the musculoskeletal system resulted in a significantly smaller burden on care partners compared to AD.

**Keywords:** Alzheimer's disease; Care partner burden; Chronic diseases; Patient-reported outcome measure.



# Conflict of interest statement

Julie H. Hahn-Pedersen is employed by Novo Nordisk inc. (Bagsvaerd, Denmark). Henrik L. Jørgensen and Murat Demirbas have nothing to disclose.

- 94 references
- 3 figures

SUPPLEMENTARY INFO

Publication types, Grant supportexpand

FULL TEXT LINKS

Review

Respir Med

. 2023 Aug;214:107284.

doi: 10.1016/j.rmed.2023.107284. Epub 2023 May 19.

# Clinical characteristics of chronic obstructive pulmonary disease in never-smokers: A systematic review

Carlota Rodríguez García[1], Alberto Ruano-Ravina[2], Mónica Pérez Ríos[3], Lucía Martín Gisbert[4], Leonor Varela-Lema[3], Cristina Candal-Pedreira[5], Cristina Represas-Represas[6], Julia Rey-Brandariz[7], Luis Valdés-Cuadrado[8], Alvar Agustí[9]

Affiliations expand

- PMID: 37211258

- DOI: 10.1016/j.rmed.2023.107284

**Free article**

## Abstract

**Introduction:** Chronic Obstructive Pulmonary Disease (COPD) is the third cause of death worldwide. While tobacco smoking is a key risk factor, COPD also occurs in never-smokers

(NS). However, available evidence on risk factors, clinical characteristics, and natural history of the disease in NS is scarce. Here, we perform a systematic review of the literature to better describe the characteristics of COPD in NS.

**Methods:** We searched different databases following the PRISMA guidelines with explicit inclusion and exclusion criteria. A purpose-designed quality scale was applied to the studies included in the analysis. It was not possible to pool the results due to the high heterogeneity of the studies included.

**Results:** A total of 17 studies that met the selection criteria were included, albeit only 2 of them studied NS exclusively. The total number of participants in these studies were 57,146 subjects, 25,047 of whom were NS and 2,655 of the latter had NS-COPD. Compared to COPD in smokers, COPD in NS is more frequent in women and older ages, and is associated with a slightly higher prevalence of comorbidities. There are not enough studies to understand if COPD progression and clinical symptoms in NS are different to that of ever-smokers.

**Conclusions:** There is a significant knowledge gap on COPD in NS. Given that COPD in NS account for about a third of all COPD patients in the world, particularly in low-middle income countries, and the decrease in tobacco consumption in high income countries, understanding COPD in NS constitutes a public-health priority.

**Keywords:** COPD; Non-smokers; Population characteristics; Systematic review.



# 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: Alberto Ruano-Ravina reports financial support was provided by Carlos III Health Institute. Alvar Agusti reports a relationship with Gold that includes: board membership.

Respir Care

. 2023 Aug;68(8):1041-1048.

doi: 10.4187/respcare.10760. Epub 2023 May 16.

# Assessment of Noninvasive Oxygen Saturation in Patients With COPD During Pulmonary Rehabilitation: Smartwatch versus Pulse Oximeter

Morten Pallisgaard Støve[1,2], Aske Hostrup Graversen[3], Johanne Sørensen[3]

Affiliations expand

- PMID: 37193599

- PMCID: PMC10353168 (available on 2024-08-01)

- DOI: 10.4187/respcare.10760

## Abstract

**Background:** Patients with COPD can have hypoxemia; hence, monitoring peripheral $S_{pO_2}$ during pulmonary rehabilitation is recommended. This study aimed to examine the accuracy of $S_{pO_2}$ readings in patients with COPD as measured by wearable devices at rest and after physical exercise.

**Methods:** Thirty-six participants with COPD (20 women), ages 52-89 years, participated in this cross-sectional study. Oxygen saturation was concurrently measured by using the Contec Pulse Oximeter CMS50D as a comparator, and the Apple Watch Series 7 and the Garmin Vivosmart 4 at rest and immediately after the 30-s sit-to-stand test and the 6-min walk test (6MWT).

**Results:** For the Apple Watch, the root mean squared error showed a deviation of 3.5% at rest, 4.1% after the 30-s sit-to-stand test, and 3.9% after the 6MWT. The level of agreement was 2.8 ± 2.4 (7.6, -1.9) at rest, 3.1 ± 2.8 (8.6, -2.3) after the 30-s sit-to-stand test, and 2.8 ± 2.9 (8.6, -2.9) after the 6MWT. For the Garmin Vivosmart, the root mean squared error showed a deviation of 3.3% at rest, 6.1% after the 30-s sit-to-stand test, and 5.4% after the 6MWT. Level of agreement was 1.9 ± 2.7 (7.2, -3.3) at rest, 2.9 ± 5.4 (13.5, -7.7) after the 30-s sit-to-stand test, and 2.3 ± 5.0 (12.1, -7.4) after the 6MWT. The limits of agreement showed considerable measurement variance and a tendency for the devices to be less accurate at lower saturation levels.

**Conclusions:** The Apple Watch Series 7 and Garmin Vivosmart 4 overestimated $S_{pO_2}$ in participants with COPD when $S_{pO_2}$ was < 95% and underestimated oxygen saturation when saturation was > 95%. These findings suggest that wearable devices should not be used to monitor oxygen saturation during pulmonary rehabilitation.

**Keywords:** COPD; Wearable devices; oxygen saturation; pulmonary rehabilitation; respiratory care; validity.

doi: 10.4187/respcare.10575. Epub 2023 Apr 25.

# Patient-Assessed Quality of Virtual Consultations as Follow-Up on Long-Term Oxygen Therapy for Patients With COPD

Hannah Clement Schmidt[1], Helle Marie Christensen[2]

Affiliations expand

- PMID: 37185114

- PMCID: PMC10353161 (available on 2024-08-01)

- DOI: 10.4187/respcare.10575

## Abstract

**Background:** Long-term oxygen therapy (LTOT) can increase survival time and relieve symptom burden in patients with COPD and chronic hypoxemia. The Department of Respiratory Medicine at Odense University Hospital invites patients with LTOT and COPD to the out-patient clinic for treatment evaluation every 6 months to regulate or terminate treatment and support patients' treatment adherence. The out-patient clinic, however, experiences many absences or cancellations from patients. For that reason, patients were offered virtual consultation as an alternative to physical attendance. This study was initiated to uncover reasons for absences and the patients' experiences of virtual consultation to promote a more patient-centered clinical practice for patients with COPD and LTOT.

**Methods:** A qualitative study encompassing semi-structured interviews with 20 subjects was conducted in the winter of 2021. The subjects had tried or been given the opportunity of virtual consultation. Data were analyzed inspired by Kvale and Brinkmann focusing on the subject's perspectives on virtual consultation.

**Results:** The analysis resulted in 3 main themes: limitations and vulnerabilities, independence and quality of life, and personal strategies. Subjects expressed that everyday life with LTOT and COPD was characterized by limited resources in terms of energy, oxygen, and time. LTOT was perceived as a necessary means to maintain a sense of

independence and quality of life. However, LTOT also meant additional limitations due to cumbersome equipment and feelings of isolation. Most subjects considered the virtual consultation to be oxygen-, energy-, and time-preserving, as it meant avoiding stressful transportation and handling of oxygen cylinders, COVID-19 exposure, waiting time, and not having to involve others for help.

**Conclusions:** The subjects' perspective showed that follow-up on LTOT as a virtual consultation was considered a valuable offer. The chosen method was found to be relevant in uncovering subjects' attitudes toward clinical practice procedures.

**Keywords:** COPD; chronic obstructive; critical psychology; home oxygen; long-term oxygen therapy; patient attitudes; patient perspective; pulmonary disease; qualitative research; telemedicine; virtual consultation.



# Conflict of interest statement

The authors have disclosed no conflicts of interest.

- 25 references



Am J Respir Cell Mol Biol

. 2023 Aug;69(2):230-241.

doi: 10.1165/rcmb.2022-0382OC.

# Diastolic Cardiomyopathy Secondary to Experimentally Induced Exacerbated Emphysema

Pierre-Edouard Grillet[1,2], Elodie Desplanche[1], Quentin Wynands[1,3], Fares Gouzi[1,4], Patrice Bideaux[1], Aurelie Fort[3], Valérie Scheuermann[1], Alain Lacampagne[1], Anne Virsolvy[1], Jérôme Thireau[1], Pieter de Tombe[1], Arnaud Bourdin[1,3], Olivier Cazorla[1]

Affiliations expand

- PMID: 37163759

- DOI: 10.1165/rcmb.2022-0382OC

## Abstract

Chronic obstructive pulmonary disease (COPD) is a clinical entity of increasing significance. COPD involves abnormalities of the airways and, in emphysema, parenchymal pulmonary destruction. Cardiovascular disease has emerged as a significant comorbidity to COPD. Heart failure with preserved ejection fraction (HFpEF) appears to be particularly associated with COPD-emphysema. Traditional treatments have shown limited efficacy in improving COPD-associated HFpEF. This lack of therapeutic efficacy highlights the need to identify potential mechanisms that link COPD-emphysema to HFpEF. Therefore, we aimed to study the delayed cardiac physiological impacts in a rat model with acute exacerbated emphysema. Emphysema was induced by four weekly 4 units elastase (ELA) intratracheal pulmonary instillations and exacerbation by one final additional lipolysaccharide (LPS) instillation in male Wistar rats. At 5 weeks after the ELA and LPS exposure, *in vivo* and *ex vivo* pulmonary and cardiac measurements were performed. Experimental exacerbated emphysema resulted in decreased pulmonary function and exercise intolerance. Histological analysis revealed parenchymal pulmonary destruction without signs of inflammation or cardiac fibrosis. *In vivo* cardiac functional analysis revealed diastolic dysfunction and tachycardia. *Ex vivo* analysis revealed a cellular cardiomyopathy with decreased myofilament $Ca^{2+}$ sensitivity, cross-bridge cycling kinetics, and increased adrenergic PKA (protein kinase A)-dependent phosphorylation of troponin-I. Experimental exacerbated emphysema was associated with exercise intolerance that appeared to be secondary to increased β-adrenergic tone and subsequent cardiac myofilament dysfunction. A $\beta_1$-receptor antagonist treatment (bisoprolol) started 24 hours after ELA-LPS instillation prevented *in vivo* and *ex vivo* diastolic dysfunction. These results suggest that novel treatment strategies targeted to the cardiac myofilament may be beneficial to combat exacerbated emphysema-associated HFpEF.

**Keywords:** calcium; cardiac myofilaments; chronic obstructive pulmonary disease; elastase; heart failure with preserved ejection fraction.



Randomized Controlled Trial

Am J Med Sci

. 2023 Aug;366(2):124-134.

doi: 10.1016/j.amjms.2023.05.005. Epub 2023 May 6.

# Non-invasive ventilatory support accelerates the oxygen uptake and heart rate kinetics and improves muscle oxygenation dynamics in COPD-HF patients

Rodrigo Polaquini Simões[1], Cássia da Luz Goulart[1], Flávia Rossi Caruso[1], Adriana S Garcia de Araújo[1], Sílvia Cristina Garcia de Moura[2], Aparecida Maria Catai[2], Polliana Batista Dos Santos[1], Patricia de Faria Camargo[1], Renan Shida Marinho[1], Renata Gonçalves Mendes[1], Audrey Borghi-Silva[3]

Affiliations expand


- PMID: 37156461

- DOI: 10.1016/j.amjms.2023.05.005


# Abstract

**Background:** The aim of this study was to explore the effects of non-invasive positive pressure ventilation (NIPPV) associated with high-intensity exercise on heart rate (HR) and oxygen uptake ($\dot{V}O_2$) recovery kinetics in in patients with coexistence of chronic obstructive pulmonary disease (COPD) and heart failure (HF).

**Methods:** This is a randomized, double blinded, sham-controlled study involving 14 HF-COPD patients, who underwent a lung function test and Doppler echocardiography. On two different days, patients performed incremental cardiopulmonary exercise testing (CPET) and two constant-work rate tests (80% of CPET peak) receiving Sham or NIPPV (bilevel mode - Astral 150) in a random order until the limit of tolerance (Tlim). During exercise, oxyhemoglobin and deoxyhemoglobin were assessed using near-infrared spectroscopy (Oxymon, Artinis Medical Systems, Einsteinweg, Netherland).

**Results:** The kinetic variables of both $\dot{V}O_2$ and HR during the high-intensity constant workload protocol were significantly faster in the NIPPV protocol compared to Sham ventilation ($P < 0.05$). Also, there was a marked improvement in oxygenation and lower deoxygenation of both peripheral and respiratory musculature in TLim during NIPPV when contrasted with Sham ventilation.

**Conclusions:** NIPPV applied during high-intensity dynamic exercise can effectively improve exercise tolerance, accelerate HR and $\dot{V}O_2$ kinetics, improve respiratory and peripheral muscle oxygenation in COPD-HF patients. These beneficial results from the effects of NIPPV may provide evidence and a basis for high-intensity physical training for these patients in cardiopulmonary rehabilitation programs.

**Keywords:** Blood flow muscle; COPD; Cardiovascular physiology; Heart failure; Oxygen consumption.



# Conflict of interest statement

Declaration of Competing Interest No potential conflict of interest was reported by the authors.

Eur J Med Chem

. 2023 Aug 5;256:115374.

doi: 10.1016/j.ejmech.2023.115374. Epub 2023 Apr 24.

# Design and synthesis of a novel class of PDE4 inhibitors with antioxidant properties as bifunctional agents for the potential treatment of COPD

Youzhi Wang[1], Huifang Wang[1], Guoqing Yang[1], Qingjing Hao[1], Kan Yang[2], Huizhen Shen[1], Yulong Wang[1], Jinxin Wang[3]

Affiliations expand

- PMID: 37150057

- DOI: 10.1016/j.ejmech.2023.115374

## Abstract

It is well known that chronic obstructive pulmonary disease (COPD) patients are always trapped in the vicious circle of inflammation and oxidative stress, therefore anti-inflammatory and antioxidant bifunctional agents may interrupt this vicious cycle in COPD. Phosphodiesterase 4 (PDE4) inhibitors, as anti-inflammatory drugs, have been used for COPD treatment in clinical, and the PDE4 inhibitors with antioxidant properties may be a good strategy to design bifunctional agents for COPD. Sappanone A was the first PDE4 inhibitor with antioxidant properties we identified from natural products in our previous study, which was used by us as a hit compound to design new bifunctional agents for COPD in this study. 27 derivatives of sappanone A including homoisoflavonoids, aurones and chalcones were designed and synthesized by innovatively fusing the antioxidant pharmacophore of catechol from polyphenols and the pharmacophore of catechol ether abstracted from the PDE4 inhibitors of the catechol ether class such as rolipram, roflumilast and apremilast respectively. All the compounds were assayed for the PDE4 inhibitory and radical scavenging against 2, 2-diphenyl-1-picrylhydrazyl (DPPH) activities in vitro. Herein we obtained a series of bifunctional compounds with better PDE4 inhibitory activity than sappanone A, and their free radical scavenging activities were superior to edaravone in vitro. In addition, they can reduce tumour necrosis factor-alpha (TNF-α) production induced by lipopolysaccharide (LPS) in RAW264.7 macrophages and malondialdehyde (MDA) production induced by $Fe^{2+}$ in mouse lung homogenate. Meanwhile, it showed outstanding abilities in reducing $Fe^{3+}$ and complexing $Fe^{2+}$. 6o, as the candidate anti-inflammatory and antioxidant bifunctional compound, exhibited good drug-likeness, ADME (Absorption, Distribution, Metabolism, Excretion) properties and human liver microsomal stability. In vivo, 6o (50 mg/kg and 100 mg/kg, i. p.) distinctly prevented LPS-induced serum levels of TNF-α in mice. In conclusion, the preliminary investigation provided a novel class of PDE4 inhibitors with antioxidant properties as bifunctional agents for the potential treatment of COPD, which can interrupt the vicious cycle of chronic inflammation and oxidative stress in COPD.

**Keywords:** Anti-inflammatory; Antioxidant; COPD; PDE4 inhibitor; Sappanone A.



# Conflict of interest statement

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

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS

Case Reports

Arch Bronconeumol

. 2023 Aug;59(8):537-539.

doi: 10.1016/j.arbres.2023.03.024. Epub 2023 Apr 20.

# Reduction in Hospital Admissions for Asthma and COPD During the First Year of COVID-19 Pandemic in Spain

[Article in English, Spanish]

Marta Galán-Negrillo[1], Eduardo García-Pachón[2]

Affiliations expand

- PMID: 37149468
- PMCID: PMC10118055
- DOI: 10.1016/j.arbres.2023.03.024

**Free PMC article**

*No abstract available*

- 20 references
- 1 figure

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS



Cite

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46

Respir Med

. 2023 Aug;214:107262.

doi: 10.1016/j.rmed.2023.107262. Epub 2023 May 2.

# There is still no established and accepted definition of COPD

Mario Cazzola[1], Francesco Blasi[2]

Affiliations expand

- PMID: 37142165

- DOI: 10.1016/j.rmed.2023.107262

*No abstract available*

**Keywords:** COPD; Definition; Treatable treats.

## Conflict of interest statement

Declaration of competing interest Nothing to declare.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS



Review

J Adv Nurs

. 2023 Aug;79(8):2802-2814.

doi: 10.1111/jan.15693. Epub 2023 May 3.

# Effectiveness of internet-based self-management interventions on pulmonary function in patients with chronic obstructive pulmonary disease: A systematic review and meta-analysis

Yan-Yan Liu[1], Ya-Jie Li[1], Han-Bing Lu[1], Chun-Yu Song[1], Ting-Ting Yang[1], Jiao Xie[1]

Affiliations expand

- PMID: 37139550

- DOI: 10.1111/jan.15693


# Abstract


**Aim:** To investigate the effectiveness of internet-based self-management interventions on pulmonary function in patients with chronic obstructive pulmonary disease (COPD).

**Design:** Systematic review and meta-analysis.

**Data sources:** Eight electronic databases including PubMed, Web of Science, Cochrane library, Embase, CINAHL, China National Knowledge Infrastructure, Wangfang and Weipu databases were systematically searched from inception of the database to January 10, 2022.

**Methods:** Statistical analysis was performed using Review Manager 5.4 and results were reported as mean difference (MD) or standard mean difference (SMD) with 95% confidence intervals (CI). Outcomes were the forced expiratory volume in 1 second (FEV1), forced volume capacity (FVC) and percent of FEV1/FVC. The Cochrane Risk of Bias Tool was used to assess the risk of bias of included studies. The study protocol was not registered.

**Results:** Eight randomized controlled trials (RCTs) including 476 participants met the inclusion criteria and were included in meta-analysis. It was found that internet-based self-management interventions showed a significant improvement in FVC(L), while FEV1 (%), FEV1 (L), FEV1/FVC (%) and FVC (%) did not significantly improve.

**Conclusions:** Internet-based self-management interventions were effective in improving pulmonary function in patients with COPD, caution should be exercised in interpreting the results. RCTs of higher quality are needed in the future to further demonstrate the effectiveness of the intervention.

**Relevance to clinical practice:** It provides evidence for internet-based self-management interventions in improving pulmonary function in patients with COPD.

**Impact:** The results suggested that internet-based self-management interventions could improve the pulmonary function in people with COPD. This study provides a promising alternative method for patients with COPD who have difficulty seeking face-to-face self-management interventions, and the intervention can be applied in clinical settings.

**Patient or public contribution:** No Patient or Public Contribution.



**Keywords:** chronic obstructive pulmonary disease; internet-based; meta-analysis; nursing; pulmonary function; self-management; systematic review.

- 48 references

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS


Proceed to details

Cite

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48

Sci Total Environ

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. 2023 Aug 1;884:163802.

doi: 10.1016/j.scitotenv.2023.163802. Epub 2023 Apr 29.

# Long-term residential exposure to air pollution and risk of chronic respiratory diseases in Italy: The BIGEPI study

Pierpaolo Marchetti[1], Jessica Miotti[1], Francesca Locatelli[1], Leonardo Antonicelli[2], Sandra Baldacci[3], Salvatore Battaglia[4], Roberto Bono[5], Angelo Corsico[6], Claudio Gariazzo[7], Sara Maio[3], Nicola Murgia[8], Pietro Pirina[9], Camillo Silibello[10], Massimo Stafoggia[11], Lorena Torroni[1], Giovanni Viegi[3], Giuseppe Verlato[1], Alessandro Marcon[12]; BIGEPI group

Affiliations expand

- PMID: 37127163

- DOI: 10.1016/j.scitotenv.2023.163802

**Free article**

# Abstract

Long-term exposure to air pollution has adverse respiratory health effects. We investigated the cross-sectional relationship between residential exposure to air pollutants and the risk of suffering from chronic respiratory diseases in some Italian cities. In the BIGEPI project, we harmonised questionnaire data from two population-based studies conducted in 2007-2014. By combining self-reported diagnoses, symptoms and medication use, we identified cases of rhinitis (n = 965), asthma (n = 328), chronic bronchitis/chronic obstructive pulmonary disease (CB/COPD, n = 469), and controls (n = 2380) belonging to 13 cohorts from 8 Italian cities (Pavia, Turin, Verona, Terni, Pisa, Ancona, Palermo, Sassari). We derived mean residential concentrations of fine particulate matter ($PM_{10}$, $PM_{2.5}$), nitrogen dioxide ($NO_2$), and summer ozone ($O_3$) for the period 2013-2015 using spatiotemporal models at a 1 km resolution. We fitted logistic regression models with controls as reference category, a random-intercept for cohort, and adjusting for sex, age, education, BMI, smoking, and climate. Mean ± SD exposures were 28.7 ± 6.0 μg/m³ ($PM_{10}$), 20.1 ± 5.6 μg/m³ ($PM_{2.5}$), 27.2 ± 9.7 μg/m³ ($NO_2$), and 70.8 ± 4.2 μg/m³ (summer $O_3$). The concentrations of $PM_{10}$, $PM_{2.5}$, and $NO_2$ were higher in Northern Italian cities. We found associations between PM exposure and rhinitis ($PM_{10}$: OR 1.62, 95%CI: 1.19-2.20 and $PM_{2.5}$: OR 1.80, 95%CI: 1.16-2.81, per 10 μg/m³) and between $NO_2$ exposure and CB/COPD (OR 1.22, 95%CI: 1.07-1.38 per 10 μg/m³), whereas asthma was not related to environmental exposures. Results remained consistent using different adjustment sets, including bi-pollutant models, and after excluding subjects who had changed residential address in the last 5 years. We found novel evidence of association between long-term PM exposure and increased risk of rhinitis, the chronic respiratory disease with the highest prevalence in the general population. Exposure to $NO_2$, a pollutant characterised by strong oxidative properties, seems to affect mainly CB/COPD.

**Keywords:** Air quality; Asthma; Chronic bronchitis; Epidemiology; Public health; Rhinitis.



# Conflict of interest statement

Declaration of competing interest Sara Maio reports financial support was provided by National Institute for Insurance against Accidents at Work.

- Cited by 1 article

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

Review

Cell Signal

. 2023 Aug;108:110689.

doi: 10.1016/j.cellsig.2023.110689. Epub 2023 Apr 28.

# Phosphodiesterase 7 as a therapeutic target - Where are we now?

Alina Zorn[1], George Baillie[2]

Affiliations expand

- PMID: 37120115

- DOI: 10.1016/j.cellsig.2023.110689

**Free article**

## Abstract

Cyclic nucleotide phosphodiesterases (PDEs) are a superfamily of enzymes that hydrolyse the intracellular second messengers cAMP and cGMP to their inactive forms 5'AMP and 5'GMP. Some members of the PDE family display specificity towards a single cyclic nucleotide messenger, and PDE4, PDE7, and PDE8 specifically hydrolyse cAMP. While the

role of PDE4 and its use as a therapeutic target have been well studied, less is known about PDE7 and PDE8. This review aims to collate the present knowledge on human PDE7 and outline its potential use as a therapeutic target. Human PDE7 exists as two isoforms PDE7A and PDE7B that display different expression patterns but are predominantly found in the central nervous system, immune cells, and lymphoid tissue. As a result, PDE7 is thought to play a role in T cell activation and proliferation, inflammation, and regulate several physiological processes in the central nervous system, such as neurogenesis, synaptogenesis, and long-term memory formation. Increased expression and activity of PDE7 has been detected in several disease states, including neurodegenerative diseases such as Parkinson's, Alzheimer's and Huntington's disease, autoimmune diseases such as multiple sclerosis and COPD, and several types of cancer. Early studies have shown that administration of PDE7 inhibitors may ameliorate the clinical state of these diseases. Targeting PDE7 may therefore provide a novel therapeutic strategy for targeting a broad range of disease and possibly provide a complementary alternative to inhibitors of other cAMP-selective PDEs, such as PDE4, which are severely limited by their side-effects.

**Keywords:** Drug development; Neurodegenerative disease; PDE7; Phosphodiesterase 7; cAMP; cancer.



# 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: Alina Zorn reports financial support was provided by Medical Research Council. Professor George Baillie is the Editor in Chief of Cellular Signalling.

. 2023 Aug;262:100-109.

doi: 10.1016/j.ahj.2023.04.016. Epub 2023 Apr 26.

# Mortality in patients with chronic obstructive pulmonary disorder undergoing transcatheter aortic valve replacement: The importance of chronic obstructive pulmonary disease exacerbation

Marie Dam Lauridsen[1], Jan Brink Valentin[2], Jarl Emanuel Strange[3], Peter A Jacobsen[4], Lars Køber[5], Ulla Weinreich[4], Søren Paaske Johnsen[2], Emil Fosbøl[5]

Affiliations expand

- PMID: 37116603

- DOI: 10.1016/j.ahj.2023.04.016

**Free article**

## Abstract

**Background:** Severe chronic obstructive pulmonary disease (COPD) has been associated with futile outcome after transcatheter aortic valve replacement (TAVR). Data on outcomes according to COPD severity are warranted to aid identification of patients who may not benefit from TAVR. We aimed to examine the association between risk of COPD exacerbation and 1-year mortality after TAVR.

**Methods:** Using Danish nationwide registries we identified patients undergoing first-time TAVR during 2008-2021 by COPD status. COPD severity levels were defined as low or high risk of acute exacerbation of COPD (AE-COPD) and treatment intensity levels (none or short-term, mono/dual, triple therapy, or home oxygen). Kaplan-Meier functions and adjusted Cox regression models were used to assess 1-year mortality comparing COPD severity groups with patients without COPD.

**Results:** We identified 7,047 patients with TAVR of whom 644 had a history of COPD (low risk of AE-COPD: 439, high risk of AE-COPD: 205). The median age of the TAVR cohort was 81.4 years (IQR: 76.8-85.1) and 55.8% were males. One-year mortality for TAVR patients without COPD was 8.5% (95% CI: 7.8-9.2) and 15.4% (95% CI: 12.5-18.2) for those with COPD (adjusted HR: 1.63 [95% CI: 1.28-2.07]). Patients with low or high risk of AE-COPD had 1-year mortality of 13.1% (95% CI: 9.8-16.3) and 20.2% (95% CI: 14.6-25.8) corresponding to adjusted HRs of 1.31 (95% CI: 0.97-1.78) and 2.44 (95% CI: 1.70-3.50) compared with patients without COPD. Patients with high risk of AE-COPD and no/short term therapy or use of home oxygen represented the subgroups of patients with the highest 1-year mortality (31.6% [95% CI: 14.5-48.7] and 30.9% [95% CI: 10.3-51.6]).

**Conclusion:** Among patients undergoing TAVR, increasing risk of exacerbation with COPD was associated with increasing 1-year mortality compared with non-COPD patients. Patients with a high risk of exacerbation with COPD not using any guideline recommended COPD medication and those using home oxygen had the highest 1-year mortality.



# Conflict of interest statement

Disclosures Dr. Lauridsen has nothing to declare. Mr. Valentin has nothing to declare. Dr. Strange has nothing to declare. Dr. Jacobsen reports personal fees from AstraZeneca outside the submitted work. Dr. Møller Weinreich reports personal fees from Astra Zeneca, Chiesi, Novartis, Boehringer Ingelheim, Pfizer, GSK, and Orion pharma outside the submitted work. Dr. Johnsen reports personal fees from BMS and Pfizer, outside the submitted work. Dr. Køber reports personal fees from Novartis, BMS, and AstraZeneca, outside the submitted work. Dr. Fosbøl reports a grant from Novo Nordisk, outside the submitted work.

J Clin Sleep Med

. 2023 Aug 1;19(8):1447-1456.

doi: 10.5664/jcsm.10600. Online ahead of print.

# Inflammation biomarkers in OSA, chronic obstructive pulmonary disease, and chronic obstructive pulmonary disease/OSA overlap syndrome

Ana Sanchez-Azofra[1,2], Wanjun Gu[1,3], Jorge A Masso-Silva[1,4], David Sanz-Rubio[5], Marta Marin-Oto[5], Pablo Cubero[5], Ana V Gil[5], Esteban A Moya[1], Laura A Barnes[1], Omar A Mesarwi[1], Traci Marin[1,6], Tatum S Simonson[1,7], Laura E Crotty Alexander[1,4], Jose M Marin[5,8], Atul Malhotra[1,7]

Affiliations expand

- PMID: 37082823

- PMCID: PMC10394367 (available on 2024-08-01)

- DOI: 10.5664/jcsm.10600

## Abstract

**Study objectives:** The coexistence of obstructive sleep apnea (OSA) and chronic obstructive pulmonary disease (COPD) in a single individual, also known as overlap syndrome (OVS), is associated with higher cardiovascular risk and mortality than either OSA or COPD alone. However, the underlying mechanisms remain unclear. We hypothesized that patients with OVS have elevated systemic inflammatory biomarkers relative to patients with either disease alone, which could explain greater cardiovascular risk observed in OVS.

**Methods:** We included 255 participants in the study, 55 with COPD alone, 100 with OSA alone, 50 with OVS, and 50 healthy controls. All participants underwent a home sleep study, spirometry, and a blood draw for high-sensitivity C-reactive protein and total blood count analysis. In a randomly selected subset of 186 participants, inflammatory protein

profiling was performed using Bio-Rad Bio-Plex Pro Human Cytokine 27-Plex Assays. Biomarker level differences across groups were identified using a mixed linear model.

**Results:** Levels of interleukin 6 (IL-6), high-sensitivity C-reactive protein (hs-CRP), and granulocyte colony stimulating factor (G-CSF) were higher in participants with OVS and COPD compared with healthy controls and participants with OSA. Furthermore, participants with OVS had higher circulating levels of leukocytes and neutrophils than those with COPD, OSA, and controls.

**Conclusions:** COPD and OVS are associated with higher systemic inflammation relative to OSA and healthy controls. This work proposes the potential utilization of interleukin 6, granulocyte colony stimulating factor, and high-sensitivity C-reactive protein as screening biomarkers for COPD in patients with OSA. Inflammatory pathways may not fully explain the higher cardiovascular risk observed in OVS, indicating the need for further investigation.

**Citation:** Sanchez-Azofra A, Gu W, Masso-Silva JA, et al. Inflammation biomarkers in OSA, chronic obstructive pulmonary disease, and chronic obstructive pulmonary disease/OSA overlap syndrome. *J Clin Sleep Med*. 2023;19(8):1447-1456.

**Keywords:** c-reactive protein; cardiovascular risk; chronic obstructive pulmonary disease; granulocyte colony stimulating factor; interleukin 6; interleukin 8; obstructive sleep apnea; overlap syndrome; sleep-disordered breathing.



# Conflict of interest statement

All authors have seen and approved this manuscript. Work for this study was performed at University of California, San Diego, La Jolla, CA, and Translational Research Unit, IIS Aragon, Hospital Universitario Miguel Servet, Zaragoza, Spain. Author's declarations: A.S.A.: Alfonso Martin Escudero Foundation grant. T.S.S.: NIH R01HL145470. O.A.M.: NIH K08HL143140. Dr. Malhotra is funded by NIH. He reports income related to medical education from LIvanova, Eli Lilly, Zoll and Jazz. ResMed provided a philanthropic donation to UCSD. L.C.A: NIH K24 HL155884, R01HL137052, R01HL147326, VA Merit 1I01BX004767, TRDRP T30IP0965. J.M.M.: Grants Number PI12/02175, PI15/01940 and PI18/01524 from the Instituto Salud Carlos III, Spanish Ministry of Health, Madrid, Spain and the European Regional Development Fund (FEDER) and by a Grant Number 01/2010 from the SADAR-Pneumo Aragón, Zaragoza, Spain. The other authors report no conflicts of interest.

J Investig Med

. 2023 Aug;71(6):613-622.

doi: 10.1177/10815589231167357. Epub 2023 Apr 13.

# E-cigarette use and prevalence of lung diseases among the U.S. population: a NHANES survey

Sudha Dirisanala[1], Srishti Laller[2], Naga Ganti[3], Shafaq Taj[4], Neel Patel[5], Kunwardeep Singh Arora[6], Inemesit Williams[7], Ayesha Hameed[8], Aasa Deepika Kuditipudi[9], Yadanar Win Lei[10], Raghavendra Tirupathi[3], Sachin Gupta[11], Urvish Patel[12], Vikramaditya Samala Venkata[13]

Affiliations expand

- PMID: 37052242

- DOI: 10.1177/10815589231167357

## Abstract

The primary aim of this study was to evaluate epidemiological characteristics and prevalence of lung disease among e-cigarettes users in the United States. A population-based, cross-sectional survey was performed using the National Health and Nutrition Examination Survey (NHANES) of 2015-2018. Adults using e-cigarettes (SMQ900), traditional smoking (SMQ020: > 100 cigarettes in lifetime or SMQ040: current cigarettes use), and dual smoking (e-cigarettes and traditional smoking) were identified and compared in their sociodemographic characteristics and prevalence of lung diseases

(Asthma: MCQ010 and COPD: MCQ160O). We used the chi square test (categorical variables) and Mann-Whitney test and unpaired-student *t* test (continuous variables). p-value <0.05 was used as a reference. We excluded respondents <18 years and missing data on demographics and outcomes. Out of 178,157 respondents, 7745 (4.35%), 48,570 (27.26%), and 23,444 (13.16%) were e-cigarette smokers, traditional smokers, and dual smokers, respectively. Overall prevalence of asthma was 15.16% and COPD was 4.26%. E-cigarette smokers were younger in comparison to traditional smokers (median: 25 years vs 62 years; p < 0.0001). In females (49.34% vs 37.97%), Mexican (19.82% vs 13.35%), annual household income above $100,000 (23.97% vs 15.56%), prevalence of e-cigarette smoking was higher in comparison to traditional smoking (p < 0.0001). The prevalence of COPD was higher among dual smokers in comparison to e-cigarette and traditional smoking (10.14% vs 0.25% vs 8.11%; p < 0.0001). Prevalence of asthma was higher among dual and e-cigarette smokers in comparison with traditional smokers and non-smokers (22.44% vs 21.10% vs 14.46% vs 13.30%; p < 0.0001). Median age (Q1-Q3) was lower at which asthma (7 years (4-12) vs 25 years (8-50)) was diagnosed first among e-cigarettes smokers in comparison with traditional smokers. In a mixed effect multivariable logistic regression analysis, we found higher odds of asthma among e-cigarette users in comparison with non-smokers (Odds ratio (OR): 1.47; 95% Confidence Interval (CI): 1.21-1.78; p = 0.0001). Chronic Obstructive Pulmonary Disease (COPD) respondents were also associated with 11.28 higher odds of e-cigarette utilization (Oddsratio (OR): 11.28; 95% Confidence Interval (CI): 5.59-22.72; p < 0.0001). We conclude the higher prevalence of e-cigarette users is seen among the younger population, female, Mexican race, and annual income above $100,000 in comparison to traditional smokers. Chronic Obstructive Pulmonary Disease (COPD) and asthma were both more prevalent in dual smokers. As asthma was more prevalent and diagnosed at an early age in e-cigarette smokers, more prospective studies are needed to understand the effects of e-cigarette among the population at risk to mitigate the sudden rise in utilization and to create awareness.

**Keywords:** COPD; ENDS; National Health and Nutrition Examination Survey; asthma; e-cigarettes; smoking; vaping; vaping-associated lung injury.

Ann Am Thorac Soc

. 2023 Aug;20(8):1116-1123.

doi: 10.1513/AnnalsATS.202211-954OC.

# Impact of a Computerized Clinical Decision Support System to Improve Chronic Obstructive Pulmonary Disease Diagnosis and Testing for Alpha-1 Antitrypsin Deficiency

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Affiliations expand

- PMID: 36989247

- DOI: 10.1513/AnnalsATS.202211-954OC

## Abstract

**Rationale:** Chronic obstructive pulmonary disease (COPD) and alpha-1 antitrypsin deficiency (AATD) are underrecognized diseases. This is in part due to the underdiagnosis and lack of confirmation of COPD but also from poor adherence to AATD screening recommendations. **Objectives:** A clinical decision support system (CDSS) to guide primary care providers improves spirometry testing and confirmation of COPD diagnosis in subjects at risk and improves AATD screening in patients with confirmed COPD. **Methods:** A CDSS was created to be applied to all Veterans attending single-center Veterans Affairs primary care clinics. The CDSS had an algorithmic dialogue with components executed in phases during different clinic visits: screening for COPD risk using the COPD population screening (COPD-PS) questionnaire, spirometry recommendation, and ordering tool for subjects with a prior diagnosis of COPD or subjects considered high risk by the COPD-PS, dialogue to confirm or discard the diagnosis of COPD, and recommendations for AATD screening in subjects with confirmed COPD. The latter was performed by ordering alpha-1 antitrypsin (AAT) serum levels. Each step of the CDSS

algorithm approach was recorded and available to be retrieved at a later date for analysis. **Results:** Over 6 years, a total of 6,235 Veterans >40 years of age completed the CDSS. According to the COPD-PS questionnaire, 962 (18.5%) subjects were identified as high risk for COPD. An additional 579 subjects with a prior diagnosis of COPD also entered the subsequent steps of the CDSS algorithm. Of the high-risk cohort, the CDSS led to an increase in spirometry testing from 24% to 83% and led to a new diagnosis of COPD in 342 (43%). In the prior COPD diagnosis group, spirometry testing increased from 58% to 84%, leading to COPD reconfirmation in only 326 (67%). A total of 489 (68%) subjects with confirmed COPD completed AAT testing prompted by the CDSS, with 23 subjects identified with AATD and one with severe AATD. **Conclusions:** In the Veterans Affairs system, the use of a clinical decision support system algorithm that incorporates screening for COPD and AATD improves COPD over- and underdiagnosis and screening rates of AATD in a primary care setting.

**Keywords:** COPD; alpha-1 antitrypsin; alpha-1 antitrypsin deficiency; screening.



Meta-Analysis

J Pharmacokinet Pharmacodyn

. 2023 Aug;50(4):297-314.

doi: 10.1007/s10928-023-09853-z. Epub 2023 Mar 22.

# Joint longitudinal model-based meta-analysis of $FEV_1$ and exacerbation rate in randomized COPD trials

Carolina Llanos-Paez[1], Claire Ambery[2], Shuying Yang[2], Misba Beerahee[2], Elodie L Plan[1], Mats O Karlsson[3,4]

Affiliations expand

- PMID: 36947282
- PMCID: PMC10374752
- DOI: 10.1007/s10928-023-09853-z

**Free PMC article**

# Abstract

Model-based meta-analysis (MBMA) is an approach that integrates relevant summary level data from heterogeneously designed randomized controlled trials (RCTs). This study not only evaluated the predictability of a published MBMA for forced expiratory volume in one second ($FEV_1$) and its link to annual exacerbation rate in patients with chronic obstructive pulmonary disease (COPD) but also included data from new RCTs. A comparative effectiveness analysis across all drugs was also performed. Aggregated level data were collected from RCTs published between July 2013 and November 2020 (n = 132 references comprising 156 studies) and combined with data used in the legacy MBMA (published RCTs up to July 2013 - n = 142). The augmented data (n = 298) were used to evaluate the predictive performance of the published MBMA using goodness-of-fit plots for assessment. Furthermore, the model was extended including drugs that were not available before July 2013, estimating a new set of parameters. The legacy MBMA model predicted the post-2013 $FEV_1$ data well, and new estimated parameters were similar to those of drugs in the same class. However, the exacerbation model overpredicted the post-2013 mean annual exacerbation rate data. Inclusion of year when the study started on the pre-treatment placebo rate improved the model predictive performance perhaps explaining potential improvements in the disease management over time. The addition of new data to the legacy COPD MBMA enabled a more robust model with increased predictability performance for both endpoints $FEV_1$ and mean annual exacerbation rate.

**Keywords:** Chronic obstructive pulmonary disease; Exacerbation rate; Forced expiratory volume in one second; Model-based meta-analysis.



# Conflict of interest statement

CL-P, ELP, and MOK declare that they have no conflict of interest. SY, CA and MB are GSK employees and hold GSK shares.

- 37 references
- 8 figures

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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J Cancer Res Clin Oncol

. 2023 Aug;149(10):7275-7283.

doi: 10.1007/s00432-023-04686-2. Epub 2023 Mar 13.

# Low diffusion capacity predicts poor prognosis in extensive stage small cell lung cancer: a single-center analysis of 10 years

Jee Seon Kim[#1], Eun Ji Kim[#2], Jong Geol Jang[2], Kyung Soo Hong[#3], June Hong Ahn[#4]

Affiliations expand

- PMID: 36912944

- PMCID: PMC10374757

- DOI: 10.1007/s00432-023-04686-2

**Free PMC article**


# Abstract


**Background:** Poor pulmonary function and chronic obstructive pulmonary disease (COPD) are associated with poorer overall survival (OS) in non-small-cell lung cancer (NSCLC) patients. Few studies have investigated the association between pulmonary function and OS in small-cell lung cancer (SCLC) patients. We compared the clinical characteristics of extensive disease SCLC (ED-SCLC) with or without moderately impaired diffusion capacity for carbon monoxide (DLco) and investigated the factors associated with survival in ED-SCLC patients.

**Methods:** This retrospective single-center study was performed between January 2011 and December 2020. Of the 307 SCLC patients who received cancer therapy during the study, 142 with ED-SCLC were analyzed. The patients were divided into DLco < 60% group and DLco ≥ 60% groups. OS and predictors of poor OS were analyzed.

**Results:** The median OS of the 142 ED-SCLC patients was 9.3 months and the median age was 68 years. In total, 129 (90.8%) patients had a history of smoking, and 60 (42.3%) had COPD. Thirty-five (24.6%) patients were assigned to the DLco < 60% group. Multivariate analysis revealed that DLco < 60% (odds ratio [OR], 1.609; 95% confidence interval [CI], 1.062-2.437; P = 0.025), number of metastases (OR, 1.488; 95% CI, 1.262-1.756; P < 0.001), and < 4 cycles of first-line chemotherapy (OR, 3.793; 95% CI, 2.530-5.686; P < 0.001) were associated with poor OS. Forty (28.2%) patients received < 4 cycles of first-line chemotherapy; the most common reason for this was death (n = 22, 55%) from grade 4 febrile neutropenia (n = 15), infection (n = 5), or massive hemoptysis (n = 2). The DLco < 60% group had a shorter median OS than the DLco ≥ 60% group (10.6 ± 0.8 vs. 4.9 ± 0.9 months, P = 0.003).

**Conclusions:** In this study, approximately one quarter of the ED-SCLC patients had DLco < 60%. Low DLco (but not forced expiratory volume in 1 s or forced vital capacity), a large number of metastases, and < 4 cycles of first-line chemotherapy were independent risk factors for poor survival outcomes in patients with ED-SCLC.



**Keywords:** Diffusion capacity (DLco); Prognosis; Small-cell lung cancer (SCLC).




# Conflict of interest statement

The authors declare no conflicts of interest.

- 28 references
- 2 figures

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS



Am J Prev Med

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. 2023 Aug;65(2):173-181.

doi: 10.1016/j.amepre.2023.01.038. Epub 2023 Mar 7.

# Cigarettes, ENDS Use, and Chronic Obstructive Pulmonary Disease Incidence: A Prospective Longitudinal Study

Steven F Cook[1], Jana L Hirschtick[1], Nancy L Fleischer[1], Douglas A Arenberg[2], Geoffrey D Barnes[3], David T Levy[4], Luz Maria Sanchez-Romero[4], Jihyoun Jeon[1], Rafael Meza[5]

Affiliations expand

- PMID: 36890083

- PMCID: PMC10363225 (available on 2024-08-01)

- DOI: 10.1016/j.amepre.2023.01.038


# Abstract


**Introduction:** Understanding the relationship between ENDS use and chronic obstructive pulmonary disease (COPD) and other respiratory conditions is critical. However, most previous studies have not fully adjusted for cigarette smoking history.

**Methods:** Using Waves 1-5 of the U.S. Population Assessment of Tobacco and Health study, the association between ENDS use and self-reported incident COPD was examined among adults aged 40+ years using discrete-time survival models. Current ENDS use was measured as a time-varying covariate, lagged by 1 wave, defined as established daily or some days of use. Multivariable models were adjusted for baseline demographics (age, sex, race/ethnicity, education), health characteristics (asthma, obesity, exposure to second-hand smoke), and smoking history (smoking status and cigarette pack years). Data were collected between 2013 and 2019, and the analysis was conducted in 2021-2022.

**Results:** Incident COPD was self-reported by 925 respondents during the 5-year follow-up. Before adjusting for other covariates, time-varying ENDS use appeared to double COPD incidence risk (hazard ratio=1.98, 95% CI=1.44, 2.74). However, ENDS use was no longer associated with COPD (adjusted hazard ratio=1.10, 95% CI=0.78, 1.57) after adjusting for current cigarette smoking and cigarette pack years.

**Conclusions:** ENDS use did not significantly increase the risk of self-reported incident COPD over a 5-year period once current smoking status and cigarette pack years were included. Cigarette pack years, by contrast, remained associated with a net increase in COPD incidence risk. These findings highlight the importance of using prospective longitudinal data and adequately controlling for cigarette smoking history to assess the independent health effects of ENDS.




SUPPLEMENTARY INFO


Grant supportexpand


FULL TEXT LINKS

Arch Phys Med Rehabil

. 2023 Aug;104(8):1243-1252.

doi: 10.1016/j.apmr.2023.01.020. Epub 2023 Feb 11.

# Validity and Accuracy of Step Count as an Indicator of a Sedentary Lifestyle in People With Chronic Obstructive Pulmonary Disease

Sonia W M Cheng [1], Jennifer A Alison [2], Emmanuel Stamatakis [3], Sarah M Dennis [4], Zoe J McKeough [5]

Affiliations expand

- PMID: 36775005

- DOI: 10.1016/j.apmr.2023.01.020

## Abstract

**Objective:** To determine the validity and accuracy of <5000 steps/day as a sedentary lifestyle indicator, and the optimal step count cut point value for indicating a sedentary lifestyle in people with chronic obstructive pulmonary disease (COPD).

**Design:** Analysis of baseline data from a randomized clinical trial.

**Setting:** Sydney, Australia.

**Participants:** Stable COPD on the waitlist for pulmonary rehabilitation.

**Interventions:** Not applicable.

**Main outcome measures:** Step count and time in sedentary behavior (SB) were assessed using thigh-worn accelerometry. A sedentary lifestyle was defined as <5000 steps/day. Pearson correlation coefficients were analyzed between step count and time spent in SB. Sensitivity, specificity, and accuracy were calculated for the <5000 steps/day threshold. Receiver operating characteristic curves with the area under the curve were computed for step count in identifying a sedentary lifestyle.

**Results:** 69 people with COPD (mean age=74 years, SD=9; forced expiratory volume in 1 second, mean=55%, SD=19 predicted) had sufficient wear data for analysis. There was a moderate inverse correlation between step count and time spent in SB (r=-0.58, P<.001). Step count had a fair discriminative ability for identifying a sedentary lifestyle (area under the curve=0.80, 95% confidence interval [CI], 0.68-0.91). The <5000 steps/day threshold had a sensitivity, specificity, and accuracy of 82% (95% CI, 70-94), 70% (95% CI, 54-86), and 78%, respectively. A lower threshold of <4300 steps/day was more accurate for ruling in a sedentary lifestyle.

**Conclusions:** Compared with thigh-worn accelerometry, <5000 steps/day is a valid and reasonably accurate indicator of a sedentary lifestyle in this population.

**Keywords:** Accelerometry; Chronic obstructive pulmonary disease; Physical activity; Rehabilitation; Sedentary behavior.

. 2023 Aug;32(15-16):4915-4931.

doi: 10.1111/jocn.16640. Epub 2023 Feb 5.

# Predictors of self-care behaviour trajectories in patients with chronic obstructive pulmonary disease: A latent class growth analysis

Bei Dou[1,2], Ting Tang[3], Chen Wang[1], Huixian Zha[4], Yu Kong[5], Kouying Liu[1,3]

Affiliations expand

- PMID: 36740779

- DOI: 10.1111/jocn.16640

## Abstract

**Aims and objectives:** To explore the trajectories of self-care behaviours in patients with chronic obstructive pulmonary disease based on the latent class growth model and investigate the predictors of each trajectory based on the capability opportunity motivation and behaviour model.

**Background:** Studies on self-care behaviours of patients with chronic obstructive pulmonary disease are mainly cross-sectional surveys. However, little is known about longitudinal trends of self-care behaviours changes among those population.

**Design:** This was a prospective observational research performed according to STROBE Checklist.

**Methods:** One hundred and nineteen patients with chronic obstructive pulmonary disease were followed up at baseline, 3 and 6 months. Data collection included the scores of self-care behaviours, specific demographic and clinical characteristics, and scores for the predictors. A latent class growth model was used to explore the self-care behaviours trajectories. Multiple logistic regression analysis was conducted to identify predictors of self-care behaviours trajectories.

**Results:** Three trajectories in the self-care behaviours of patients with chronic obstructive pulmonary disease were found: a persistently negative trajectory, a maintenance trajectory after a slight increase and an active trajectory with a slow upward improvement in self-care behaviours. Medical insurance and access to medical resources were the predictors of self-care behaviours.

**Conclusion:** The patients with poor medical resources and medical insurance are at high risk for the poor self-care behaviours and the negative trajectory. Thus, dynamic and individualised intervention should be continuously provided to ensure patients acquire adequate medical resources to comprehensively improve self-care behaviours.

**Relevance to clinical practice:** People with better self-care trajectory may be patients who receive more medical resources or have less financial burden, which will help with the early identification of high-risk patients with a negative self-care trajectory. Intervention guided by Behaviour Change Wheel Theory should be conducted dynamically for patients for patients with different trajectories.

**Patient or public contribution:** Thank the patients and their families for their cooperation in data collecting in this study.

**Keywords:** chronic obstructive pulmonary disease; latent class growth model; self-care.



- 67 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

FULL TEXT LINKS

J Ultrasound Med

. 2023 Aug;42(8):1899.

doi: 10.1002/jum.16188. Epub 2023 Feb 1.

# Comment on: Diagnostic Accuracy of Optic Nerve Sheath Diameter Measured With Ocular Ultrasonography in Acute Attack of Chronic Obstructive Pulmonary Disease

Danilo Biondino[1], Martina De Luca[1], Marco Gioia[1], Aniello La Marca[1]

Affiliations expand

- PMID: 36723388

- DOI: 10.1002/jum.16188

*No abstract available*

## Comment on

- Diagnostic Accuracy of Optic Nerve Sheath Diameter Measured With Ocular Ultrasonography in Acute Attack of Chronic Obstructive Pulmonary Disease. Copcuoglu Z, Oruc OA.J Ultrasound Med. 2023 May;42(5):989-995. doi: 10.1002/jum.16106. Epub 2022 Sep 23.PMID: 36149357

Review

Infection

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. 2023 Aug;51(4):813-829.

doi: 10.1007/s15010-022-01960-2. Epub 2023 Jan 20.

# The clinical spectrum of aspergillosis in chronic obstructive pulmonary disease

Akaninyene Otu [1], Chris Kosmidis [2], Alexander G Mathioudakis [3,4], Chibuike Ibe [5], David W Denning [6]

Affiliations expand

- PMID: 36662439

- PMCID: PMC9857914

- DOI: 10.1007/s15010-022-01960-2

**Free PMC article**

## Abstract

Chronic obstructive pulmonary disease (COPD) is the third leading cause of death worldwide. In this review, we present the clinical spectrum and pathogenesis of syndromes caused by Aspergillus in COPD namely invasive aspergillosis (IA), community-acquired Aspergillus pneumonia, chronic pulmonary Aspergillosis and Aspergillus sensitisation. Some of these entities are clearly linked to COPD, while others may coexist, but are less

clearly liked directly to COPD. We discuss current uncertainties as these pertain to IA in COPD cohorts and explore areas for future research in this field.

**Keywords:** Aspergillosis; Bronchiectasis; Chronic pulmonary disease.



# Conflict of interest statement

Denning and family hold Founder shares in F2G Ltd, a University of Manchester spin-out antifungal discovery company. He acts, or has recently acted, as a consultant to Pulmatrix, Pulmocide, Zambon, iCo Therapeutics, Mayne Pharma, Biosergen, Bright Angel Therapeutics, Cipla and Metis. He sits on the DSMB for a SARS CoV2 vaccine trial. In the last three years, he has been paid for talks on behalf of Dynamiker, Hikma, Gilead, Merck, Mylan and Pfizer. The other co-authors have no conflict of interest to declare.


- 157 references
- 6 figures

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Ann Pharmacother

. 2023 Aug;57(8):993-994.

doi: 10.1177/10600280221136254. Epub 2022 Nov 14.

# Comment: "Co-Prescribing of Central Nervous System-Active Medications for COPD Patients: Impact on Emergency Room Visits and Hospitalization"

Sloan Smith[1], Sarah Beth Tucker[1], Ismaeel Yunusa[1]

Affiliations expand

- PMID: 36373627

- DOI: 10.1177/10600280221136254

*No abstract available*

**Keywords:** CNS stimulants; antidepressants; benzodiazepines; chronic obstructive pulmonary disease; drug interactions; opioids; outcomes research/analysis.



Ann Pharmacother

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. 2023 Aug;57(8):995-996.

doi: 10.1177/10600280221136243. Epub 2022 Nov 14.

# Author's Reply "Considerations Regarding a Cohort Study on Concomitant Use of Central Nervous System–Active Medications in Patients With COPD"

Akhil Sood, Yong-Fang Kuo, Gulshan Sharma, Mukaila A Raji


- PMID: 36373620

- DOI: 10.1177/10600280221136243


*No abstract available*

**Keywords:** COPD; analgesics; anxiolytics; benzodiazepines; opioids.



Thorax

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. 2023 Aug;78(8):760-766.

doi: 10.1136/thorax-2022-219039. Epub 2022 Oct 31.

# Frequency and severity of respiratory infections prior to COPD diagnosis and risk of subsequent postdiagnosis COPD exacerbations and mortality: EXACOS-UK health care data study

Hannah Whittaker[1], Clementine Nordon[2], Annalisa Rubino[2], Tamsin Morris[3], Yang Xu[3], Enrico De Nigris[4], Hana Müllerová[2], Jennifer K Quint[5]

Affiliations expand

- PMID: 36316117

- PMCID: PMC10359568

- DOI: 10.1136/thorax-2022-219039

**Free PMC article**

## Abstract

**Objective:** Little is known about how lower respiratory tract infections (LRTIs) before chronic obstructive pulmonary disease (COPD) are associated with future exacerbations and mortality. We investigated this association in patients with COPD in England.

**Methods:** Clinical Practice Research Datalink Aurum, Hospital Episode Statistics and Office of National Statistics data were used. Start of follow-up was patient's first ever COPD diagnosis date and a 1-year baseline period prior to start of follow-up was used to find mild LRTIs (general practice (GP) events/no antibiotics), moderate LRTIs (GP events+antibiotics) and severe LRTIs (hospitalised). Patients were categorised as having: none, 1 mild only, 2+ mild only, 1 moderate, 2+ moderate and 1+ severe. Negative binomial regression modelled the association between baseline LRTIs and subsequent COPD exacerbations and Cox proportional hazard regression was used to investigate mortality.

**Results:** In 215 234 patients with COPD, increasing frequency and severity of mild and moderate LRTIs were associated with increased rates of subsequent exacerbations compared with no recorded LRTIs (1 mild adjusted IRR 1.16, 95% CI 1.14 to 1.18, 2+ mild

IRR 1.51, 95% CI 1.46 to 1.55, 1 moderate IRR 1.81, 95% CI 1.78 to 1.85, 2+ moderate IRR 2.55, 95% CI 2.48 to 2.63). Patients with 1+ severe LRTI (vs no baseline LRTIs) also showed an increased rate of future exacerbations (adjusted IRR 1.75, 95% CI, 1.70 to 1.80). This pattern of association was similar for risk of all-cause and COPD-related mortality; however, patients with 1+ severe LRTIs had the highest risk of all-cause and COPD mortality.

**Conclusion:** Increasing frequency and severity of LRTIs prior to COPD diagnosis were associated with increasing rates of subsequent exacerbations, and increasing risk of all-cause and COPD-related mortality.

**Keywords:** COPD epidemiology.



# Conflict of interest statement

Competing interests: JKQ has received grants from The Health Foundation, MRC, GSK, Bayer, BI, AUK-BLF, Chiesi, and AZ, and personal fees for advisory board participation or speaking fees from GlaxoSmithKline, Boehringer Ingelheim, AstraZeneca and Bayer. HW has nothing to disclose. CL, AR, HM, TM and YX are employees of AstraZeneca and holds stock and/or options in the company. EDN is a former employee of AstraZeneca, but was employed by AstraZeneca at the time of the study.

Am J Hosp Palliat Care

. 2023 Aug;40(8):856-871.

doi: 10.1177/10499091221134777. Epub 2022 Oct 20.

# Knowledge and Attitudes of Allied Health Professionals Towards End-Of-Life and Advance Care Planning Discussions With People With COPD: A Cross-Sectional Survey Study

Rebecca Disler[1,2], Brooke Henwood[2], Tim Luckett[3], Amy Pascoe[1], Doranne Donesky[4,5], Louis Irving[6], David C Currow[7], Natasha Smallwood[1,8]

Affiliations expand

- PMID: 36266239

- DOI: 10.1177/10499091221134777

## Abstract

Chronic obstructive pulmonary disease (COPD) is a progressive, life-limiting condition. End-of-life (EOL) and Advance Care Planning (ACP) discussions are essential, yet access and support remain inadequate. Allied health professionals (AHPs) commonly have ongoing relationships with patients and opportunities to discuss care outside acute crises as is considered best practice. Australian and New Zealand AHPs were invited to complete an anonymous, online, cross-sectional survey that aimed to explore knowledge, attitudes and practices, and associated perceived triggers and barriers to EOL and ACP discussions with patients with COPD. Closed survey responses were summarized descriptively and free-text thematically analysed. One hundred and one AHPs (physiotherapists, social workers and occupational therapists) participated. Many held positive attitudes towards ACP but lacked procedural knowledge. Half (50%) of participants routinely discussed EOL care with patients when perceiving this to be appropriate but only 21% actually discussed ACP with the majority of their patients. Many cited lack of training to engage in sensitive EOL discussions, with barriers including: 1) clinician lack of confidence/fear of distressing

patients (75%); 2) perceived patient and family reluctance (51%); 3) organizational challenges (28%); and 4) lack of role clarity (39%). AHPs commonly have ongoing relationships with patients with chronic conditions but lack the confidence and role clarity to utilise this position to engage ongoing EOL and ACP discussions. While AHPs may not traditionally consider EOL and ACP discussions as part of their role, it is crucial that they feel prepared to respond if patients broach the topic.

**Keywords:** advance care planning; allied health; chronic obstructive pulmonary disease; end of life; palliative care; survey.



Physiother Theory Pract

. 2023 Aug 3;39(8):1681-1691.

doi: 10.1080/09593985.2022.2045658. Epub 2022 Feb 28.

# Experiences of physical activity and exercise among women with obstructive pulmonary disease

Marian E Papp[1,2], Cecilia Berg[3], Petra Lindfors[4], Per E Wändell[2], Malin Nygren-Bonnier[1,5]

Affiliations expand

- PMID: 35225744

- DOI: 10.1080/09593985.2022.2045658

# Abstract

**Background:** With more women being diagnosed with obstructive pulmonary disease, it is important to know how women experience non-pharmacological rehabilitation including different types of physical activity and exercise.

**Objective:** This study aimed to explore how women with obstructive pulmonary disease experienced participating in pulmonary rehabilitation including yoga or strength- and endurance training to promote physical activity. A second aim included exploring experiences of physical activity and exercise through life.

**Methods:** Fifteen women with asthma or chronic obstructive pulmonary disease were interviewed about their experiences of participating in an exercise intervention and about their experiences of physical activity and exercise in their lives. The transcribed interviews were analyzed using qualitative content analysis.

**Results:** An overall theme, "Wishing to succeed in attending physical activity and exercise," emerged. Three categories were identified: 1) strategies to overcome insecurity; 2) a life situation which enables and hinders; and 3) an inner drive and focus on myself.

**Conclusions:** The women's wishes to be physically activity and exercise involved hindering and enabling factors. Specifically, their gender roles as women were described as a hinder. This suggests a need to include a gender perspective when promoting physical activity and exercise to women with obstructive pulmonary disease.

**Keywords:** Gender; physiotherapy; qualitative; yoga.

Minerva Surg

. 2023 Aug;78(4):457-459.

doi: 10.23736/S2724-5691.21.09390-4. Epub 2022 Jan 28.

# Effect of pulmonary rehabilitation nursing model on pulmonary function and quality of life in patients with stable chronic obstructive pulmonary disease

Yi Jiang[1], Lin Liu[1], Meifang Jiang[2]

Affiliations expand

- PMID: 35088995

- DOI: 10.23736/S2724-5691.21.09390-4

**Free article**

*No abstract available*

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

1

Review

Sci Total Environ

. 2023 Aug 2;166010.

doi: 10.1016/j.scitotenv.2023.166010. Online ahead of print.

# Associations of long-term particulate matter exposure with cardiometabolic diseases: A systematic review and meta-analysis

Mengqi Sun[1], Tianyu Li[1], Qinglin Sun[1], Xiaoke Ren[1], Zhiwei Sun[1], Junchao Duan[2]

Affiliations expand

- PMID: 37541522

- DOI: 10.1016/j.scitotenv.2023.166010

## Abstract

**Background:** This review aimed to establish a holistic perspective of long-term PM exposure and cardiometabolic diseases, identify long-term PM-related cardiovascular and metabolic risk factors, and provide practical significance to preventative measures.

**Method:** A combination of computer and manual retrieval was used to search for keywords in PubMed (2903 records), Embase (2791 records), Web of Science (5488

records) and Cochrane Library (163 records). Finally, a total of 82 articles were considered in this meta-analysis. Stata 13.0 was accustomed to inspecting the studies' heterogeneity and calculating the combined effect value (RR) by selecting the matching models. The subgroup analysis, sensitivity analysis and publication bias tests were also performed.

**Results:** Meta-analysis figured an association between PM and cardiometabolic diseases. $PM_{2.5}$ (per 10 μg/$m^3$ increase) boosted the risk of hypertension (RR = 1.14, 95 % CI: 1.09-1.19), coronary heart disease (CHD) (RR = 1.21, 95 % CI: 1.08-1.35), diabetes (RR = 1.16, 95 % CI: 1.11-1.21) and stroke (including ischemic stroke and hemorrhagic stroke). $PM_{10}$ (per 10 μg/$m^3$ increase) elevated the incidence of hypertension (RR = 1.11, 95 % CI: 1.07-1.16) and diabetes (RR = 1.26, 95 % CI: 1.08-1.47). $PM_1$ (per 10 μg/$m^3$ increase) exposure increased the risk of total dyslipidemia, yielding the RR of 1.10 (95 % CI: 1.01-1.18). Furthermore, the elderly, overweight and higher background pollutant level were potentially susceptible to related diseases.

**Conclusion:** There was a virtual connection between long-term exposure to PM and cardiometabolic diseases. $PM_{2.5}$ or $PM_{10}$ (per 10 μg/$m^3$) increased the risk of hypertension, CHD, diabetes, stroke and dyslipidemia, causing cardiovascular "multimorbidity" in high-risk populations.

**Keywords:** Air pollution; Cardiometabolic diseases; Meta-analysis; Particulate matter.





Geriatr Nurs

. 2023 Aug 2;53:181-190.

doi: 10.1016/j.gerinurse.2023.07.016. Online ahead of print.

# Spanish version of the self-care self-efficacy scale: A validation study in community-dwelling older adults with chronic multimorbidity

Anabel Chica-Pérez[1], Iria Dobarrio-Sanz[2], Matías Correa-Casado[3], Cayetano Fernández-Sola[4], María Dolores Ruiz-Fernández[5], José Manuel Hernández-Padilla[5]

Affiliations expand

- PMID: 37540914

- DOI: 10.1016/j.gerinurse.2023.07.016

## Abstract

**Objective:** To test the psychometric properties of the Spanish version of the Self-Care Self-Efficacy Scale (SCSES-Sp) in community-dwelling older adults with chronic multimorbidity.

**Methods:** A sample of 1013 community-dwelling older adults with chronic multimorbidity participated in an observational cross-sectional study that was carried out in 3 phases.

**Results:** Confirmatory factor analysis showed that the SCSES-Sp has 4 dimensions: "self-efficacy in self-care behaviours based on clinical knowledge", "self-efficacy in self-care maintenance", "self-efficacy in self-care monitoring", and "self-efficacy in self-care management". A panel of independent experts considered the content of the SCSES-Sp valid. Convergent validity analysis showed moderate-strong correlations between all of the SCSES-Sp's dimensions and the reference criteria chosen. Reliability was good for the SCSES-Sp and all its dimensions. Test-retest reliability analysis showed that the SCSES-Sp was temporally stable.

**Conclusions:** The SCSES-Sp is a valid and reliable tool to assess self-efficacy in self-care in Spanish-speaking, community-dwelling older adults with chronic multimorbidity.

**Keywords:** Multimorbidity; Older adults; Psychometrics; Self-care; Self-efficacy.

## Conflict of interest statement

Declaration of Competing Interest None.



PLoS One

. 2023 Aug 4;18(8):e0289502.

doi: 10.1371/journal.pone.0289502. eCollection 2023.

# Assessment of health-related quality of life among patients with obesity, hypertension and type 2 diabetes mellitus and its relationship with multimorbidity

Shahid Shah[1], Ghulam Abbas[2], Ayesha Aslam[3], Fawad Ahmad Randhawa[4], Faiz Ullah Khan[5], Haris Khurram[6], Usman Rashid Chand[1], Muhammad Hammad Butt[7], Tauqeer Hussain Mallhi[8], Yusra Habib Khan[8]

Affiliations expand

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- DOI: 10.1371/journal.pone.0289502

# Abstract

Obesity, hypertension (HTN) and type 2 diabetes (T2D) are among the multifactorial disorders that occur at higher prevalence in a population. This study aims to assess the health-related quality of life (HRQoL) of patients with obesity, HTN and T2D individually and in the form of multimorbidity. A questionnaire-based cross-sectional study was conducted among the patients in 15 private clinics of Punjab, Pakistan. A stratified random sampling technique was used to collect the data from patients with obesity, HTN and T2D or their comorbidity. A total of 1350 patients responded by completing the questionnaire. The HRQoL of these patients was assessed using the EQ-5D-5L questionnaire (a standardized instrument for measuring generic health status). Statistical analysis was performed using chi-square test, Mann-Whitney U test, and Kruskal-Wallis test. Multivariate linear regression model was used to model the visual analogue scale (VAS) score. In total, 15% of patients had combined obesity, HTN and T2D; 16.5% had HTN and T2D; 13.5% had obesity and HTN and 12.8% had obesity and T2D. Only 15.8% of patients had obesity, 14.3% had HTN, and 12% had T2D. Mann Whitney-U test gave the statistically significant ($p = <0.001$) HRQoL VAS score55.1 (±23.2) of patients with the obesity. HRQoL VAS scores of patients with obesity were found to be higher when compared to patients with both T2D 49.8 (±15.4) and HTN 48.2 (±21). Diagnosis of one, two and three diseases showed significant results in VAS with all variables including gender ($p = 0.004$), educational level ($p = <0.001$), marital status ($p<0.001$), residence ($p = <0.001$), financial situation ($p = <0.001$) and monthly income ($p = <0.001$). The most frequently observed extremely problematic dimension was anxiety/ depression (47%) and the self-care (10%) was the least affected. Patient HRQoL is decreased by T2D, HTN, and obesity. The impact of these diseases coexisting is more detrimental to HRQoL.




# Conflict of interest statement

The authors have declared that no competing interests exist.

4

Nurs Ethics

. 2023 Aug 4;9697330231191280.

doi: 10.1177/09697330231191280. Online ahead of print.

# Alleviating suffering of individuals with multimorbidity and complex needs: A descriptive qualitative study

Ahtisham Younas [1], Shahzad Inayat [2]

Affiliations expand

- PMID: 37540492

- DOI: 10.1177/09697330231191280

## Abstract

**Background:** Individuals living with multimorbidity and/or mental health issues, low education, socioeconomic status, and polypharmacy are often called complex patients. The complexity of their health and social care needs can make them prone to disease burden and suffering. Therefore, they frequently access health care services to seek guidance for managing their illness and suffering.

**Aims:** The aim of this research was to describe the approaches used by nurses to alleviate the suffering of individuals with multimorbidity and complex needs in acute care settings.

**Research design:** A qualitative descriptive approach.

**Participants and research context:** Semi-structured interviews were conducted with 19 nurses working in general, medical-surgical, specialized, and intensive care settings across five hospitals in Pakistan. Reflexive thematic analysis was used for analysis.

**Ethical considerations:** Ethical approval was obtained from the Ethical Committee of Al-Nafees Medical College Islamabad, Pakistan.

**Findings:** Four themes were generated: Deeper Exploration of Patients' Health-Illness Situation and Complexity, Prioritizing Patient Psychosocial and Emotional Needs, Instilling Hope and Encouragement in Patients, and Creating a Comforting Environment to Foster Sharing of felt needs.

**Discussion:** Nurses emphasized the need of deeper inquiry into patients illness situation and complexity to discern the impact of determinants on their well-being and develop care plans that are tailored to address psychosocial, emotional, and physical suffering of this patient population.

**Conclusions:** Alleviation of patient suffering is integral to compassionate nursing care. Nurses use a multifaceted approach entailing sensitive understanding, recognizing sociocultural and structural determinants impact on patient situation, and individual and interdisciplinary altruistic actions to alleviate patient suffering.

**Keywords:** Multimorbidity; comorbidities: complex patients; nursing; qualitative; suffering.



BMJ Open Qual

. 2023 Aug;12(3):e002188.

doi: 10.1136/bmjoq-2022-002188.

# Improving outpatient clinic experience: the future of chronic kidney disease care and associated multimorbidity

Saif Al-Chalabi[1,2], Helen Alderson[3], Natalie Garratt[4], Darren Green[3,2], Philip A Kalra[3,2], James Ritchie[3,2], Schanhave Santhirasekaran[3], Dimitrios Poulikakos[3,2], Smeeta Sinha[3,2]

Affiliations expand


- PMID: 37532458
- PMCID: PMC10401237
- DOI: 10.1136/bmjoq-2022-002188


**Free PMC article**

# Abstract


**Background:** Chronic kidney disease (CKD) is estimated to affect more than 2.5 million adults in England, and this is expected to rise to 4.2 million by 2036 (1). Population-level digital healthcare systems have the potential to enable earlier detection of CKD providing an opportunity to introduce interventions that attenuate progression and reduce the risk of end-stage kidney disease (ESKD) and cardiovascular diseases (CVD). Services that can support patients with CKD, CVD, and diabetes mellitus (DM) have the potential to reduce fragmented clinical care and optimise pharmaceutical management.

**Methods and results:** The Salford renal service has established an outpatient improvement programme which aims to address these issues via two projects. Firstly, the development of a CKD dashboard that can stratify patients by their kidney failure risk equation (KFRE) risk. High-risk patients would be invited to attend an outpatient clinic if appropriate. Specialist advice and guidance would be offered to primary care providers looking after patients with medium risk. Patients with lower risk would continue with standard care via their primary care provider unless there was another indication for a nephrology referral. The CKD dashboard identified 11546 patients (4.4% of the total adult population in Salford) with T2DM and CKD. The second project is the establishment of the Metabolic CardioRenal (MRC) clinic. It provided care for 209 patients in the first 8 months of its establishment with a total of 450 patient visits. Initial analysis showed clustering of cardiorenal metabolic diseases with 85% having CKD stages 3 and 4 and 73.2% having DM. In addition, patients had a significant burden of CVD with 50.2% having hypertension and 47.8% having heart failure.

**Conclusion:** There is a pressing need to create new outpatient models of care to tackle the rising epidemic of cardio-renal metabolic diseases. This model of service has potential benefits at both organisational and patient levels including improving patient management via risk stratification, increased care capacity and reduction of variation of care. Patients will benefit from earlier intervention, appropriate referral for care, reduction in CKD-related complications, and reduction in hospital visits and cardiovascular events. In

addition, this combined digital and patient-facing model of care will allow rapid translation of advances in cardio-renal metabolic diseases into clinical practice.

**Keywords:** Chronic disease management; Diabetes mellitus; Electronic Health Records; Multiple Chronic Conditions; Outpatients.



# Conflict of interest statement

Competing interests: JR reports conference registration and travel costs from Bayer. SS reports research funding from Amgen, Ethicon, and AstraZeneca; consultancy agreements with Sanifit and honoraria from Astra Zeneca, Napp Pharmaceuticals, Vifor Pharma, Novartis, Bayer, Sanofi-Genzyme, Travere and GSK. PAK reports speaker/lecture fees from AstraZeneca, Napp, Bayer, Novartis, Vifor Pharma, Pharmacosmos, Boehringer Ingelheim, Lilly, advisory Boards: AstraZeneca, Vifor Clinical consultancy: Bayer, Astellas, Otsuka, Unicyte. Grants: Astellas, Vifor, BergenBio, Evotec. DG reports speaker fees from AZ, Novartis, and Vifor Pharma. SA-C, SS, NG, and HA report no COI.

- 6 references
- 1 figure



Age Ageing

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. 2023 Aug 1;52(8):afad134.

doi: 10.1093/ageing/afad134.

# New horizons in the role of digital data in the healthcare of older people

Jane A H Masoli[1,2], Oliver Todd[3], Jennifer K Burton[4], Christopher Wolff[2], Katherine E Walesby[5], Jonathan Hewitt[6], Simon Conroy[7], James van Oppen[8], Chris Wilkinson[9,10], Ruth Evans[3], Atul Anand[11], Joe Hollinghurst[12], Cini Bhanu[6], Victoria L Keevil[13], Emma R L C Vardy[14,15]; Geridata Group

Collaborators, Affiliations expand

- PMID: 37530442

- PMCID: PMC10394991

- DOI: 10.1093/ageing/afad134

**Free PMC article**

## Abstract

There are national and global moves to improve effective digital data design and application in healthcare. This New Horizons commentary describes the role of digital data in healthcare of the ageing population. We outline how health and social care professionals can engage in the proactive design of digital systems that appropriately serve people as they age, carers and the workforce that supports them.

**Key points:** Healthcare improvements have resulted in increased population longevity and hence multimorbidity. Shared care records to improve communication and information continuity across care settings hold potential for older people. Data structure and coding are key considerations. A workforce with expertise in caring for older people with relevant knowledge and skills in digital healthcare is important.

**Keywords:** data; digital; frailty; older people; workforce.



## Conflict of interest statement

C.W. has received research funding from Bristol Myer Squibb. E.R.L.C.V. has received speaker honoraria from GE healthcare.

- 59 references

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

FULL TEXT LINKS

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Commun Med (Lond)

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. 2023 Jul 31;3(1):105.

doi: 10.1038/s43856-023-00335-4.

# Association of birth and childhood weight with risk of chronic diseases and multimorbidity in adulthood

Yue Zhang[#1,2], Yaguan Zhou[#1,2], Yangyang Cheng[1,2], Rodrigo M Carrillo-Larco[3], Muhammad Fawad[1,2], Shu Chen[4,5], Xiaolin Xu[6,7,8]

Affiliations expand

- PMID: 37524882

- PMCID: PMC10390459

- DOI: 10.1038/s43856-023-00335-4

**Free PMC article**

# Abstract

**Background:** Little is known about the relationship between early life body size and occurrence of life-course multiple chronic diseases (multimorbidity). We aim to evaluate associations of birth weight, childhood body size, and their changes with the risks of chronic diseases and multimorbidity.

**Methods:** This prospective cohort study included 246,495 UK Biobank participants (aged 40-69 years) who reported birth weight and childhood body size at 10 years old. Birth weight was categorized into low, normal, and high; childhood body size was reported as being thinner, average, or plumper. Multimorbidity was defined as having two or more of 38 chronic conditions retrieved from inpatient hospital data until 31 December, 2020. The Cox regression and quasi-Poisson mixed effects models were used to estimate the associations.

**Results:** We show that 57,071 (23.2%) participants develop multimorbidity. Low birth weight (hazard ratio [HR] 1.29, 95% confidence interval [CI] 1.26-1.33), high birth weight (HR 1.02, 95% CI > 1.00-1.05), thinner (HR 1.21, 95% CI 1.18-1.23) and plumper body size (HR 1.06, 95% CI 1.04-1.09) are associated with higher risks of multimorbidity. A U-shaped relationship between birth weight and multimorbidity is observed. Changing to be thinner or plumper is associated with multimorbidity and many conditions, compared to changing to be average.

**Conclusions:** Low birth weight, being thinner and changing to have a thinner body size in childhood are associated with higher risks of developing multimorbidity and many chronic conditions in adulthood. Early monitoring and maintaining a normal body size in childhood could have life-course benefits for preventing multimorbidity above and beyond individual conditions.

# Plain language summary

Little is known about the relationship between childhood body size and the risk of developing more than one chronic disease later in life. Using data from the UK, we found that low birth weight, high birth weight, and being thinner or plumper than average during childhood were all associated with higher risks of developing more than one chronic disease in adulthood. In addition, changing body shape during childhood to be either thinner or plumper, was associated with being more likely to develop more than one chronic disease later in life. Our results highlight the importance of early monitoring and

maintenance of average body size in childhood, as this might prevent the occurrence of chronic diseases later in life.



## Conflict of interest statement

The authors declare no competing interests.

- 45 references
- 4 figures



Br J Gen Pract

. 2023 Jul 27;73(733):373-376.

doi: 10.3399/bjgp23X734661. Print 2023 Aug.

# Defining and measuring complex multimorbidity: a critical analysis

Sanghamitra Pati[1], Clare MacRae[2], David Henderson[3], David Weller[2], Bruce Guthrie[2], Stewart Mercer[4]

Affiliations expand

- PMID: 37500453

- DOI: 10.3399/bjgp23X734661

*No abstract available*

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS



Geriatr Gerontol Int

. 2023 Aug;23(8):628-638.

doi: 10.1111/ggi.14638. Epub 2023 Jul 11.

# Questionnaire survey of geriatricians and primary care physicians' approaches to treating older patients with multimorbidity

Takuma Kimura[1], Ken Shinmura[2]

Affiliations expand

- PMID: 37433747

- DOI: 10.1111/ggi.14638

# Abstract

**Aim:** Geriatricians and primary care physicians in Japan are expected to provide care to older patients with multimorbidity.

**Methods:** A questionnaire survey was carried out to understand the current approaches to older patients with multimorbidity. A total of 3300 participants, including 1650 geriatric specialists (G) and 1650 primary care specialists (PC) were enrolled. A 4-point Likert scale was used to score the following items: diseases that cause difficulty in treatment (diseases), patient backgrounds that cause difficulty in treatment (backgrounds), important clinical factors and important clinical strategies. Statistical comparisons were made between the groups. In the Likert scale, higher scores show a greater degree of difficulty.

**Results:** We obtained responses from 439 and 397 specialists in the G and PC, respectively (response rates 26.6 and 24.1%). The overall scores for "diseases" and "backgrounds" were significantly higher in the G than those in the PC ($P < 0.001$ and $P = 0.018$). The top 10 items in the "backgrounds" and in the "important clinical strategies" were all matched between the groups. The overall score of the "important clinical factors" was not statistically different between the groups; however, "low nutrition," "bedridden activities of daily living," "living alone" and "frailty" were found only in the top 10 items of the G, and "financial problems" was found in those of the PC.

**Conclusions:** Geriatricians and primary care physicians have many similarities and differences in their approaches to multimorbidity management. Therefore, there is an urgent need to establish a system in which they can share a common understanding to manage older patients with multimorbidity. Geriatr Gerontol Int 2023; 23: 628-638.



**Keywords:** family medicine; geriatrician; multimorbidity; older adults; primary care physician.




- 19 references

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

FULL TEXT LINKS


Proceed to details

Cite

J Epidemiol Community Health

. 2023 Aug;77(8):507-514.

doi: 10.1136/jech-2023-220654. Epub 2023 Jun 7.

# What can death records tell us about multimorbidity?

Mohammad Reza Baneshi[1], James Eynstone-Hinkins[2], Paul McElwee[1], Gita D Mishra[1], Lauren Moran[2], Michael Waller[1], Annette Dobson[3]

Affiliations expand

- PMID: 37286346

- DOI: 10.1136/jech-2023-220654

## Abstract

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

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

**Results:** The prevalence of deaths with multimorbidity was 81.0% for medically certified deaths, 61.1% for coroner-referred deaths with natural underlying causes and 82.4% for coroner-referred deaths with external underlying causes. For medically certified deaths,

multimorbidity increased with age: incidence rate ratio (IRR 1.070, 95% CI 1.068, 1.072) was lower for women than men (0.954, 95% CI 0.952, 0.956) and changed little over time. For coroner-referred deaths with natural underlying causes, multimorbidity showed the expected pattern increasing with age (1.066, 95% CI 1.062, 1.070) and being higher for women than men (1.025, 95% CI 1.015, 1.035) and in more recent periods. For coroner-referred deaths with external underlying causes, there were marked increases over time that differed by age group due to changes in coding processes.

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

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



# Conflict of interest statement

Competing interests: None declared.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS


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Prev Med Rep

. 2023 Jun 2;34:102265.

doi: 10.1016/j.pmedr.2023.102265. eCollection 2023 Aug.

# Physical activity matters for everyone's health, but individuals with multimorbidity benefit more

Layan Fessler[1], Silvio Maltagliati[1], Stefan Sieber[2], Stéphane Cullati[3,4], Elena Tessitore[5], Cecilia Craviari[6,7], Christophe Luthy[8], Eliana Hanna[8], Philippe Meyer[9], Dan Orsholits[10], Philippe Sarrazin[1], Boris Cheval[11,12]

Affiliations expand

- PMID: 37284656

- PMCID: PMC10240419

- DOI: 10.1016/j.pmedr.2023.102265

**Free PMC article**

## Abstract

Multimorbidity, defined as the presence of two or more chronic conditions, is increasingly prevalent and is a major contributor to ill health in old age. Physical activity (PA) is a key protective factor for health and individuals with multimorbidity could particularly benefit from engaging in PA. However, direct evidence that PA has greater health benefits in people with multimorbidity is lacking. The objective of the present study was to investigate whether the associations between PA and health were more pronounced in individuals with (vs. without) multimorbidity. We used data from 121,875 adults aged 50 to 96 years (mean age = 67 ± 10 years, 55% women) enrolled in the Survey of Health, Ageing and Retirement in Europe (SHARE). Multimorbidity and PA were self-reported. Health indicators were assessed using tests and validated scales. Variables were measured up to seven times over a 15-year period. Confounder-adjusted linear mixed-effects models were used to investigate the moderating role of multimorbidity on the associations of PA with the levels and trajectories of health indicators across aging. Results showed that multimorbidity was associated with declines in physical, cognitive, and mental health, as well as poorer general health. Conversely, PA was positively associated with these health indicators. We found a significant interaction between multimorbidity and PA, revealing that positive associations between PA and health indicators were strengthened in people with multimorbidity - although this stronger association became less pronounced in advanced age. These

findings suggest that the protective role of PA for multiple health indicators is enhanced in individuals with multimorbidity.

**Keywords:** Aging; Chronic conditions; Europe; Health; Multimorbidity; Physical activity.



## Conflict of interest statement

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

- 64 references
- 2 figures



Review

Pharmacol Rep

- 
- 
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. 2023 Aug;75(4):755-770.

doi: 10.1007/s43440-023-00501-4. Epub 2023 Jun 6.

# Polypharmacology: promises and new drugs in 2022

Piotr Ryszkiewicz[1], Barbara Malinowska[2], Eberhard Schlicker[3]

Affiliations expand


- PMID: 37278927
- PMCID: PMC10243259
- DOI: 10.1007/s43440-023-00501-4


**Free PMC article**

# Abstract

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

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



# Conflict of interest statement

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

- 71 references

- 6 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

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Aging Clin Exp Res

- 
- 
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. 2023 Aug;35(8):1671-1678.

doi: 10.1007/s40520-023-02455-2. Epub 2023 Jun 5.

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

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

Affiliations expand

- PMID: 37273091

- PMCID: PMC10363082

- DOI: 10.1007/s40520-023-02455-2

**Free PMC article**

# Abstract

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

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

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

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

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



# Conflict of interest statement

None.

- 42 references
- 1 figure

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

FULL TEXT LINKS

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14

Int J Soc Psychiatry

. 2023 Aug;69(5):1250-1259.

doi: 10.1177/00207640231157253. Epub 2023 Feb 24.

# Health status and quality of life in comorbid physical multimorbidity and depression among adults aged ⩾50 years from low- and middle-income countries

Mireia Felez-Nobrega[1,2], Ai Koyanagi[1,2,3]

Affiliations expand

- PMID: 36825661

- DOI: 10.1177/00207640231157253

## Abstract

**Background:** Data on the clinical and functional significance of comorbid depression in physical multimorbidity in middle-aged and older adults and from low- and middle-income countries (LMICs) are lacking.

**Aims:** This study aims to determine the association of comorbid depression in physical multimorbidity with health outcomes and quality of life among adults aged ⩾50 years from six LMICs.

**Methods:** Cross-sectional, nationally representative data from the Study on Global Ageing and Adult Health were analyzed. DSM-IV Depression was based on past 12-month symptoms. Eleven chronic physical conditions were assessed. Health status was based on scales ranging from 0 (best) to 100 (worse). The quality of life (8-item WHO Quality of Life) scale ranged from 0 (worse) to 100 (best). Multivariable linear regression analyses were conducted.

**Results:** Data on 34,129 individuals aged ⩾50 years [mean (SD) age 62.4 (16.0) years; 52.1% females] were analyzed. Among people with physical multimorbidity, having comorbid depression was associated with significantly worse health status in terms of sleep/energy (β = 14.71: 95% CI [12.23, 17.20]), self-care (13.23: [8.66, 17.82]), pain/discomfort (13.03: [9.59, 16.47]), mobility (11.06: [6.91, 15.21]), cognition (10.41: [7.31, 13.50]), perceived stress (8.35: [4.71, 11.99]), interpersonal activities (7.81: [3.71, 11.91]), and lower quality of life (-8.81: [-10.74, -6.88]).

**Conclusions:** Comorbid depression in physical multimorbidity was associated with lower quality of life and poorer scores in multiple domains of health status. Treatment of depression in people with physical multimorbidity may potentially lead to better clinical outcomes, but future studies are needed to determine the most effective intervention to address this comorbidity in LMICs.

**Keywords:** Depression; comorbidity; health outcomes; low- and middle-income countries; multimorbidity.

Multicenter Study

Int Urol Nephrol

. 2023 Aug;55(8):2047-2057.

doi: 10.1007/s11255-023-03516-1. Epub 2023 Feb 21.

# Multimorbidity prevalence and patterns in chronic kidney disease: findings from an observational multicentre UK cohort study

Grace Hawthorne[1], Courtney J Lightfoot[2], Alice C Smith[2], Kamlesh Khunti[3], Thomas J Wilkinson[3 2]

Affiliations expand

- PMID: 36806100

- PMCID: PMC10329585

- DOI: 10.1007/s11255-023-03516-1

**Free PMC article**

## Abstract

**Purpose:** Multimorbidity [defined as two or more long-term conditions (LTCs)] contributes to increased treatment and medication burden, poor health-related quality of life, and worse outcomes. Management strategies need to be patient centred and tailored depending on existing comorbidities; however, little is known about the prevalence and patterns of comorbidities in people with chronic kidney disease (CKD). We investigated the prevalence of multimorbidity and comorbidity patterns across all CKD stages.

**Methods:** Multimorbidity was assessed, using a composite of self-report and clinical data, across four CKD groups stratified by eGFR [stage 1-2, stage 3a&b, stage 4-5, and kidney transplant (KTx)]. Principal component analysis using varimax rotation was used to identify comorbidity clusters across each group.

**Results:** Of the 978 participants (mean 66.3 ± 14 years, 60% male), 96.0% had multimorbidity. In addition to CKD, the mean number of comorbidities was 3.0 ± 1.7. Complex multimorbidity (i.e. ≥ 4 multiple LTCs) was identified in 560 (57.3%) participants. When stratified by CKD stage, the two most prevalent comorbidities across all stages were hypertension (> 55%) and musculoskeletal disorders (> 40%). The next most prevalent comorbidity for CKD stages 1-2 was lung conditions and for CKD stages 3 and 4-5 it was heart problems. CKD stages 1-2 showed different comorbidity patterns and clustering compared to other CKD stages.

**Conclusion:** Most people across the spectrum of CKD have multimorbidity. Different patterns of multimorbidity exist at different stages of CKD, and as such, clinicians should consider patient comorbidities to integrate care and provide effective treatment strategies.

**Keywords:** Chronic kidney disease; Comorbidity; Multimorbidity; Transplant.



# Conflict of interest statement

None to declare. The results presented in this paper have not been published previously in whole or part, except in abstract format.

- 44 references
- 4 figures

16

J Aging Health

. 2023 Aug;35(7-8):511-524.

doi: 10.1177/08982643221143828. Epub 2022 Dec 2.

# Association of Psychological distress and Physical Health with Subjective and Objective Memory in Older Adults

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Affiliations expand

- PMID: 36459693

- DOI: 10.1177/08982643221143828

## Abstract

ObjectivesTo investigate how indicators of psychological stress and physical health differentially influence subjective and objective memory in older adults. **Methods:** 404 adults aged ≥55 without cognitive impairment participated in remote assessment of physical health (PHY; multimorbidity, body-mass-index), psychological distress (PDS; perceived stress, anxiety, depression), subjective memory complaints (SM), and task-based objective memory performance (OM). **Results:** Separately, both PHY and PDS significantly predicted SM ($p < 0.01$), but only PHY was associated with OM ($p = 0.05$). Combined models showed that PHY and PDS maintained significant association with SM ($p < 0.01$, $R^2 = 0.30$), while only PHY was associated with OM ($p = .07$, $R^2 = 0.03$; for associative OM, $p = 0.04$). **Discussion:** SM is associated with participants' psychological profile, highlighting the importance of addressing these factors when assessing SM. The results also reveal that remotely-administered OM tasks are more immune to participants' psychological profile, and support previously-established links between physical health and objective and subjective memory function.

**Keywords:** aging; objective memory; physical health; psychological distress; subjective memory.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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

1
J Allergy Clin Immunol Pract

. 2023 Aug 2;S2213-2198(23)00809-7.

doi: 10.1016/j.jaip.2023.07.035. Online ahead of print.

# Sex, ethnicity, BMI, and environmental exposures associated with NSAID-Exacerbated Respiratory Disease symptom sequence

Kelley Nicole Dages[1], Olufemi Sofola-James[2], Esha Sehanobish[3], Prudhvi Regula[4], Chien-Chang Chen[5], Sergio Elias Chiarella[6], Rohit Dilip Divekar[7], Hillel W Cohen[8], Elina Jerschow[9]

Affiliations expand

- PMID: 37541619

- DOI: 10.1016/j.jaip.2023.07.035

# Abstract

**Background:** Nonsteroidal anti-inflammatory drugs-exacerbated respiratory disease (N-ERD) has a triad of symptoms: nasal polyposis, asthma, and NSAID hypersensitivity. Little is known about symptom timing and disease progression.

**Objective:** The aim of this study is to characterize disease progression in N-ERD.

**Methods:** Patients with N-ERD were prospectively interviewed and classified into four groups based on their first symptom at initial N-ERD onset (asthma, nasal polyps, NSAID hypersensitivity, or all concurrently). Associations of patient characteristics with the four groups were examined, along with associations within the "asthma first" group.

**Results:** Patients (n=240) were mostly female (68%) and self-identified as non-White (77%). Half (n=119) reported asthma as the earliest symptom in the N-ERD triad. Compared to other groups, "asthma first" was associated with younger age of onset (25 years, SE ±1.3, p<0.001) and higher BMI (OR=1.3, 95%CI 1.06-1.7, p=0.02). In this group, age of onset <20 years was associated with female sex, Latino ethnicity, and higher BMI (all p<0.05). The "NSAID-sensitivity first" group was significantly associated with male sex (OR=3.3, 95%CI 1.5-7.4, p=0.004) and pollution exposure (OR=4.4, 95%CI 1.6-11.9, p=0.003). At the initial presentation, 27% of patients were unaware of their N-ERD diagnosis. Black and Latino patients were more likely to be unaware of their N-ERD diagnosis compared to White (p=0.003). Median diagnostic delay was 3 years (IQR 0-5).

**Conclusions:** In this cohort, N-ERD is highly variable in onset and progression, with sex, BMI, race and ethnicity, and environmental exposures significantly associated with disease patterns and diagnostic delay.

**Keywords:** AERD; N-ERD; NSAID hypersensitivity; NSAID-exacerbated respiratory disease; aspirin-exacerbated respiratory disease; asthma; nasal polyposis.

J Allergy Clin Immunol

. 2023 Aug 2;S0091-6749(23)00973-9.

doi: 10.1016/j.jaci.2023.06.027. Online ahead of print.

# High plasma IL-6 levels may enhance the adverse effects of mouse allergen exposure in urban schools on asthma morbidity in children

Nicole Akar-Ghibril[1], Kimberly F Greco[2], Medina Jackson-Browne[3], Wanda Phipatanakul[4], Perdita Permaul[5]

Affiliations expand

- PMID: 37541489

- DOI: 10.1016/j.jaci.2023.06.027

## Abstract

**Background:** Few data on the relationships between environmental exposures, asthma morbidity, and systemic IL-6 inflammation exist.

**Objective:** We sought to determine whether baseline plasma IL-6 level is associated with increased asthma morbidity in children exposed to mouse allergen in inner-city classrooms.

**Methods:** Data from the longitudinal School Inner-City Asthma Studies of 215 children with asthma, aged 4 to 14 years and recruited from urban elementary schools, were analyzed. Given the unknown threshold of IL-6 risk levels and skewness of the distribution, the children were stratified into tertiles as follows: low baseline IL-6 level (<0.013 pg/mL), moderate baseline IL-6 level (0.013-0.302 pg/mL), and high baseline IL-6 level (>0.302 pg/mL). Relationships between plasma IL-6 level and body mass index (BMI) percentile,

inflammatory markers, lung function, mouse allergen exposure, and asthma outcomes were assessed.

**Results:** Cross-sectional analysis demonstrated that increasing IL-6 level was associated with higher BMI percentile (P < .0001), C-reactive protein level (P = .0006), and blood neutrophil count (P = .0024). IL-6 was not associated with type 2 inflammatory markers, including blood eosinophil count, allergic sensitization, or fractional exhaled nitric oxide level. Longitudinal analysis showed that children with high IL-6 levels had a higher number of days with asthma symptoms than did those children with moderate (incidence rate ratio = 1.74 [95% CI = 1.10-2.77]; P = .0187) or low (incidence rate ratio =1.83 [95% CI = 1.21-2.77]; P = .0043) IL-6 levels. Children with high IL-6 levels who were exposed to increasing levels of mouse allergen exhibited lower ratios of $FEV_1$ value to forced vital capacity than did children with moderate IL-6 levels (β = -0.0044 [95% CI = -0.0073 to -0.0015]; pairwise interaction P = .0028) or low IL-6 levels (β = -0.0042 [95% CI = - 0.0070 to -0.0013]; pairwise interaction P = .0039) levels.

**Conclusions:** Inner-city children with asthma and high plasma IL-6 levels are more likely to have an increased BMI, elevated C-reactive protein level, elevated blood neutrophil count, and greater asthma symptoms. High IL-6 level appears to increase susceptibility to the effects of classroom exposure to mouse allergen on lung function in urban children.

**Keywords:** BMI; IL-6; allergen; asthma; body mass index; children; inner-city; metabolic dysfunction; obesity.



Eur Arch Otorhinolaryngol

. 2023 Aug 4.

doi: 10.1007/s00405-023-08141-3. Online ahead of print.

# How can we identify subglottic stenosis in patients with suspected obstructive disease?

Eleftherios Ntouniadakis[1], Josefin Sundh[2], Jeanette Söderqvist[3], Mathias von Beckerath[4,5]

Affiliations expand

- PMID: 37540269

- DOI: 10.1007/s00405-023-08141-3

## Abstract

**Purpose:** Subglottic stenosis, a rare condition of the upper airway, is frequently misdiagnosed as obstructive lung disease. The aim of this study was to investigate whether subglottic stenosis could be identified and distinguished from asthma and chronic obstructive pulmonary disease (COPD) using spirometry or the dyspnea index (DI).

**Methods:** The study population included 43 patients with asthma, 31 patients with COPD and 50 patients with subglottic stenosis planned to undergo endoscopic intervention. All patients completed the DI and underwent dynamic spirometry registering both inspiratory and expiratory volumes and flows, including the expiratory disproportion index (EDI), the ratio of forced expiratory volume in 1 s to peak expiratory flow. One-way analysis of variance assessed the discrepancy of the variables among the study groups, and receiver operating curve (ROC) analysis determined the measurement with the best discriminatory power providing a cutoff value, maximizing both sensitivity and specificity.

**Results:** The only statistically significant variables differing between all three groups were the EDI and the DI. The EDI showed an excellent area under the ROC curve (0.99, $p < 0.001$) with a cutoff value of 0.39 (98% sensitivity, 96% specificity), followed by DI (0.87, $p < 0.001$) with a cutoff score of > 25 (83% sensitivity and 78% specificity).

**Conclusion:** In patients with dyspnea of unknown cause, an increase in EDI should arouse a suspicion of extrathoracic airway obstruction, advocating for further evaluation with laryngotracheoscopy.

**Keywords:** Asthma; COPD; Dyspnea Index; Expiratory Disproportion Index; Functional assessment; Subglottic stenosis.

- 32 references

SUPPLEMENTARY INFO

Grant supportexpand

FULL TEXT LINKS

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Acta Biomed

. 2023 Aug 3;94(4):e2023172.

doi: 10.23750/abm.v94i4.14239.

# Safety and adverse reactions in subcutaneous allergen immunotherapy: a review

Cristoforo Incorvaia[1], Carlo Cavaliere[2], Jan W Schroeder[3], Gualtiero Leo[4], Francesca Nicoletta[5], Alessandro Barone[6], Erminia Ridolo[7]

Affiliations expand

- PMID: 37539607

- DOI: 10.23750/abm.v94i4.14239

## Abstract

**Background:** Allergen immunotherapy (AIT) is the only treatment which acts on the causes of allergic diseases by modifying their natural history. In the eighties subcutaneous immunotherapy (SCIT) with high biological power allergen extracts caused a number of severe systemic reactions and also fatalities in the UK and the US, resulting in its limitation and in the introduction of other routes of administration. A decisive advance for SCIT safety was understanding that the major cause of mortality was injecting the allergen extract to patients with uncontrolled asthma at the time of injection.

**Areas covered:** This awareness resulted in a significant decrease in fatalities, but not in their abolition. In 2019, an increase in SCIT-related mortality was observed, suggesting to continue the research for still unidentified factors favoring severe reactions, such as the administration of a wrong extract or of allergen doses higher than listed, unintentional intravenous administration, and missed dose reduction after protracted interruption. Moreover, in the context of the improving of the safety, the role played in tolerance-promoting by adjuvants such as CpG oligodeoxynucleotides has to be taken into account, as well as the potential preventive effect performed by the monoclonal anti-IgE antibody omalizumab against the exacerbation of severe reactions during SCIT.

**Conclusion:** The safety of SCIT is good, but the research to improve it further must continue. In particular, the pathophysiological mechanisms related to AIT for inhalants and for Hymenoptera venom should be studied, based on the evident diversity demonstrated by the complete absence of fatal reactions to Hymenoptera venom immunotherapy from its introduction in comparison with the history of serious and fatal offenses examined in this review.



Review

Ther Adv Chronic Dis

. 2023 Aug 1;14:20406223231190480.

doi: 10.1177/20406223231190480. eCollection 2023.

# Fractional nitric oxide measurement in exhaled air (FeNO): perspectives in the management of respiratory diseases

Beatrice Ragnoli[1], Alessandro Radaeli[2], Patrizia Pochetti[1], Stefano Kette[1], Jaymin Morjaria[3], Mario Malerba[1,4]

Affiliations expand

- PMID: 37538344

- PMCID: PMC10395178

- DOI: 10.1177/20406223231190480

## Abstract

Exhaled nitric oxide (NO) production, upregulated by inflammatory cytokines and mediators in central and peripheral airways, can be easily and non-invasively detected in exhaled air in asthma and other respiratory conditions as a promising tool for disease monitoring. The American Thoracic Society and European Respiratory Society released recommendations that standardize the measurement of the fractional exhaled NO (FeNO). In asthma, increased FeNO reflects eosinophilic-mediated inflammatory pathways and, as a biomarker of T2 inflammation can be used to identify asthma T2 phenotype. In this setting its measurement has shown to be an important tool especially in the diagnostic process, in the assessment and evaluation of poor adherence or predicting positive response to inhaled corticosteroids treatment, in phenotyping severe asthma patients and as a biomarker to predict the response to biologic treatments. The discovery of the role of NO in the pathogenesis of different diseases affecting the airways and the possibility to estimate the predominant site of increased NO production has provided new insight on its regulatory role in the airways, making it suitable for a potential extended use in clinical practice for different pulmonary diseases, even though its role remains less clear than in asthma. Monitoring FeNO in pulmonary obstructive lung diseases including chronic bronchitis and emphysema, interstitial lung diseases, obstructive sleep apnea and other pulmonary diseases is still under debate but has opened up a window to the role NO may play in the management of these diseases. The use of FeNO is reliable, cost effective and

recommendable in both adults and children, and should be implemented in the management of patients with asthma and other respiratory conditions.

**Keywords:** asthma management; central and peripheral airways; fractional exhaled nitric oxide; respiratory diseases.



# Conflict of interest statement

Jaymin Morjaria has received honoraria for speaking and financial support to attend meetings/advisory boards from Wyeth, Chiesi, Pfizer, MSD, Boehringer Ingelheim, Teva, GSK/Allen & Hanburys, Napp, Almirall, AstraZeneca, Trudell, Cook Medical, Medela AG, Medtronics and Novartis. He has been an expert witness in a court case relating to the impact of smoking on illness severity, ITU admissions and mortality from Covid-19 in South Africa in 2020. The entire proceeds of the work were donated to multiple charities. Mario Malerba has received honoraria for speaking and financial support for attending meetings and/or serving on the advisory boards from Chiesi, Astra-Zeneca, GSK, Laboratori Guidotti, Boehringer Ingelheim, Vitalaire, Grifols, CLS Behring. All the authors have no other relevant affiliations of financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed. Jaymin Morjaria is also an Associate Editor of Therapeutic Advances in Chronic Disease; therefore, the peer-review process was managed by alternative members of the Board, and he had no involvement in the decision-making process. Beatrice Ragnoli and Mario Malerba are members of the Editorial Board of Therapeutic Advances in Chronic Disease and had no involvement in the peer review process.

Editorial

Eur Respir J

. 2023 Aug 3;62(2):2301052.

doi: 10.1183/13993003.01052-2023. Print 2023 Aug.

# From small to big, using microRNA profiling to investigate infant origins of childhood asthma

Weston T Powell[1,2], Stephen R Reeves[3,2]

Affiliations expand

- PMID: 37536728

- DOI: 10.1183/13993003.01052-2023

*No abstract available*

## Conflict of interest statement

Conflict of interest: W.T. Powell reports grants from the Parker B. Francis Foundation and the Sleep Research Society Foundation, outside the submitted work. S.R. Reeves reports support for the present manuscript from NHLBI (R03HL156916).

## Comment on

- Nasal airway microRNA profiling of infants with severe bronchiolitis and risk of childhood asthma: a multicentre prospective study.
  Zhu Z, Freishtat RJ, Harmon B, Hahn A, Teach SJ, Pérez-Losada M, Hasegawa K, Camargo CA Jr; MARC-35 Investigators.Eur Respir J. 2023 Aug 3;62(2):2300502. doi: 10.1183/13993003.00502-2023. Print 2023 Aug.PMID: 37321621

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS



Mucosal Immunol

. 2023 Aug 1;S1933-0219(23)00055-7.

doi: 10.1016/j.mucimm.2023.07.003. Online ahead of print.

# Airway epithelium IgE-FcεRI Cross-Link Induces Epithelial Barrier Disruption in Severe T2-high Asthma

Chih-Ming Weng[1], Meng-Jung Lee[2], Wei Chao[3], Yuh-Rong Lin[3], Chun-Ju Chou[3], Mei-Chuan Chen[4], Chun-Liang Chou[5], I Lin Tsai[6], Chien-Huang Lin[7], Kian Fan Chung[8], Han-Pin Kuo[9]

Affiliations expand

- PMID: 37536562

- DOI: 10.1016/j.mucimm.2023.07.003

## Abstract

Although high affinity IgE receptor (FcεRI) expression is up-regulated in Type 2 (T2)-high asthmatic airway epithelium, its functional role in airway epithelial dysfunction has not

been elucidated. Here we report the up-regulated expression of FcεRI and p-EGFR, associated with decreased expression of E-cadherin and claudin-18 in bronchial biopsies of severe T2-high asthmatics compared to mild allergic asthmatics and non-T2 asthmatics. Monomeric IgE (mIgE) decreased the expression of junction proteins, E-cadherin, claudin-18 and ZO-1, and increased alarmin mRNA and protein expression in cultured PBEC from T2-high asthmatics. Epithelial FcεRI ligation with mIgE decreased TEER in air-liquid interface (ALI) cultured epithelial cells. FcεRI ligation with mIgE or IgE-DNP or serum of high level allergen specific IgE activated EGFR and Akt via activation of Src family kinases, mediating alarmin expression, junctional protein loss, and increased epithelial permeability. Furthermore, tracheal instillation of mIgE in HDM-sensitized mice induced airway hyper-responsiveness, junction protein loss, epithelial cell shedding, and increased epithelial permeability. Thus, our results suggest that IgE-FcεRI cross-linking in the airway epithelium is a potential and unnoticed mechanism for impaired barrier function, increased mucosal permeability, EGFR-mediated alarmin production in T2-high asthma.

**Keywords:** EGFR phosphorylation; FcεRI; T2-high asthma; impaired barrier function; junctional proteins loss.



Respir Physiol Neurobiol

. 2023 Aug 1;104135.

doi: 10.1016/j.resp.2023.104135. Online ahead of print.

# 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

## 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.

Respir Med

. 2023 Aug 1;107375.

doi: 10.1016/j.rmed.2023.107375. Online ahead of print.

# Bronchodilator response does not associate with asthma control or symptom burden among patients with poorly controlled asthma

David A Kaminsky[1], Jiaxian He[2], Robert Henderson[2], Anne E Dixon[3], Charles G Irvin[3], John Mastronarde[4], Lewis J Smith[5], Elizabeth A Sugar[2], Robert A Wise[6], Janet T Holbrook[2]

Affiliations expand

- PMID: 37536444

- DOI: 10.1016/j.rmed.2023.107375

## Abstract

**Purpose:** The purpose of this study was to determine how four different definitions of bronchodilator response (BDR) relate to asthma control and asthma symptom burden in a large population of participants with poorly controlled asthma.

**Procedures:** We examined the baseline change in FEV1 and FVC in response to albuterol among 931 participants with poorly controlled asthma pooled from three clinical trials conducted by the American Lung Association - Airways Clinical Research Centers. We defined BDR based on four definitions and analyzed the association of each with asthma

control as measured by the Asthma Control Test or Asthma Control Questionnaire, and asthma symptom burden as measured by the Asthma Symptom Utility Index.

**Main findings:** A BDR was seen in 31-42% of all participants, depending on the definition used. There was good agreement among responses (kappa coefficient 0.73 to 0.87), but only 56% of participants met all four definitions for BDR. A BDR was more common in men than women, in Blacks compared to Whites, in non-smokers compared to smokers, and in non-obese compared to obese participants. Among those with poorly controlled asthma, 35% had a BDR compared to 25% of those with well controlled asthma, and among those with a high symptom burden, 34% had a BDR compared to 28% of those with a low symptom burden. After adjusting for age, sex, height, race, obesity and baseline lung function, none of the four definitions was associated with asthma control or symptom burden.

**Conclusion:** A BDR is not associated with asthma control or symptoms in people with poorly controlled asthma, regardless of the definition of BDR used. These findings question the clinical utility of a BDR in assessing asthma control and symptoms.

**Keywords:** Asthma; Asthma control; Asthma symptoms; Bronchodilator response.



# Conflict of interest statement

Declaration of competing interest DAK – David A. Kaminsky reports article publishing charges and statistical analysis were provided by American Lung Association. David A. Kaminsky reports a relationship with MGC Diagnostics Corporation that includes: speaking and lecture fees. David A. Kaminsky reports a relationship with UptoDate Inc that includes: consulting or advisory. Editor, Netter Respiratory Disease, Elsevier, Inc. - DAK CGI – Charles G Irvin reports a relationship with Medical Graphics Corp that includes: board membership and travel reimbursement. AED – Anne Dixon reports a relationship with American Lung Association that includes: board membership. Anne Dixon reports a relationship with American Board of Internal Medicine that includes: consulting or advisory. Anne Dixon reports a relationship with UptoDate Inc that includes: consulting or advisory. LJS- Lewis Smith reports financial support was provided by American Lung Association. RAW – Consultant: Astra-Zeneca, Boehringer Ingelheim, GlaxoSmithKline, Glenmark Pharmaceuticals, USA, Verona. JH, RH, JM, EAS, JTH – no declarations.

Review

J Allergy Clin Immunol

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# Advancing Precision Medicine in Asthma: Evolution of Treatment Outcomes

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Affiliations expand

- PMID: 37531979

- DOI: 10.1016/j.jaci.2023.07.009

## Abstract

The article discusses the historical evolution of asthma treatment and highlights recent advancements in personalized medicine, specifically the use of biologics in severe asthma therapy and its potential combination with allergen immunotherapy (AIT). One of the major breakthroughs of biologics is their potential effect on airway remodeling, a crucial aspect of asthma chronicity. The article introduces the concept of Disease Modifying Anti Asthmatic Drugs (DMAADs), which aim to modify the course of asthma and possibly modulate or prevent airway remodeling. Furthermore, the critical importance of patient-centered outcome measures to evaluate the efficacy and effectiveness of asthma treatments is emphasized, with the innovative concept of asthma remission introduced as a potential outcome. Recent studies suggest that AIT can be used as an additional therapy to biologic agents for the treatment of allergic asthma. The combination of these treatments

has been shown to induce improved clinical outcomes. However , AIT is actually not recommended for use in severe asthma patients, but encouraging results from studies investigating the combined use of AIT and biologics indicate a novel approach to exploring these treatment modalities. In conclusion, the introduction of biologics and AIT have changed the scenario of respiratory allergy treatment, from a "one size fits all" approach to embracing "individual treatments."

**Keywords:** Airways Remodelling; Allergen Immunotherapy; Asthma Treatments; Biologics; Clinical Remission.





Pediatr Pulmonol

. 2023 Aug 2.

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# The association between PM2.5 concentration and the severity of acute asthmatic exacerbation in hospitalized children: A retrospective study in Chongqing, China

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Affiliations expand

- PMID: 37530510

- DOI: 10.1002/ppul.26557

# Abstract

**Background:** Ambient PM2.5 is associated with asthma exacerbation. The association between the concentration of PM2.5 and the severity of asthma exacerbation has yet to be thoroughly clarified. The study aims to explore the association between the piror 30 days average concentration of PM2.5 and the severity of acute asthma exacerbation in hospitalized children.

**Methods:** A total of 269 children with acute exacerbation of asthma were enrolled and divided into three groups according to the PM2.5 exposure concentrations: group 1 (PM2.5: <37.5 μg/m$^3$ ), group 2 (PM2.5: 37.5-75 μg/m$^3$ ), group 3 (PM2.5: ≥75 μg/m$^3$ ), respectively. The ordered logistic regression modeling was conducted to explore the influence of daily PM2.5 concentration on the clinical severity of children's asthma exacerbation. Multiple linear regression was conducted to explore the association between the concentration of PM2.5 and the length of stay in the hospital (LOS). We also conducted a receiver operating characteristic (ROC) curve analysis to explore the cutoff value of PM2.5 to predict the children's asthma exacerbation.

**Results:** There was no statistical difference among the three groups of children in gender, age, body mass index, ethnicity, the first diagnosis of asthma, allergic history, passive smoke exposure, or family history of asthma. There was a statistically significant difference in many hospitalization characteristics ($p < 0.05$) among the three groups of children. Significant differences were found in terms of accessory muscles of respiration ($p = 0.005$), respiratory failure ($p = 0.012$), low respiratory tract infectious ($p = 0.020$), and the severity of asthma exacerbation ($p < 0.001$) among the three groups. PM2.5 concentration was primarily positively correlated to neutrophile inflammation. The ordered multivariate logistic regression model showed that higher PM2.5 concentrations were significantly associated with greater odds of more severe asthma exacerbation in one and two-pollutant models. The adjusted odds ratio of severe asthma exacerbation was 1.029 (1.009, 1.049) in the one-pollutant model. The most significant odds ratio of severe asthma exacerbation was 1.050 (1.027, 1.073) when controlling $NO_2$ in the two-pollutant models. Multiple linear regression showed that PM2.5 concentration was significantly associated with longer LOS in both one-pollutant and two-pollutant models. By performing ROC analysis, the average daily concentration of 44.5 μg/m$^3$ of PM2.5 (AUC = 0.622, $p = 0.002$)

provided the best performance to predict severe asthma of children exacerbation with a sensitivity of 59.2% and a specificity of 63.8%.

**Conclusion:** The increased prior 30 days average concentration of PM2.5 was associated with greater asthma exacerbation severity and longer length of stay in the hospital of children with asthma exacerbation.

**Keywords:** PM2.5; asthma; children; exacerbation severity.



- 38 references

SUPPLEMENTARY INFO

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12

Pediatr Pulmonol

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. 2023 Aug 2.

doi: 10.1002/ppul.26617. Online ahead of print.

# High flow nasal cannula use is associated with increased hospital length of stay for pediatric asthma

Colin Rogerson[1,2], Arthur Owora[1], Tian He[3], Aaron Carroll[1], Titus Schleyer[2], Samer AbuSultaneh[1], Wanzhu Tu[3], Eneida Mendonca[1,4]

Affiliations expand


- PMID: 37530483

- DOI: 10.1002/ppul.26617


# Abstract


**Background:** High flow nasal cannula (HFNC) is a respiratory device increasingly used to treat asthma. Recent mechanistic studies have shown that nebulized medications may have reduced delivery with HFNC, which may impair asthma treatment. This study evaluated the association between HFNC use for pediatric asthma and hospital length of stay (LOS).

**Methods:** This was a retrospective matched cohort study. Cases included patients aged 2-18 years hospitalized between January 2010 and December 2021 with asthma and received HFNC treatment. Controls were selected using logistic regression propensity score matching based on demographics, vital signs, medications, imaging, and social and environmental determinants of health. The primary outcome was hospital LOS.

**Results:** A total of 23,659 encounters met eligibility criteria, and of these 1766 cases included HFNC treatment with a suitable matched control. Cases were well-matched in demographics, social and environmental determinants of health, and clinical characteristics including use of adjunctive asthma therapies. The median hospital LOS for study cases was significantly higher at 87 h (interquartile range [IQR]: 61-145) compared to 66 h (IQR: 43-105) in the matched controls ($p < 0.01$). There was no significant difference in the rate of intubation and mechanical ventilation (8.9% vs. 7.6%, $p = .18$); however, the use of NIV was significantly higher in the cases than the control group (21.3% vs. 6.7%, $p < .01$).

**Conclusion:** In this study of children hospitalized for asthma, HFNC use was associated with increased hospital LOS compared to matched controls. Further research using more granular data and additional relevant variables is needed to validate these findings.


**Keywords:** critical care; informatics; pediatrics; pulmonology.



- 38 references

SUPPLEMENTARY INFO

Grant supportexpand

FULL TEXT LINKS

J Asthma

. 2023 Aug 2;1-5.

doi: 10.1080/02770903.2023.2244590. Online ahead of print.

# Efficacy of Mepolizumab and Omalizumab Combination Therapy in Uncontrolled Asthma

Mehmet Emin Sezgin[1], Mustafa Çolak[2], Özge Çağlayan[1], Merve Yumrukuz Şenel[2], Esma Nur Aktepe Sezgin[3], Hikmet Çoban[2], Nurhan Sarıoğlu[2], Bilun Gemicioğlu[4], Fuat Erel[1]

Affiliations expand

- PMID: 37530447

- DOI: 10.1080/02770903.2023.2244590

## Abstract

**Objective:** Results of biological therapies are often encouraging for devere asthma who are phenotyped as Type 2 inflammation. Unfortunately, some patients do not achieve the desired responses. In this group of patients, there are often switches between anti Ig E and anti IL-5s and partial improvements are often is deemed sufficient.

**Method:** We planned to start combination therapy with mepolizumab and omalizumab in a 52-year-old patient with uncontrolled allergic asthma whose asthma could not be controlled with omalizumab and mepolizumab treatment, respectively. After complete

asthma control was achieved, we aimed to discontinue mepolizumab and continue with omalizumab because it was allergic asthma.

**Result:** The combination of omalizumab 300 mg/month and mepolizumab 100 mg/month was tried and emergency admissions and oral corticosteroids were stopped. At the same time, significant improvement was observed in asthma control test, pulmonary function test and comfort of life.

**Conclusion:** Combined use of Anti-Ig E (omalizumab) and Anti IL 5 (mepolizumab) with a synergistic effect by acting through both pathways, especially in patients with allergic asthma and high levels of both total Ig E and eosinophilia, was found to be effective and no side effects were observed in long-term follow-up. Combination therapy with omalizumab and mepolizumab may become a safe option in patients with severe allergic asthma with a Type 2 inflammatory phenotype who cannot be controlled with each biologic agent.

**Keywords:** Biological Therapy; Combination; Mepolizumab; Omalizumab; Severe Asthma.



ERJ Open Res

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doi: 10.1183/23120541.00158-2023. eCollection 2023 Jul.

# Healthcare costs and resource utilisation in bronchiectasis, asthma and COPD

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Affiliations expand

- PMID: 37529638

- PMCID: PMC10388176

- DOI: 10.1183/23120541.00158-2023

**Free PMC article**

# Abstract

**Direct healthcare costs for patients with asthma are less than half (-52%) and for patients with COPD are 41% higher if compared to those of patients with bronchiectasis. The leading expense items in bronchiectasis are hospitalisations and antibiotics.** https://bit.ly/3Iq8AUP.



# Conflict of interest statement

Conflict of interest: G. Corrao received research support from the European Community, the Italian Medicines Agency (AIFA), and the Italian Ministry of Education, Universities and Research. He took part in a variety of projects that were funded by pharmaceutical companies (Novartis, GSK, Roche, AMGEN and BMS). He also received honoraria as a member of the Advisory Board of Roche. S. Aliberti received consulting fees, honoraria for lectures, presentations or educational events and participation on a data safety monitoring board or advisory board from Insmed, Zambon, AstraZeneca, CLS Behring, Grifols, Fondazione Internazionale Menarini, MSD, Brahms, Physioassist SAS, GlaxoSmithKline Spa and Thermofisher Scientific. He also received royalties from McGraw-Hill. No other potential conflicts of interest were declared for the other authors.

- 11 references

Review

Nat Rev Drug Discov

.

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doi: 10.1038/s41573-023-00750-1. Online ahead of print.

# Type 2 chronic inflammatory diseases: targets, therapies and unmet needs

Pavel Kolkhir[1,2], Cezmi A Akdis[3], Mübeccel Akdis[3], Claus Bachert[4,5,6], Thomas Bieber[7,8,9], Giorgio Walter Canonica[10,11], Emma Guttman-Yassky[12], Martin Metz[13,14], Joaquim Mullol[15], Oscar Palomares[16], Harald Renz[17,18], Sonja Ständer[19], Torsten Zuberbier[13,14], Marcus Maurer[20,21]

Affiliations expand

- PMID: 37528191

- DOI: 10.1038/s41573-023-00750-1

## Abstract

Over the past two decades, significant progress in understanding of the pathogenesis of type 2 chronic inflammatory diseases has enabled the identification of compounds for more than 20 novel targets, which are approved or at various stages of development, finally facilitating a more targeted approach for the treatment of these disorders. Most of these newly identified pathogenic drivers of type 2 inflammation and their corresponding treatments are related to mast cells, eosinophils, T cells, B cells, epithelial cells and sensory nerves. Epithelial barrier defects and dysbiotic microbiomes represent exciting future drug targets for chronic type 2 inflammatory conditions. Here, we review common targets, current treatments and emerging therapies for the treatment of five major type 2 chronic inflammatory diseases - atopic dermatitis, chronic prurigo, chronic urticaria, asthma and

chronic rhinosinusitis with nasal polyps - with a high need for targeted therapies. Unmet needs and future directions in the field are discussed.



- 304 references

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. 2023 Aug 1;382:1774.

doi: 10.1136/bmj.p1774.

# Organisational change needed to move towards net zero for asthma care

David McKelvey[1]

Affiliations expand

- PMID: 37527845

- DOI: 10.1136/bmj.p1774

*No abstract available*

## Conflict of interest statement

Competing interests: None declared.

## Comment on

- Towards net zero: asthma care.
  Smith LE, Bhugra R, Kelani RY, Smith J.BMJ. 2023 Jun 19;381:e072328. doi: 10.1136/bmj-2022-072328.PMID: 37336559 No abstract available.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS



Pulm Ther

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doi: 10.1007/s41030-023-00234-y. Online ahead of print.

# Triple Therapy with Mometasone/Indacaterol/Glycopyrroni

# um or Doubling the ICS/LABA Dose in GINA Step 4: IRIDIUM Analyses

Richard N van Zyl-Smit[1], Huib A M Kerstjens[2], Jorge Maspero[3], Ana-Maria Tanase[4], David Lawrence[4], Karen Mezzi[4], Peter D'Andrea[5], Kenneth R Chapman[6]

Affiliations expand

- PMID: 37526856

- DOI: 10.1007/s41030-023-00234-y

**Free article**

## Abstract

**Introduction:** GINA guidelines recommend increasing the dose of inhaled corticosteroids (ICS) as a step-up option for patients with inadequately controlled asthma at GINA step 4 [inadequately controlled asthma on medium-dose ICS/long-acting beta-2 agonist (LABA)]. The aim of this study was to compare the efficacy and safety of long-acting muscarinic antagonists (LAMA) add-on to medium-dose ICS/LABA in patients at GINA 2022 step 4.

**Methods:** This post hoc analysis of the IRIDIUM study evaluated the change from baseline in trough forced expiratory volume ($FEV_1$) in patients receiving medium-dose MF/IND/GLY versus high-dose MF/IND and high-dose FLU/SAL at Week 26. Other outcomes included improvement in lung functions [peak expiratory flow (PEF), forced vital capacity (FVC), forced expiratory flow between 25% and 75% of the FVC ($FEF_{25-75\%}$)], asthma control [Asthma Control Questionnaire (ACQ-7)], responder analysis (≥ 0.5 unit improvement in ACQ-7), and reduction in asthma exacerbations at Weeks 26 and 52.

**Results:** A total of 1930 patients were included in this analysis. Medium-dose MF/IND/GLY improved trough $FEV_1$ versus high-dose MF/IND (Δ 41 mL; 95% CI - 7-90) and high-dose FLU/SAL (Δ 88 mL; 95% CI 39-137) at Week 26 which were sustained until Week 52. Exacerbation rates were 16% lower with medium-dose MF/IND/GLY versus high-dose MF/IND for all (mild, moderate, and severe) exacerbations and 21-30% lower versus high-dose FLU/SAL for all (mild, moderate, and severe), moderate or severe, and severe exacerbations over 52 weeks. Further improvements in other lung functions were observed with medium-dose MF/IND/GLY. No new safety signals were identified.

**Conclusion:** Medium-dose MF/IND/GLY improved lung function and reduced asthma exacerbations compared to high-dose ICS/LABA and may be an undervalued option in patients at GINA 2022 step 4.

**Trial registration:** ClinicalTrials.gov Identifier: NCT02571777.

**Keywords:** Asthma exacerbations; GINA step 4; Glycopyrronium; ICS/LABA; IRIDIUM; Inadequately controlled asthma; LAMA add-on; Lung function.



- 21 references

SUPPLEMENTARY INFO

Associated dataexpand

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Allergy Asthma Clin Immunol

. 2023 Jul 31;19(1):66.

doi: 10.1186/s13223-023-00822-2.

# The impact of CFTR modulator triple therapy on type 2 inflammatory response in patients with cystic fibrosis

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Affiliations expand

- PMID: 37525180

- PMCID: PMC10391773

- DOI: 10.1186/s13223-023-00822-2

**Free PMC article**


# Abstract


**Background:** Treatment of cystic fibrosis (CF) has been revolutionized by the use of cystic fibrosis transmembrane conductance regulator (CFTR) protein modulators such as elexacaftor/tezacaftor/ivacaftor (ETI) triple therapy. Prior studies support a role for type 2 (T2) inflammation in many people with CF (PwCF) and CF-asthma overlap syndrome (CFAOS) is considered a separate clinical entity. It is unknown whether initiation of ETI therapy impacts T2 inflammation in PwCF. We hypothesized that ETI initiation decreases T2 inflammation in PwCF.

**Methods:** A single center retrospective chart review was conducted for adult PwCF. As markers of T2 inflammation, absolute eosinophil count (AEC) and total immunoglobulin E (IgE) data were collected longitudinally 12 months prior to ETI therapy initiation and 12 months following therapy initiation. Multivariable analyses adjusted for the age, gender, CFTR mutation, disease severity, inhaled steroid use, and microbiological colonization.

**Results:** There was a statistically significant reduction (20.10%, $p < 0.001$) in 12-month mean total IgE following ETI initiation; this change remained statistically significant in the multivariate model. The longitudinal analysis demonstrated no change in AEC following therapy initiation.

**Conclusion:** This study demonstrates that there is a statistically significant percent reduction in mean total IgE but no change in AEC following ETI initiation. ETI may lead to decreased antigen and superantigen load in the airway as a result of improved mucociliary clearance and these changes may drive the decline in total IgE, without influencing the epigenetic drivers of eosinophilic inflammation. Further studies are warranted to determine the underlying mechanism of ETI impact on T2 inflammation and possible role for asthma immunomodulator therapy post ETI initiation in CFAOS.




# Conflict of interest statement

None of the authors have any competing interests to declare.


- 27 references
- 3 figures

SUPPLEMENTARY INFO

Grant supportexpand

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Thorax

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. 2023 Jul 31;thorax-2022-219757.

doi: 10.1136/thorax-2022-219757. Online ahead of print.

# Recent trends in asthma diagnosis, preschool wheeze diagnosis and asthma exacerbations in English children and adolescents: a SABINA Jr study

Constantinos Kallis[1], Ekaterina Maslova[2], Ann D Morgan[1], Ian Sinha[3,4], Graham Roberts[5,6,7], Ralf J P van der Valk[2], Jennifer K Quint[1], Trung N Tran[8]

Affiliations expand

- PMID: 37524391

- DOI: 10.1136/thorax-2022-219757

**Free article**

# Abstract

**Background:** Asthma-related burden remains poorly characterised in children in the UK. We quantified recent trends in asthma prevalence and burden in a UK population-based cohort (1–17-year-olds).

**Methods:** The Clinical Practice Research Datalink Aurum database (2008–2018) was used to assess annual asthma incidence and prevalence in 1–17-year-olds and preschool wheeze in 1–5-year-olds, stratified by sex and age. During the same period, annual asthma exacerbation rates were assessed in those with either a diagnosis of preschool wheeze or asthma.

**Results:** Annual asthma incidence rates decreased by 51% from 1403.4 (95% CI 1383.7 to 1423.2) in 2008 to 688.0 (95% CI 676.3 to 699.9) per $10^5$ person-years (PYs) in 2018, with the most pronounced decrease observed in 1–5-year olds (decreasing by 65%, from 2556.9 (95% CI 2509.8 to 2604.7) to 892.3 (95% CI 866.9 to 918.3) per $10^5$ PYs). The corresponding decreases for the 6–11- and 12–17-year-olds were 36% (1139.9 (95% CI 1110.6 to 1169.7) to 739.9 (95% CI 720.5 to 759.8)) and 20% (572.3 (95% CI 550.4 to 594.9) to 459.5 (95% CI 442.9 to 476.4)) per $10^5$ PYs, respectively. The incidence of preschool wheeze decreased over time and was slightly more pronounced in the 1–3 year-olds than in the 4-year-olds. Prevalence of asthma and preschool wheeze also decreased over time, from 18.0% overall in 2008 to 10.2% in 2018 for asthma. Exacerbation rates increased over time from 1.33 (95% CI 1.31 to 1.35) per 10 PYs in 2008 to 1.81 (95% CI 1.78 to 1.83) per 10 PYs in 2018.

**Conclusion:** Paediatric asthma incidence decreased in the UK since 2008, particularly in 1-5-year-olds; this was accompanied by a decline in asthma prevalence. Preschool wheeze incidence also decreased in this age group. However, exacerbation rates have been increasing.



**Keywords:** Asthma Epidemiology; Paediatric asthma.




# Conflict of interest statement

Competing interests: EM is an employee of AstraZeneca and owns stock in AstraZeneca. IS received consultancy from AstraZeneca to their institutions for this work. GR received consultancy from AstraZeneca to their institutions for this work. RJPvdV is an employee of AstraZeneca and owns stock in AstraZeneca and GlaxoSmithKline. JKQ reports grants from AUK-BLF and The Health Foundation; grants and personal fees from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline and Bayer; and grants from Chiesi, outside the submitted work. JKQ's research group received funding from AstraZeneca for this work.

TNT is an employee of AstraZeneca and owns stock in AstraZeneca. CK and ADM have nothing to declare.



Review

Aust Occup Ther J

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doi: 10.1111/1440-1630.12899. Online ahead of print.

# Occupations and balance during the transition to motherhood with a lifetime chronic illness: A scoping review examining cystic fibrosis, asthma, and Type-1 diabetes

Alena Jane Haines[1], Lynette Mackenzie[1], Anne Honey[1], Peter G Middleton[1,2]

Affiliations expand

- PMID: 37524324

- DOI: 10.1111/1440-1630.12899

# Abstract

**Introduction:** Throughout the transition to motherhood, changes are experienced across a woman's physical, mental, social, and occupational self. Maternal chronic illness adds the complexity of increased healthcare needs and navigating a high-risk, medicalised pregnancy, birth, and post-natal period. Literature concerning motherhood transitions in chronic illness generally focusses on the mother's medical health and pregnancy outcomes; little is known about the impacts on women's occupations, balance, and quality of life. Understanding these issues may help support women in a more tailored and holistic way.

**Objective:** This scoping review aims to gather, analyse, and synthesise existing empirical research on occupational engagement and occupational balance as they impact on wellbeing and quality of life in women with a lifetime chronic illness before and during pregnancy and in early motherhood.

**Method:** The review follows the nine-stage framework described in the Joanna Briggs Institute Manual for Evidence Synthesis (2020). Five databases were searched: Embase, Medline, PsycINFO, CINAHL, Scopus, and OT Seeker. Data were extracted and examined via content analysis, described in narrative synthesis, summarised into a conceptual framework, and tabulated.

**Findings:** A total of 8,655 papers were discovered on initial search. Following title and abstract screening, 220 full-text studies were assessed for eligibility, and 46 papers were finally included. Analysis generated four major themes: The Disrupted Transition Journey; Adaptation, Compromise and Choice; Outcomes; and Drawing on What's Available. The themes were conceptualised into a framework to explain how women sought to balance motherhood and illness-related occupations. Adequate access to information, social support, expert care, and financial resources improved both quality of life and healthcare compliance.

**Conclusion:** Findings of this scoping review deepen the understanding of occupational balance during the transition to motherhood in the context of lifetime chronic illness. Healthcare providers and supportive family and friends can use this knowledge to adapt their approach to assisting women with chronic illness on the motherhood journey. These findings may also inform further inquiry into the scope of occupational therapy practice with this population.



**Keywords:** chronic disease; mothers; occupations; quality of life.




- 87 references

SUPPLEMENTARY INFO

Am J Respir Crit Care Med

. 2023 Jul 31.

doi: 10.1164/rccm.202301-0041OC. Online ahead of print.

# Circulating CC16 and Asthma: A Population-Based, Multi-Cohort 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[2], Monica Kraft[1], Duane L Sherrill[1], John A Curtin[3], Clare S Murray[3], Adnan Custovic[4], Inger Kull[5], Jenny Hallberg[5], Anna Bergström[6], Esther Herrera-Luis[7], Marilyn Halonen[1], Fernando D Martinez[1], Angela Simpson[3], Erik Melén[5], Stefano Guerra[8]

Affiliations expand

- PMID: 37523710

- DOI: 10.1164/rccm.202301-0041OC

## Abstract

**Rationale:** CC16 is an anti-inflammatory 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: TCRS (years 6-36; N-participants=814, N-observations=3042), BAMSE (years 8-24; Ns=2547, 3438), and MAAS (years 5-18, Ns=745, 1626). 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:** 1) After adjusting for covariates, CC16 deficits were associated with increased risk for the presence of asthma in all cohorts (meta-analyzed adjOR per 1-SD CC16 decrease: 1.20[95%CI 1.12-1.28];*P*<0.0001). The association was particularly strong for asthma with frequent symptoms (meta-analyzed adjRRR: 1.40[1.24-1.57];*P*<0.0001), was confirmed for both atopic and non-atopic asthma, and was independent of lung function impairment. 2) After adjustment for known predictors of persistent asthma, asthmatic children in the lowest CC16 tertile had a nearly 4-fold increased risk for having frequent symptoms persisting into adult life, compared with asthmatic children in the other two CC16 tertiles (meta-analyzed adjOR: 3.72[1.78-7.76];*P*<0.0001).

**Conclusions:** Circulating CC16 deficits are associated with the presence of asthma with frequent symptoms from childhood through mid-adult 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.

. 2023 Aug 1;61(4):320-327.

doi: 10.4193/Rhin22.408.

# Efficacy and safety of switching between biologics in chronic rhinosinusitis with nasal polyps or N-ERD

F F Brkic[1], D T Liu[1], R Klimbacher[1], N J Campion[1], T J Bartosik[1], E Vyskocil[1], V Stanek[1], A Tu[1], T Arnoldner[2], C Bangert[2], K Gangl[1], J Eckl-Dorna[1], S Schneider[1]

Affiliations expand

- PMID: 37515811

- DOI: 10.4193/Rhin22.408

## Abstract

**Background and objective:** The effectiveness of biologics in chronic rhinosinusitis with nasal polyps (CRSwNP) is well-established. However, real-world experience on the effectiveness of transitioning between two monoclonal antibodies is scarce. Therefore, we aimed to analyze the safety and efficacy of antibody switching in treatment of chronic rhinosinusitis.

**Methods:** All patients with CRSwNP or nonsteroidal anti-inflammatory drugs-exacerbated respiratory disease (N-ERD) requiring a switch between biologics were retrospectively studied. Analysis included changes in polyp size, quality of life parameters, asthma control, and side effects.

**Results:** Out of 195 patients treated with biologics for CRSwNP or N-ERD in our center, 23 (11.8%) required transition to a different monoclonal antibody. The majority switched from omalizumab to dupilumab (17/23, 73.9%), mostly due to inadequate symptom control. Nine out of these 17 patients (52.9%) were switched without a washout period. All patients showed significant improvement in nasal polyp score, asthma control test and sino-nasal outcome test-22 after changing to dupilumab. Keratoconjunctivitis sicca was the side-effect (4.3%) reported after the switch from omalizumab to dupilumab, which lead to

termination of therapy in one patient. Due to limited sample size, other antibody transitions were reported in a descriptive manner.

**Conclusion:** The transition to dupilumab is an effective option in patients with inadequate treatment response or side-effects of omalizumab in nasal polyposis. Our preliminary results indicate that a wash-out period may not be necessary when switching between biologics, however, these findings require further investigations. Other monoclonal antibody transitions also show promising results, but warrant validations in larger cohorts due to small patient samples in our study.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS


Proceed to details

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23

Pediatrics

. 2023 Aug 1;152(2):e2022060531.

doi: 10.1542/peds.2022-060531.

# Patterns in the Development of Pediatric Allergy

Stanislaw J Gabryszewski[1], Jesse Dudley[2], Di Shu[2,3], Jennifer A Faerber[2], Robert W Grundmeier[2], Alexander G Fiks[2], David A Hill[1,4]

Affiliations expand

- PMID: 37489286

- PMCID: PMC10389774 (available on 2024-08-01)

- DOI: 10.1542/peds.2022-060531

# Abstract

**Objectives:** Describe clinical and epidemiologic patterns of pediatric allergy using longitudinal electronic health records (EHRs) from a multistate consortium of US practices.

**Methods:** Using the multistate Comparative Effectiveness Research through Collaborative Electronic Reporting EHR database, we defined a cohort of 218 485 children (0-18 years) who were observed for ≥5 years between 1999 and 2020. Children with atopic dermatitis (AD), immunoglobulin E-mediated food allergy (IgE-FA), asthma, allergic rhinitis (AR), and eosinophilic esophagitis (EoE) were identified using a combination of diagnosis codes and medication prescriptions. We determined age at diagnosis, cumulative incidence, and allergic comorbidity.

**Results:** Allergic disease cumulative (and peak age of) incidence was 10.3% (4 months) for AD, 4.0% (13 months) for IgE-FA, 20.1% (13 months) for asthma, 19.7% (26 months) for AR, and 0.11% (35 months) for EoE. The most diagnosed IgE-FAs were peanut (1.9%), egg (0.8%), and shellfish (0.6%). A total of 13.4% of children had ≥2 allergic conditions, and respiratory allergies (ie, asthma, AR) were commonly comorbid with each other, and with other allergic conditions.

**Conclusions:** We detail pediatric allergy patterns using longitudinal, health care provider-based data from EHR systems across multiple US states and varied pediatric practice types. Our results support the population-level allergic march progression and indicate high rates of comorbidity among children with food and respiratory allergies.



# Conflict of interest statement

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

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grant supportexpand

FULL TEXT LINKS

J Allergy Clin Immunol Glob

. 2023 Aug;2(3):100122.

doi: 10.1016/j.jacig.2023.100122. Epub 2023 May 30.

# Maternal asthma in relation to infant size and body composition

Danielle R Stevens[1,2], Edwina Yeung[2], Stefanie N Hinkle[2,3], William Grobman[4], Andrew Williams[5], Marion Ouidir[2], Rajesh Kumar[6], Leah M Lipsky[2], Matthew C H Rohn[2,7], Jenna Kanner[2], Seth Sherman[8], Zhen Chen[9], Pauline Mendola[2,10]

Affiliations expand

- PMID: 37485032

- PMCID: PMC10361394

- DOI: 10.1016/j.jacig.2023.100122

**Free PMC article**

## Abstract

**Background:** Asthma affects 10% of pregnancies and may influence offspring health, including infant size and body composition, through hypoxic and inflammatory pathways.

**Objective:** We sought to determine associations between maternal asthma and asthma phenotypes during pregnancy and infant size and body composition.

**Methods:** The B-WELL-Mom study (2015-19) is a prospective cohort of 418 pregnant persons with and without asthma recruited in the first trimester of pregnancy from 2 US obstetric clinics. Exposures were maternal self-reported active asthma (n = 311) or no asthma (n = 107), and asthma phenotypes were classified on the bases of atopy, onset, exercise induced, control, severity, symptomology, and exacerbations. Outcomes were infant weight, length, head circumference, and skinfold measurements at birth and postnatal follow-up, as well as fat and lean mass assessed by air displacement plethysmography at birth. Adjusted multivariable linear regression examined associations of maternal asthma and asthma phenotypes with infant outcomes.

**Results:** Offspring were born at a mean ± SD of 38 ± 2.3 weeks' gestation and were 18 ± 2.2 weeks of age at postnatal follow-up. Infants of participants with asthma had a mean ± SD fat mass of 11.0 ± 4.2%, birth weight of 3045.8 ± 604.3 g, and postnatal follow-up weight of 6696.4 ± 964.2 g, which were not different from infants of participants without asthma (respectively, β [95% confidence interval]: -0.1 [-1.4, 1.3], -26.7 [-156.9, 103.4], and 107.5 [-117.3, 332.3]). Few associations were observed between asthma or asthma phenotypes and infant size or body composition.

**Conclusions:** In a current obstetric cohort, maternal asthma during pregnancy was not associated with differential infant size or body composition.

**Keywords:** Infant; adiposity; anthropometry; asthma; atopy; pregnancy; prospective study.

# Conflict of interest statement

DISCLOSURE STATEMENT Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interest.

- 67 references
- 3 figures

Eur Respir J

. 2023 Aug 3;62(2):2300245.

doi: 10.1183/13993003.00245-2023. Print 2023 Aug.

# The impact of steroid-sparing biologic therapies on weight loss in obese individuals with severe eosinophilic asthma

Alexandra M Nanzer[1,2], Victoria Taylor[3], Andrew P Hearn[3,2], Joanne E Kavanagh[3,2], Tanya Patrick[3], Linda Green[3], Louise Thomson[3], Jodie Lam[3], Mariana Fernandes[3], Cris Roxas[3], Grainne d'Ancona[3,2], Brian D Kent[3,4,5], Jaideep Dhariwal[3], David J Jackson[3,2]

Affiliations expand

- PMID: 37474156

- DOI: 10.1183/13993003.00245-2023

*No abstract available*

## Conflict of interest statement

Conflict of interest: A.M. Nanzer reports speaker fees and conference travel support from AstraZeneca, Sanofi, Teva, Chiesi and Napp. J.E. Kavanagh reports travel support from Teva. L. Thomson reports speaker fees and conference travel support from AstraZeneca. C. Roxas reports speaker fees from AstraZeneca, Chiesi, NAPP and Novartis, and conference travel support from AstraZeneca, Chiesi, GlaxoSmithKline, NAPP and Novartis. G. d'Ancona reports advisory board, speaker fees and congress travel support from GlaxoSmithKline, AstraZeneca, Chiesi, Napp and Teva Pharmaceuticals. B.D. Kent reports advisory board fees from AstraZeneca, GlaxoSmithKline and Chiesi, speaker fees from GlaxoSmithKline and AstraZeneca, and travel support to attend ERS meetings from A Menarini. J. Dhariwal

reports congress support from Sanofi. D.J. Jackson reports investigator-initiated research grants from AstraZeneca, advisory board and speaker fees from AstraZeneca, Sanofi and GlaxoSmithKline. The rest of the authors declare that they have no relevant conflicts of interest.

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS



Hosp Pediatr

. 2023 Aug 1;13(8):688-694.

doi: 10.1542/hpeds.2022-007020.

# Decreasing Goal Oxygen Saturations in Bronchiolitis Is Associated With Decreased Length of Stay

Shivani Briggs[1], Vedant Gupta[2], Nehal Thakkar[2], Jamie Librizzi[2], Hamy Temkit[2], Richard Engel[2]

Affiliations expand

- PMID: 37449328

- DOI: 10.1542/hpeds.2022-007020

# Abstract

**Objectives:** For patients hospitalized with bronchiolitis, many hospitals have implemented clinical practice guidelines to decrease variability in care. Our hospital updated its bronchiolitis clinical pathway by lowering goal oxygen saturation from 90% to 88%. We compared clinical outcomes before and after this change within the context of the pathway update.

**Methods:** This was a retrospective analysis of patients <24 months old admitted to a pediatric tertiary care center from 2019 to 2021 with bronchiolitis. Patients with congenital heart disease, asthma, home oxygen, or admitted to an ICU were excluded. The data were stratified for patients admitted before and after the clinical pathway update. Statistical methods consisted of 2 group comparisons using the $\chi$-square test for categorical variables, the Wilcoxon rank-sum test for continuous variables, and multiple regression analysis.

**Results:** A total of 1386 patients were included, 779 preupdate and 607 postupdate. There was no statistically significant difference in the admission rate of patients presenting to the emergency department with bronchiolitis between the 2 groups (P value .60). The median time to room air was 40.0 hours preupdate versus 30.0 hours postupdate (P value < .001). The median length of stay was 48.0 hours preupdate versus 41.0 hours postupdate (P value < .001). Readmission rate was 2.7% within 7 days of discharge preupdate, and 2.1% postupdate (P value .51).

**Conclusions:** Decreasing goal oxygen saturation to 88% was associated with a statistically significant decrease in time spent on oxygen and length of stay for patients admitted with bronchiolitis with no increase in readmissions.

. 2023 Aug;59(8):502-509.

doi: 10.1016/j.arbres.2023.05.014. Epub 2023 Jun 1.

# Validation of a Pathological Score for the Assessment of Bronchial Biopsies in Severe Uncontrolled Asthma: Beyond Blood Eosinophils

[Article in English, Spanish]

Borja G Cosio[1], Hanaa Shafiek[2], Amanda Iglesias[3], Mar Mosteiro[4], Ana Gonzalez-Piñeiro[4], Marta Rodríguez[5], Mónica García-Cosío[6], Eladio Busto[7], Javier Martin[8], Luis Mejías[9], Amparo Benito[6], Laura López Vilaro[10], Cristina Gómez[11]

Affiliations expand

- PMID: 37414638

- DOI: 10.1016/j.arbres.2023.05.014

**Free article**

## Abstract

**Background:** Blood eosinophil count (BEC) is currently used as a surrogate marker of T2 inflammation in severe asthma but its relationship with tissue T2-related changes is elusive. Bronchial biopsy could add reliable information but lacks standardization.

**Objectives:** To validate a systematic assessment of the bronchial biopsy for the evaluation of severe uncontrolled asthma (SUA) by standardizing a pathological score.

**Methods:** A systematic assessment of submucosal inflammation, tissue eosinophilic count/field (TEC), goblet cells hyperplasia, epithelial changes, basement membrane thickening, prominent airway smooth muscle and submucosal mucous glands was initially agreed and validated in representative bronchial biopsies of 12 patients with SUA by 8 independent pathologists. In a second phase, 62 patients with SUA who were divided according to BEC≥300cells/mm$^3$ or less underwent bronchoscopy with bronchial biopsies and the correlations between the pathological findings and the clinical characteristics were investigated.

**Results:** The score yielded good agreement among pathologists regarding submucosal eosinophilia, TEC, goblet cells hyperplasia and mucosal glands (ICC=0.85, 0.81, 0.85 and 0.87 respectively). There was a statistically significant correlation between BEC and TEC (r=0.393, p=0.005) that disappeared after correction by oral corticosteroids (OCS) use (r=0.170, p=0.307). However, there was statistically significant correlation between FeNO and TEC (r=0.481, p=0.006) that was maintained after correction to OCS use (r=0.419, p=0.021). 82.4% of low-BEC had submucosal eosinophilia, 50% of them moderate to severe.

**Conclusion:** A standardized assessment of endobronchial biopsy is feasible and could be useful for a better phenotyping of SUA especially in those receiving OCS.

**Keywords:** Biologic therapy; Bronchial biopsy; Eosinophil; Severe asthma.





Review

Thorac Surg Clin

. 2023 Aug;33(3):299-308.

doi: 10.1016/j.thorsurg.2023.04.016. Epub 2023 May 29.

# Thermoablative Techniques to Treat Excessive Central Airway Collapse

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Affiliations expand

- PMID: 37414486

- DOI: 10.1016/j.thorsurg.2023.04.016

## Abstract

Excessive central airway collapse (ECAC) is a condition characterized by the excessive narrowing of the trachea and mainstem bronchi during expiration, which can be caused by Tracheobronchomalacia (TBM) or Excessive Dynamic Airway Collapse (EDAC). The initial standard of care for central airway collapse is to address any underlying conditions such as asthma, COPD, and gastro-esophageal reflux. In severe cases, when medical treatment fails, a stent-trial is offered to determine if surgical correction is a viable option, and tracheobronchoplasty is suggested as a definitive treatment approach. Thermoablative bronchoscopic treatments, such as Argon plasma coagulation (APC) and laser techniques (potassium-titanyl-phosphate [KTP], holmium and yttrium aluminum pevroskyte [YAP]) are a promising alternative to traditional surgery. However, further research is needed to assess their safety and effectiveness in humans before being widely used.

**Keywords:** Argon plasma coagulation; Excessive central airway collapse; Excessive dynamic airway collapse; Laser tracheobronchoplasty; Thermal ablation; Tracheobronchomalacia.

Mol Immunol

. 2023 Aug;160:95-102.

doi: 10.1016/j.molimm.2023.06.011. Epub 2023 Jul 4.

# Pro-inflammatory action of formoterol in human bronchial epithelia

Xing-Jian Liu[1], Hao Pang[2], Yu-Qian Long[2], Ji-Qing Wang[2], Ya Niu[3], Rui-Gang Zhang[4]

Affiliations expand

- PMID: 37413911

- DOI: 10.1016/j.molimm.2023.06.011

## Abstract

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

(1 μM) was used. Taken together, our results suggest that formoterol stimulates IL-6 and IL-8 release which involves PKA/Src/ERK1/2 and/or β-arrestin2 signaling pathways.

**Keywords:** Bronchail epithelia; ERK1/2; PKA; β(2)-adrenoceptor; β-arrestin2.



## Conflict of interest statement

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



Editorial

Drug Ther Bull

. 2023 Aug;61(8):114.

doi: 10.1136/dtb.2023.000013. Epub 2023 Jul 4.

# Improving asthma prescribing: is FeNO the answer?

Jo Congleton[1]

Affiliations expand

- PMID: 37402644

- DOI: 10.1136/dtb.2023.000013


*No abstract available*


**Keywords:** Asthma; Inappropriate Prescribing.


## Conflict of interest statement

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

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS



Editorial


Respirology

- 
- 
- 

. 2023 Aug;28(8):694-695.

doi: 10.1111/resp.14551. Epub 2023 Jul 4.


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

Fanny Wai San Ko [1], Sundeep Salvi [2 3]

Affiliations expand

- PMID: 37402501

- DOI: 10.1111/resp.14551

**Free article**

*No abstract available*

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

# Comment on

- The burden of systemic corticosteroid use in asthma management in Asia.
  Dhar R, Rhee CK, Perng DW, Fukunaga K, Ip MS, Juthong S, Koh MS, Li J, Sharma S, Wiyono WH.Respirology. 2023 Aug;28(8):744-757. doi: 10.1111/resp.14533. Epub 2023 Jun 10.PMID: 37301540 Review.

- 14 references



Randomized Controlled Trial

. 2023 Aug;7(8):567-576.

doi: 10.1016/S2352-4642(23)00128-1. Epub 2023 Jun 26.

# Inhaled corticosteroids to improve lung function in children (aged 6–12 years) who were born very preterm (PICSI): a randomised, double-blind, placebo-controlled trial

Rhea C Urs[1], Denby J Evans[2], Tiffany K Bradshaw[3], James T D Gibbons[4], Elizabeth F Smith[1], Rachel E Foong[1], Andrew C Wilson[4], Shannon J Simpson[5]

Affiliations expand

- PMID: 37385269

- DOI: 10.1016/S2352-4642(23)00128-1

## Abstract

**Background:** Despite the substantial burden of lung disease throughout childhood in children who were born very preterm, there are no evidence-based interventions to improve lung health beyond the neonatal period. We tested the hypothesis that inhaled corticosteroid improves lung function in this population.

**Methods:** PICSI was a randomised, double-blind, placebo-controlled trial at Perth Children's Hospital (Perth, WA, Australia) to assess whether fluticasone propionate, an inhaled corticosteroid, improves lung function in children who had been born very preterm (<32 weeks of gestation). Eligible children were aged 6-12 years and did not have severe congenital abnormalities, cardiopulmonary defects, neurodevelopmental impairment, diabetes, or any glucocorticoid use within the preceding 3 months. Participants were randomly assigned (1:1) to receive 125 µg fluticasone propionate or placebo twice daily for 12 weeks. Participants were stratified for sex, age, bronchopulmonary dysplasia diagnosis, and recent respiratory symptoms using the biased-coin minimisation technique. The primary outcome was change in pre-bronchodilator forced expiratory volume in 1 s ($FEV_1$) after 12 weeks of treatment. Data were analysed by intention-to-treat (ie, all participants who were randomly assigned and took at least the tolerance dose of the drug). All

participants were included in the safety analyses. This trial is registered at the Australian and New Zealand Clinical Trials Registry, number 12618000781246.

**Findings:** Between Oct 23, 2018, and Feb 4, 2022, 170 participants were randomly assigned and received at least the tolerance dose (83 received placebo and 87 received inhaled corticosteroid). 92 (54%) participants were male and 78 (46%) were female. 31 participants discontinued treatment before 12 weeks (14 in the placebo group and 17 in the inhaled corticosteroid group), mostly due to the impact of the COVID-19 pandemic. When analysed by intention-to-treat, the change in pre-bronchodilator $FEV_1$ Z score over 12 weeks was -0·11 (95% CI -0·21 to 0·00) in the placebo group and 0·20 (0·11 to 0·30) in the inhaled corticosteroid group (imputed mean difference 0·30, 0·15-0·45). Three of 83 participants in the inhaled corticosteroid group had adverse events requiring treatment discontinuation (exacerbation of asthma-like symptoms). One of 87 participants in the placebo group had an adverse event requiring treatment discontinuation (inability to tolerate the treatment with dizziness, headaches, stomach pains, and worsening of a skin condition).

**Interpretation:** As a group, children born very preterm have only modestly improved lung function when treated with inhaled corticosteroid for 12 weeks. Future studies should consider individual phenotypes of lung disease after preterm birth and other agents to improve management of prematurity-associated lung disease.

**Funding:** Australian National Health and Medical Research Council, Telethon Kids Institute, and Curtin University.



# Conflict of interest statement

Declaration of interests SJS received funding from the Australian National Health and Medical Research Council to conduct this study. All other authors declare no competing interests.

# Comment in

- Next steps in treatment of prematurity-associated respiratory disease.
  Pijnenburg MW.Lancet Child Adolesc Health. 2023 Aug;7(8):523-524. doi: 10.1016/S2352-4642(23)00139-6. Epub 2023 Jun 26.PMID: 37385268 No abstract available.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated dataexpand

FULL TEXT LINKS

Review

Curr Opin Allergy Clin Immunol

. 2023 Aug 1;23(4):319-326.

doi: 10.1097/ACI.0000000000000922. Epub 2023 Jun 23.

# New approaches in childhood asthma treatment

Riccardo Castagnoli[1,2], Ilaria Brambilla[1,2], Mattia Giovannini[3,4], Gian Luigi Marseglia[1,2], Amelia Licari[1,2]

Affiliations expand

- PMID: 37357774
- PMCID: PMC10317303
- DOI: 10.1097/ACI.0000000000000922

**Free PMC article**

## Abstract

**Purpose of review:** This review aims to summarize the most recent advances in asthma management, focusing on novel approaches to pediatric asthma.

**Recent findings:** In recent years, the therapeutic tools for pediatric asthma have expanded significantly for both the nonsevere and severe forms. The use of anti-inflammatory treatment, even for the mildest cases, and the withdrawal of symptomatic bronchodilation as monotherapy have been included in the most recent guidelines. Also, different biological therapies have revolutionized the therapeutical approach for severe uncontrolled asthma in children and adolescents.

**Summary:** With the expanding landscape of novel therapeutic approaches for pediatric asthma, further evidence is needed to help clinicians choose the best option for patients, particularly those with severe asthma. The identification of novel predictive biomarkers may also help pediatricians in selecting children and adolescents for innovative therapies.



# Conflict of interest statement

There are no conflicts of interest.

- 68 references
- 2 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS



Eur Respir J

. 2023 Aug 3;62(2):2300502.

doi: 10.1183/13993003.00502-2023. Print 2023 Aug.

# Nasal airway microRNA profiling of infants with severe bronchiolitis and risk of childhood asthma: a multicentre prospective study

Zhaozhong Zhu[1], Robert J Freishtat[2,3,4], Brennan Harmon[2], Andrea Hahn[2,4,5], Stephen J Teach[3,4], Marcos Pérez-Losada[6], Kohei Hasegawa[7], Carlos A Camargo Jr[7]; MARC-35 Investigators

Affiliations expand

- PMID: 37321621

- DOI: 10.1183/13993003.00502-2023

## Abstract

**Background:** Severe bronchiolitis (*i.e.* bronchiolitis requiring hospitalisation) during infancy is a major risk factor for childhood asthma. However, the exact mechanism linking these common conditions remains unclear. We examined the longitudinal relationship between nasal airway miRNAs during severe bronchiolitis and the risk of developing asthma.

**Methods:** In a 17-centre prospective cohort study of infants with severe bronchiolitis, we sequenced their nasal microRNA at hospitalisation. First, we identified differentially expressed microRNAs (DEmiRNAs) associated with the risk of developing asthma by age 6 years. Second, we characterised the DEmiRNAs based on their association with asthma-related clinical features, and expression level by tissue and cell types. Third, we conducted pathway and network analyses by integrating DEmiRNAs and their mRNA targets. Finally, we investigated the association of DEmiRNAs and nasal cytokines.

**Results:** In 575 infants (median age 3 months), we identified 23 DEmiRNAs associated with asthma development (*e.g.* hsa-miR-29a-3p; false discovery rate (FDR) <0.10), particularly in infants with respiratory syncytial virus infection (FDR for the interaction <0.05). These DEmiRNAs were associated with 16 asthma-related clinical features (FDR <0.05), *e.g.* infant eczema and corticosteroid use during hospitalisation. In addition, these DEmiRNAs were highly expressed in lung tissue and immune cells (*e.g.* T-helper cells, neutrophils). Third, DEmiRNAs were negatively correlated with their mRNA targets (*e.g.* hsa-miR-324-3p/*IL13*), which were enriched in asthma-related pathways (FDR <0.05), *e.g.* toll-like receptor, PI3K-Akt and FcεR signalling pathways, and validated by cytokine data.

**Conclusion:** In a multicentre cohort of infants with severe bronchiolitis, we identified nasal miRNAs during illness that were associated with major asthma-related clinical features, immune response, and risk of asthma development.



# Conflict of interest statement

Conflict of interest: Z. Zhu reports grants from National Institutes of Health during the conduct of the study. A. Hahn reports personal fees from Johnson & Johnson, outside the submitted work. S.J. Teach reports grants from National Institutes of Health during the conduct of the study. K. Hasegawa reports grants from National Institutes of Health during the conduct of the study, and grants from Novartis, outside the submitted work. C.A. Camargo Jr reports grants from National Institutes of Health during the conduct of the study. All other authors have indicated that they have no financial relationships relevant to this article to disclose.

# Comment in

- From small to big, using microRNA profiling to investigate infant origins of childhood asthma.
  Powell WT, Reeves SR.Eur Respir J. 2023 Aug 3;62(2):2301052. doi: 10.1183/13993003.01052-2023. Print 2023 Aug.PMID: 37536728 No abstract available.

doi: 10.3345/cep.2023.00290. Epub 2023 Jun 14.

# Association between dyslipidemia and asthma in children: a systematic review and multicenter cohort study using a common data model

Ji Eun Lim[1], Hye Min Kim[1], Ju Hee Kim[1,2], Hey Sung Baek[1], Man Yong Han[3]

Affiliations expand

- PMID: 37321588
- PMCID: PMC10397992
- DOI: 10.3345/cep.2023.00290

**Free PMC article**

## Abstract

**Background:** The association between dyslipidemia and asthma in children remains unclear.

**Purpose:** This study investigated the association between dyslipidemia and cholesterol levels in children.

**Methods:** A systematic literature review was performed to identify studies investigating the association between dyslipidemia and asthma in children. The PubMed database was searched for articles published from January 2000-March 2022. Data from a cohort study using electronic health records from 5 hospitals, converted to the Observational Medical Outcomes Partnership Common Data Model (OMOP-CDM), were used to identify the association between total cholesterol (TC) levels and asthma in children. This cohort study used the Cox proportional hazards model to examine hazard ratio (HR) of asthma after propensity score matching, and included an aggregate meta-analysis of HR.

**Results:** We examined 11 studies reporting an association between dyslipidemia and asthma in children. Most were cross-sectional; however, their results were inconsistent. In OMOP-CDM multicenter analysis, the high TC (>170 mg/dL) group included 29,038

children, while the normal TC (≤170 mg/dL) group included 88,823 children including all hospital datasets. In a meta-analysis of this multicenter cohort, a significant association was found between high TC levels and later development of asthma in children <15 years of age (pooled HR, 1.30; 95% confidence interval, 1.12-1.52).

**Conclusion:** Elevated TC levels in children may be associated with asthma.

**Keywords:** Childhood asthma; Dyslipidemia; Hypercholesterolemia.

## Conflict of interest statement

Conflicts of interest
No potential conflict of interest relevant to this article was reported.

- 29 references
- 4 figures



Clin Exp Pediatr

. 2023 Aug;66(8):339-347.

doi: 10.3345/cep.2022.01109. Epub 2023 Jun 14.

# Trends of vitamin D in asthma in the pediatric population for two decades: a systematic review

Myongsoon Sung[1]

Affiliations expand


- PMID: 37321572
- PMCID: PMC10397993
- DOI: 10.3345/cep.2022.01109


**Free PMC article**

# Abstract

Vitamin D exhibits anti-inflammatory properties through multiple mechanisms. Vitamin D deficiency is associated with increased inflammation, exacerbations, and overall worse outcomes in pediatric asthma and is observed in asthmatic children with obesity. In addition, given the increase in the prevalence of asthma over the last few decades, there has been enormous interest in vitamin D supplementation as a potential therapeutic option. However, recent studies have suggested no strong association between vitamin D levels or supplementation and childhood asthma. Recent studies have reported that obesity and vitamin D deficiency are associated with increased asthma symptoms. Thus, this review summarizes the findings of clinical trials regarding the role of vitamin D in pediatric asthma and analyzes the study trends of vitamin D over the past 2 decades.

**Keywords:** Asthma; Child; Clinical trials; Obesity; Vitamin D.

# Conflict of interest statement

Conflicts of interest
No potential conflict of interest relevant to this article was reported.

- 50 references
- 1 figure

Colloids Surf B Biointerfaces

. 2023 Aug;228:113364.

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# A large particle size is required by a nano/micron sized-fluticasone propionate inhalable suspension for asthma treatment

Mi Zhang[1], Su Jia Si[1], Wen Jin Dai[1], Jian Yang[2], Yan Wang[1], Xiang Rong Wei[1], Shuo Liu[1], Cheng Yi Xu[1], Cong Zhang[3], Fang Jin[4], Li Qun Jiang[5]

Affiliations expand

- PMID: 37290201

- DOI: 10.1016/j.colsurfb.2023.113364

## Abstract

The nano/micron sized-fluticasone propionate inhalable suspension (FPs) is used for asthma treatment, and this study aimed to elucidate the effects of particle size on the absorption of FPs by various pulmonary cells and the subsequent therapeutic efficacy for asthma. FPs of 727, 1136 and 1612 nm were prepared, and an increase in diameter diminished the endocytosis and macropinocytosis of FPs by alveolar epithelial cells (A549 and Calu-3 cells) but facilitated their uptake by M2-like macrophages; results about the transport across Calu-3 monolayer showed the mucus layer was the main rate-limiting step for the uptake of FPs by epithelial cells; the animal tests showed that although a decrease in diameter improved the pulmonary absorption of FPs, the particle size did not affect the lung distribution of FPs; a further detection revealed that larger FPs were taken more effectively by alveolar macrophages and lymphocytes and exerted a better therapeutic effect on asthma than the smaller ones. This study showed that the particle size of FPs had a significant impact on their absorption, elimination and cellular distribution in the lung

after inhalation and further on their effectiveness in asthma treatment, and the particle size of the nano/micron sized-FPs should be designed and optimized for asthma treatment on the premise of meeting the requirements of inhalation preparations.

**Keywords:** Asthma; Fluticasone propionate inhalable suspension; Macrophages; Particle size; Pulmonary epithelium absorption.



## 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.



Am J Physiol Lung Cell Mol Physiol

. 2023 Aug 1;325(2):L206-L214.

doi: 10.1152/ajplung.00074.2022. Epub 2023 Jun 6.

# Mechanical forces suppress antiviral innate immune responses from asthmatic airway epithelial cells following rhinovirus infection

Punnam Chander Veerati[1,2], Andrew T Reid[1,2], Kristy S Nichol[1,3], Peter A B Wark[1,3,4], Darryl A Knight[5,6,7], Nathan W Bartlett[3,5], Christopher L Grainge[1,2,4]

Affiliations expand

- PMID: 37280545

- PMCID: PMC10396277

- DOI: 10.1152/ajplung.00074.2022

**Free PMC article**

# Abstract

Bronchoconstriction is the main physiological event in asthma, which leads to worsened clinical symptoms and generates mechanical stress within the airways. Virus infection is the primary cause of exacerbations in people with asthma, however, the impact that bronchoconstriction itself on host antiviral responses and viral replication is currently not well understood. Here we demonstrate how mechanical forces generated during bronchoconstriction may suppress antiviral responses at the airway epithelium without any difference in viral replication. Primary bronchial epithelial cells from donors with asthma were differentiated at the air-liquid interface. Differentiated cells were apically compressed (30 $cmH_2O$) for 10 min every hour for 4 days to mimic bronchoconstriction. Two asthma disease models were developed with the application of compression, either before ("poor asthma control model," $n$ = 7) or following ("exacerbation model," $n$ = 4) rhinovirus (RV) infection. Samples were collected at 0, 24, 48, 72, and 96 h postinfection (hpi). Viral RNA, interferon (IFN)-β, IFN-λ, and host defense antiviral peptide gene expressions were measured along with IFN-β, IFN-λ, TGF-$\beta_2$, interleukin-6 (IL-6), and IL-8 protein expression. Apical compression significantly suppressed RV-induced IFN-β protein from 48 hpi and IFN-λ from 72 hpi in the poor asthma control model. There was a nonsignificant reduction of both IFN-β and IFN-λ proteins from 48 hpi in the exacerbation model. Despite reductions in antiviral proteins, there was no significant change in viral replication in either model. Compressive stress mimicking bronchoconstriction inhibits antiviral innate immune responses from asthmatic airway epithelial cells when applied before RV infection.**NEW & NOTEWORTHY** Bronchoconstriction is the main physiological event in asthma, which leads to worsened clinical symptoms and generates mechanical stress within the airways. Virus infection is the primary cause of exacerbations in people with asthma, however, the impact of bronchoconstriction on host antiviral responses and viral replication is unknown. We developed two disease models, in vitro, and found suppressed IFN response from cells following the application of compression and RV-A1 infection. This explains why people with asthma have deficient IFN response.

**Keywords:** antiviral innate immune responses; asthma; bronchoconstriction; mechanical forces; rhinovirus.

## Conflict of interest statement

Nathan Bartlett is an editor of American Journal of Physiology-Lung Cellular and Molecular Physiology and was not involved and did not have access to information regarding the peer-review process or final disposition of this article. An alternate editor oversaw the peer-review and decision-making process for this article. None of the other authors has any conflicts of interest, financial or otherwise, to disclose.



Am J Physiol Lung Cell Mol Physiol

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. 2023 Aug 1;325(2):L125-L134.

doi: 10.1152/ajplung.00058.2023. Epub 2023 Jun 6.

# Baseline reticular basement membrane morphology is related to subsequent spirometry deterioration in pediatric

# chronic airway inflammation: a follow-up study

Václav Koucký[1,2], Jiří Uhlík[2], Lenka Hoňková[1,2], Arnošt Komárek[3], Petr Pohunek[1]

Affiliations expand

- PMID: 37280505

- DOI: 10.1152/ajplung.00058.2023

## Abstract

Reticular basement membrane (RBM) thickening may occur in children with allergic bronchial asthma (BA), cystic fibrosis (CF), and primary ciliary dyskinesia (PCD). Its functional consequences remain unknown. We investigated the relationship between baseline RBM thickness and subsequent spirometry. In our cohort follow-up study, patients aged 3-18 yr with BA, CF, and PCD and controls underwent baseline lung clearance index (LCI) measurement, spirometry, and endobronchial biopsy sampling. Total RBM and collagen IV-positive layer thickness were measured. Trends in forced vital capacity (FVC), forced expired volume in 1 s ($FEV_1$), and $FEV_1$/FVC were analyzed during follow-up, and their relationship to baseline characteristics was studied using univariate analysis and multiple regression models. Complete baseline data were available in 19 patients with BA, 30 patients with CF, 25 patients with PCD, and 19 controls. The RBM was thicker in patients with BA (6.33 ± 1.22 µm), CF (5.60 ± 1.39 µm), and PCD (6.50 ± 1.87 µm) than in controls (3.29 ± 0.55 µm) (all $P < 0.001$). The LCI was higher in patients with CF (15.32 ± 4.58, $P < 0.001$) and PCD (10.97 ± 2.46, $P = 0.002$) than in controls (7.44 ± 0.43). The median follow-up times were 3.6, 4.8, 5.7, and 1.9 years in patients with BA, CF, PCD, and controls, respectively. The *z*-scores of $FEV_1$ and $FEV_1$/FVC deteriorated significantly in all groups except in controls. In patients with CF and PCD, trends in $FEV_1$ *z*-scores correlated with baseline LCI and RBM; in BA, it correlated with collagen IV. In multiple regression models, RBM morphology and ventilation inhomogeneity could predict up to 84.4% of variability in spirometry trends. In conclusion, baseline LCI value and RBM morphology may predict trends in subsequent spirometry.**NEW & NOTEWORTHY** This paper deals with the relationship between reticular basement membrane (RBM) morphology at baseline and follow-up spirometry in children with asthma, cystic fibrosis, and primary ciliary dyskinesia. For the first time, to our knowledge, the possibility to predict subsequent lung function development using selected baseline characteristics (reticular basement membrane morphology from endobronchial biopsy and ventilation inhomogeneity from nitrogen multiple breath washout test) is proposed. Corresponding predictive models are presented.

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



Review

Indian J Pediatr

. 2023 Aug;90(8):790-797.

doi: 10.1007/s12098-023-04588-8. Epub 2023 Jun 1.

# Lung Function Tests in Infants and Children

Kana Ram Jat[1], Sheetal Agarwal[2,3]

Affiliations expand

- PMID: 37261706

- PMCID: PMC10233185

- DOI: 10.1007/s12098-023-04588-8

**Free PMC article**

# Abstract

Lung function testing is an essential modality of investigation in children as it provides objective evidence of lung disease/health. With advances in technology, various tests are available that can aid in the diagnosis of lung disease, assess the progression and response to therapy and document the lung development and evolving lung diseases in infants. This narrative review discusses lung function tests in infants and children. Currently, lung function tests can be performed in every age group, from neonates to the elderly. Spirometry and peak expiratory flow rate (PEFR) are the most employed tests in children more than six years of age. Spirometry helps diagnose and monitoring of both obstructive and restrictive diseases. There is a need for expertise to perform and interpret spirometry correctly. The forced oscillation technique (FOT) or impulse oscillometry (IOS) is done with tidal volume breathing and is feasible even in preschool children. Their utility is mainly restricted to asthma in children at present. Lung function tests can be performed in neonates, infants and children using infant pulmonary function test (PFT) equipment, although their availability is limited. Diffusion capacity for carbon monoxide (DLCO) is a valuable tool in restrictive lung diseases. Lung volumes can be assessed by body plethysmography and multiple washout technique. The latter can also assess lung clearance index. It is essential to perform and interpret the lung function test results correctly and correlate them with the clinical condition for optimum treatment and outcome.

**Keywords:** Diffusion capacity; Impulse oscillometry; Infant PFT; Multiple wash out; Pediatrics; Pulmonary function tests; Spirometry.



# Conflict of interest statement

None.

- Cited by 1 article
- 43 references
- 3 figures

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

Multicenter Study

Respir Med

. 2023 Aug-Sep;215:107299.

doi: 10.1016/j.rmed.2023.107299. Epub 2023 May 29.

# Development of a diagnostic score using FeNO and symptoms to predict asthma

Benjamin Brunn[1], Alexander Hapfelmeier[2], Rudolf A Jörres[3], Konrad Schultz[4], Antonius Schneider[5]

Affiliations expand

- PMID: 37257788

- DOI: 10.1016/j.rmed.2023.107299

## Abstract

**Background:** Fractional exhaled nitric oxide (FeNO) is known as effective for ruling-in asthma. The diagnostic value might be increased in combination with clinical signs and symptoms (CSS). The aim was to develop a new model for ruling-in and ruling-out asthma.

**Methods:** Diagnostic multi-centre study in three practices of pneumologists in Germany. Whole-body plethysmography was combined with bronchodilation tests or bronchial

provocation as diagnostic reference standard. Follow-up was performed after 3 months. An expert committee evaluated test results, symptoms, and course of disease for the final diagnosis. Relevant CSS known from guidelines were used to enable combinatorial development of decision rules. Outcomes of multiple logistic regression modeling were translated into a diagnostic score and internally validated by ten-fold cross validation.

**Results:** 308 patients with complete follow-up were included. 186 (60.4%) were female, average age was 44.7 years and 161 (52.5%) had asthma. The average area under the receiver operating curve (AUC) of the diagnostic score was 0.755 (interquartile range 0.721-0.814). Allergic rhinitis, wheezing, dyspnea on exertion, coughing attacks at night, and awakening by shortness of breath were leading symptoms for ruling-in asthma. Frequent coughing and frequent respiratory infections were leading symptoms for ruling-out. The combination of FeNO and CSS allowed ruling-in asthma with a probability of up to 99%, and ruling-out with a post-test probability down to 9%.

**Conclusion:** The diagnostic scoring model increased the diagnostic value of FeNO in combination with CSS. The new decision rule allowed to rule-in asthma with high certainty, and also to rule-out with acceptable certainty.

**Keywords:** Asthma; Clinical decision rule; Diagnostic study; Fractional exhaled nitric oxide; Primary health care; Symptoms.



# Conflict of interest statement

Declaration of competing interest AS is an external expert for the Federal Joint Committee (Gemeinsamer Bundesausschuss) with regard to the development of the disease management programs for asthma and COPD; he received regular remuneration for taking part in the sessions. AS and KS are members of the National Asthma Guideline Board (Nationale Versorgungsleitlinie Asthma). The other authors declare that no conflicts of interest exist.

Meta-Analysis

Respir Med

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. 2023 Aug-Sep;215:107300.

doi: 10.1016/j.rmed.2023.107300. Epub 2023 May 29.

# Short-term and long-term effects of cesarean section on asthma and wheezing: A cohort study and meta-analysis

Yuxiu Liang[1], Jiatao Zhang[1], Shuoxin Bai[2], Shuang Du[1], Xiwei Yang[3], Zhiping Wang[4]

Affiliations expand

- PMID: 37257787

- DOI: 10.1016/j.rmed.2023.107300

## Abstract

**Objective:** To describe the short-term and long-term effects of cesarean section on childhood asthma and wheezing.

**Method:** Firstly, in the cohort study, 6640 infants were included in the cohort baseline from January 2018 to December 2019, in which 6501 children completed the follow-up study for respiratory diseases at age 2 years. The effect of cesarean section on asthma and wheezing was estimated by the logistic regression model. Secondly, we conducted a meta-analysis of studies with outcomes of childhood asthma and wheezing under 2 years of age and over 2 years of age, respectively, to investigate the short-term and long-term effects of cesarean section on asthma and wheezing.

**Results:** In our cohort study, the cumulative incidence of asthma and wheezing was 1.3% (84/6501). 45.5% of children (2961/6501) were born by cesarean section. The adjusted odds ratio for the effect of cesarean section on asthma and wheezing in children under 2 years of age was 1.14 (95%CI 0.73-1.78). Combining previous studies (outcomes of asthma and wheezing under 2 years of age) with our results for a meta-analysis, the odds ratio was 1.15 (95%CI 1.05-1.25, $I^2$ = 46.82%). Meanwhile, cesarean section had a long-term effect on asthma and wheezing in the child population over 2 years of age (OR = 1.17, 95%CI 1.11-1.24, P < 0.001, $I^2$ = 79.38%).

**Conclusion:** Cesarean section had a short-term effect on asthma and wheezing before the age of 2, in addition, the long-term effect of cesarean section on asthma and wheezing persisted in the child population (under 18).

**Keywords:** Asthma; Cesarean section; Child; Cohort study; Meta-analysis; Wheezing.



# Conflict of interest statement

Declaration of competing interest The authors declared that they have no conflicts of interest to this work.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS


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Cite

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43

Meta-Analysis

Complement Ther Med

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. 2023 Aug;75:102956.

doi: 10.1016/j.ctim.2023.102956. Epub 2023 May 29.

# Clinical evidence for acupuncture for adult asthma: Systematic review and meta-analysis of randomised sham/placebo-controlled trials

Jintao Pang[1], Johannah Linda Shergis[2], Lici Zheng[1], Shaonan Liu[3], Xinfeng Guo[3], Anthony Lin Zhang[2], Lin Lin[4], Charlie Changli Xue[5], Lei Wu[6]

Affiliations expand

- PMID: 37257728

- DOI: 10.1016/j.ctim.2023.102956

**Free article**

## Abstract

**Objective:** Acupuncture is a widely used asthma therapy, but the benefits remain uncertain. This study aimed to access the effectiveness of acupuncture for treatment of asthma in adults.

**Methods:** Five English databases and four Chinese databases were searched from inception to November 2021. Randomised sham/placebo-controlled trials meeting inclusion criteria were included. Risk of bias was evaluated according to the Cochrane Review Handbook, and data analysis was performed in RevMan 5.4.1. Quality of evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluations (GRADE) profiler.

**Results:** Sixteen randomised controlled trials (RCTs) were included in the meta-analysis. Results indicated that acupuncture was well-tolerated and could improve FEV1% compared with sham/placebo acupuncture [MD 6.11, 95% CI 0.54-11.68, $I^2$ = 93%, number of participants (n) = 603]. Acupuncture also improved Cai's Asthma Quality of Life Questionnaire (AQLQ) (MD 7.26, 95% CI 5.02-9.50, $I^2$ = 0, n = 358), and reduced the asthma symptom score (SMD -2.73, 95% CI -3.59 to -1.87, $I^2$ = 65%, n = 120). One study showed acupuncture increased the Asthma Control Test (ACT) score (MD 2.00, 95% CI 0.90-3.10, n

= 111), and decreased exacerbation frequency (MD -1.00, 95% CI -1.55 to -1.45, n = 111). Other lung function and medication use parameters were not statistically significant.

**Conclusions:** Acupuncture versus sham/placebo control appeared to improve quality of life, FEV1%, symptoms, and asthma control, and reduced exacerbation frequency per year. Further studies with appropriate controls, more participants, and high-quality evidence are needed.

**Keywords:** Acupuncture; Adult Asthma; Evidence; Meta-Analysis; Placebo; Sham.



# Conflict of interest statement

Declaration of Competing Interest The authors declare that they have no conflicts of interest.



Review

Respir Med

. 2023 Aug-Sep;215:107246.

doi: 10.1016/j.rmed.2023.107246. Epub 2023 May 26.

# Extracorporeal membrane oxygenation (ECMO) and beyond in near fatal asthma: A comprehensive review

María Lozano-Espinosa[1], Darío Antolín-Amérigo[2], Jordi Riera[3], Federico Gordo Vidal[4], Santiago Quirce[5], Joaquín Álvarez Rodríguez[1]

Affiliations expand

- PMID: 37245648

- DOI: 10.1016/j.rmed.2023.107246

## Abstract

The treatment of choice in severe asthma exacerbations with respiratory failure includes ventilatory support, both invasive and/or non-invasive, along with different kinds of asthma medication. Of note, the rate of mortality of patients with asthma has decreased substantially in recent years mainly due to significant advances in pharmacological treatment and other management strategies. However, the risk of death in patients with severe asthma who require invasive mechanical ventilation has been estimated between 6.5% and 10.3%. When conventional measures fail, rescue strategies, such as extracorporeal membrane oxygenation (ECMO) or extracorporeal CO2 removal (ECCO2R) may need to be implemented. While ECMO does not constitute a definitive treatment per se, it can minimize further ventilator associated lung injury (VALI) and can enable diagnostic-therapeutic maneuvers that cannot be performed without ECMO such as bronchoscopy and transfer for diagnostic imaging. Asthma is one of the diseases that is associated with excellent outcomes for patients with refractory respiratory failure requiring ECMO support, as shown by the Extracorporeal Life Support Organization (ELSO) registry. Moreover, in such situations, the use of ECCO2R for rescue has been described and utilized in both children and adults and is more widely spread in different hospitals than ECMO. In this article, we aim to review the evidence for the usefulness of extracorporeal respiratory support measures in the management of severe asthma exacerbations that lead to respiratory failure.

**Keywords:** ECCO2R; ECMO; Extracorporeal membrane oxygenation; ICU; Intensive care; Near fatal asthma; Severe asthma exacerbations.



## Conflict of interest statement

Declaration of competing interest The authors of the article “Near Fatal Asthma and Extracorporeal Respiratory Support: a comprehensive review report no conflicts of interest.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS


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Pediatr Pulmonol

. 2023 Aug;58(8):2424-2426.

doi: 10.1002/ppul.26500. Epub 2023 May 24.

# Prospective follow up after omalizumab discontinuation in a cohort of children with severe asthma

Valentina Agnese Ferraro [1], Amelia Licari [2 3], Alessandro Volpini [4], Grazia Fenu [5], Maria Francesca Patria [6], Manuela Seminara [7], Elena Spada [8], Franca Rusconi [9]

Affiliations expand

- PMID: 37222415

- DOI: 10.1002/ppul.26500

*No abstract available*

Review

Respirology

. 2023 Aug;28(8):709-721.

doi: 10.1111/resp.14520. Epub 2023 May 24.

# Biologics for severe asthma-Which, when and why?

Peer Ameen Shah[1], Chris Brightling[1]

Affiliations expand

- PMID: 37222237

- DOI: 10.1111/resp.14520

## Abstract

Asthma is a common chronic inflammatory condition of the airways that affects about 350 million people globally. In 5%-10% of individuals, it is severe, with considerable morbidity

and high health care utilization. The goal of asthma management is disease control by reducing symptoms and exacerbations and reducing corticosteroid-related morbidity. The era of biologics has revolutionized the management of severe asthma. Biologics have changed our expectations for severe asthma, especially in those people with type-2 mediated immunity. We can now explore the potential for changing disease trajectory and inducing remission. However, biologics are not a panacea for all severe asthma sufferers and despite their success there remains substantial unmet clinical need. We review the pathogenesis of asthma, phenotyping the heterogeneity of asthma, currently licensed and future biologic agents, how to choose the initial biologic, assessing the response, remission and switching of biologic therapies.

**Keywords:** asthma; asthma control; biologics; biologics switching; biomarkers; exacerbations; remission; severe asthma.



- 114 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grant supportexpand

FULL TEXT LINKS

WILEY Full Text Article UNIMORE

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Respir Care

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. 2023 Aug;68(8):1058-1066.

doi: 10.4187/respcare.10464. Epub 2023 May 23.

# Validity, Reproducibility, and Minimal Detectable Difference of the Functional Upper Extremity Function Test – Simplified Version – for Adults With Moderate to Severe Asthma and COPD

Natielly Soares Correia[1], Joice Mara de Oliveira[1], Diery Rugila Fernandes[1], Denner Idelmar Feitosa[1], Daniel Martins Pereira[2], Daniel Pereira do Amaral[3], Rafael Mesquita[4], Fabio Pitta[5], Simone Dal Corso[3], Karina Couto Furlanetto[6]

Affiliations expand

- PMID: 37221086

- PMCID: PMC10353162 (available on 2024-08-01)

- DOI: 10.4187/respcare.10464

## Abstract

**Background:** Upper-limbs (ULs) functional tests which are valid and reliable for individuals with chronic respiratory disease (CRD) are scarce. The aim of this study was to investigate the intra-rater reproducibility, validity, minimal detectable difference (MDD), and learning effect of the Upper Extremity Function Test - simplified version (UEFT_S) functional test and to characterize its performance for adults with moderate-severe asthma and COPD.

**Methods:** The UEFT_S was performed twice, and the number of elbow flexions in 20 s was the outcome. In addition, spirometry, 6-min walk test (6MWT), handgrip dynamometry (HGD), and usual and maximum timed-up-and-go tests (TUG_usual and TUG_max) were also performed.

**Results:** Eighty-four individuals with moderate-severe CRD and 84 control individuals matched by anthropometric data were analyzed. Individuals with CRD presented better performance in the UEFT_S than controls ($P$ = .023). UEFT_S correlated significantly with HGD, TUG_usual, TUG_max, and 6MWT ($P$ < .047 for all). The test-retest intraclass correlation coefficient was 0.91 [0.86-0.94], and the MDD was 0.4%.

**Conclusions:** The UEFT_S is a valid and reproducible tool to assess the functionality of the ULs in people with moderate-severe asthma and COPD. When applied in the modified form, the test can be considered simple, fast, and inexpensive, with an easy outcome to interpret.

**Keywords:** COPD; asthma; upper extremity; validation study.



## Conflict of interest statement

The authors have disclosed no conflicts of interest.



Review

Am J Med

. 2023 Aug;136(8):738-744.

doi: 10.1016/j.amjmed.2023.05.001. Epub 2023 May 18.

# An Update on Monoclonal Antibody Therapy to Treat Moderate-to-Severe

# Asthma: Benefits, Choices, and Limitations

Matthew R Elliott[1], Charles E Grogan[1], Gailen D Marshall[2]

Affiliations expand

- PMID: 37210021

- DOI: 10.1016/j.amjmed.2023.05.001

## Abstract

Moderate or severe asthma is a complex disease process clinically manifesting as at least partially reversible airway obstruction due to airway hyperresponsiveness. Asthma therapy was based primarily on symptom control until recent studies of its mechanisms have led to a host of new targeted, safe, and effective therapies. These biologic therapies directly attack culprit inflammatory mediators at the molecular level. In this article we review currently available biologic agents for the treatment of moderate-to-severe asthma. We provide information deemed necessary to optimally consult with an asthma specialist to choose, assist in financial arrangements for, and coordinate the use of these new, promising, Food and Drug Administration-approved biologic agents. We will also briefly review the molecular pathways targeted with each class of biologic to provide a more in-depth understanding of why these targeted therapies are effective. These biologics are the first of many to come that modify newly discovered components of the immune system with which many physicians are unfamiliar.

**Keywords:** Asthma; Biologics; Monoclonal antibody; Treatment.

Ann Allergy Asthma Immunol

. 2023 Aug;131(2):209-216.e2.

doi: 10.1016/j.anai.2023.05.011. Epub 2023 May 19.

# Biomarkers for predicting type 2-high and uncontrolled asthma in real-world practice

Seong-Dae Woo[1], Hee Sun Park[1], Jae-Hyuk Jang[2], Youngsoo Lee[2], Eun-Mi Yang[2], Ga-Young Ban[3], Seung-Hyun Kim[2], Yoo Seob Shin[2], Young-Min Ye[2], Hae-Sim Park[4]

Affiliations expand

- PMID: 37209833

- DOI: 10.1016/j.anai.2023.05.011

## Abstract

**Background:** Blood eosinophil count (BEC), immunoglobulin (Ig) E, and fractional exhaled nitric oxide (FeNO) are key clinical indicators for identifying type 2 (T2) asthma.

**Objective:** To provide optimal cutoff points of T2 markers for assessing T2-high or uncontrolled asthma in real-world practice.

**Methods:** Various clinical and laboratory parameters were analyzed according to the result of T2 markers (BEC, serum-free IgE, and FeNO) in adults with asthma who had maintained antiasthmatic medications. The cutoff levels for representing uncontrolled asthma were determined using receiver operating characteristic analysis. Blood levels of periostin and eosinophil-derived neurotoxin were measured by enzyme-linked immunosorbent assay. Activation markers of circulating eosinophils (Siglec8+) and neutrophils (CD66+) were analyzed by flow cytometry.

**Results:** Of 133 patients with asthma, 23 (17.3%) had 3 T2 markers (BEC ≥ 300 cells/μL, serum-free IgE ≥ 120 ng/mL, and FeNO ≥ 25 parts per billion) and significantly higher levels of sputum eosinophils, blood eosinophil-derived neurotoxin, and Siglec8+ eosinophils but lower 1-second forced expiratory volume percentage, in addition to a higher rate of uncontrolled status (P < .05 for all). Furthermore, patients with uncontrolled asthma had significantly higher levels of FeNO and BEC with lower 1-second forced expiratory volume percentage (P < .05 for all). The optimal cutoff values for predicting uncontrolled asthma were found to be 22 parts per billion of FeNO levels, 161.4 cells/L of BECs, and 85.9 ng/mL of serum-free IgE levels.

**Conclusion:** We suggest the optimal cutoff values of BEC, IgE, and FeNO for classifying T2-high or uncontrolled asthma, which could be applied as candidate biomarkers for targeting patients with asthma who require T2 biologics.



Editorial

Respirology

. 2023 Aug;28(8):696-698.

doi: 10.1111/resp.14517. Epub 2023 May 10.

# Mepolizumab attenuates ILC2s proliferation and activity in adults with severe eosinophilic asthma

Guy Brusselle[1], Sebastian Riemann[1], Tania Maes[1]

Affiliations expand

- PMID: 37164907

- DOI: 10.1111/resp.14517

**Free article**

*No abstract available*

**Keywords:** asthma; clinical allergy and immunology; cytokine; eosinophil; inflammation.

# Comment on

- Severe asthma ILC2s demonstrate enhanced proliferation that is modified by biologics.
  Malik B, Bartlett NW, Upham JW, Nichol KS, Harrington J, Wark PAB.Respirology. 2023 Aug;28(8):758-766. doi: 10.1111/resp.14506. Epub 2023 Apr 28.PMID: 37114915

- 13 references



Editorial

. 2023 Aug;90(8):750-751.

doi: 10.1007/s12098-023-04638-1. Epub 2023 May 10.

# Single Breath Counting: Is it a Reliable, Tool Independent Measure to Predict Asthma Exacerbation?

Swathi Nakka[1], Rashmi Ranjan Das[2]

Affiliations expand

- PMID: 37162732

- DOI: 10.1007/s12098-023-04638-1

*No abstract available*

- 5 references

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS



Case Reports

Arch Bronconeumol

. 2023 Aug;59(8):512-513.

doi: 10.1016/j.arbres.2023.04.002. Epub 2023 Apr 20.

# Cystic Fibrosis-Asthma Overlap Syndrome. Combination of Cystic Fibrosis Transmembrane Conductance Regulator Modulators and Type 2 Targeted Biologic Treatment for Asthma

[Article in English, Spanish]

Miguel Jiménez-Gómez[1], Rocío Magdalena Díaz Campos[2], Layla Diab Cáceres[3]

Affiliations expand

- PMID: 37127448

- DOI: 10.1016/j.arbres.2023.04.002

*No abstract available*

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

Sci Total Environ

. 2023 Aug 1;884:163802.

doi: 10.1016/j.scitotenv.2023.163802. Epub 2023 Apr 29.

# Long-term residential exposure to air pollution and risk of chronic respiratory diseases in Italy: The BIGEPI study

Pierpaolo Marchetti[1], Jessica Miotti[1], Francesca Locatelli[1], Leonardo Antonicelli[2], Sandra Baldacci[3], Salvatore Battaglia[4], Roberto Bono[5], Angelo Corsico[6], Claudio Gariazzo[7], Sara Maio[3], Nicola Murgia[8], Pietro Pirina[9], Camillo Silibello[10], Massimo Stafoggia[11], Lorena Torroni[1], Giovanni Viegi[3], Giuseppe Verlato[1], Alessandro Marcon[12]; BIGEPI group

Affiliations expand

- PMID: 37127163

- DOI: 10.1016/j.scitotenv.2023.163802

**Free article**

## Abstract

Long-term exposure to air pollution has adverse respiratory health effects. We investigated the cross-sectional relationship between residential exposure to air pollutants and the risk of suffering from chronic respiratory diseases in some Italian cities. In the BIGEPI project, we harmonised questionnaire data from two population-based studies conducted in 2007-2014. By combining self-reported diagnoses, symptoms and medication use, we identified cases of rhinitis (n = 965), asthma (n = 328), chronic bronchitis/chronic obstructive pulmonary disease (CB/COPD, n = 469), and controls (n = 2380) belonging to 13 cohorts from 8 Italian cities (Pavia, Turin, Verona, Terni, Pisa, Ancona, Palermo, Sassari). We derived mean residential concentrations of fine particulate matter ($PM_{10}$, $PM_{2.5}$), nitrogen dioxide

($NO_2$), and summer ozone ($O_3$) for the period 2013-2015 using spatiotemporal models at a 1 km resolution. We fitted logistic regression models with controls as reference category, a random-intercept for cohort, and adjusting for sex, age, education, BMI, smoking, and climate. Mean ± SD exposures were 28.7 ± 6.0 µg/m³ ($PM_{10}$), 20.1 ± 5.6 µg/m³ ($PM_{2.5}$), 27.2 ± 9.7 µg/m³ ($NO_2$), and 70.8 ± 4.2 µg/m³ (summer $O_3$). The concentrations of $PM_{10}$, $PM_{2.5}$, and $NO_2$ were higher in Northern Italian cities. We found associations between PM exposure and rhinitis ($PM_{10}$: OR 1.62, 95%CI: 1.19-2.20 and $PM_{2.5}$: OR 1.80, 95%CI: 1.16-2.81, per 10 µg/m³) and between $NO_2$ exposure and CB/COPD (OR 1.22, 95%CI: 1.07-1.38 per 10 µg/m³), whereas asthma was not related to environmental exposures. Results remained consistent using different adjustment sets, including bi-pollutant models, and after excluding subjects who had changed residential address in the last 5 years. We found novel evidence of association between long-term PM exposure and increased risk of rhinitis, the chronic respiratory disease with the highest prevalence in the general population. Exposure to $NO_2$, a pollutant characterised by strong oxidative properties, seems to affect mainly CB/COPD.

**Keywords:** Air quality; Asthma; Chronic bronchitis; Epidemiology; Public health; Rhinitis.



# Conflict of interest statement

Declaration of competing interest Sara Maio reports financial support was provided by National Institute for Insurance against Accidents at Work.

. 2023 Aug;28(8):758-766.

doi: 10.1111/resp.14506. Epub 2023 Apr 28.

# Severe asthma ILC2s demonstrate enhanced proliferation that is modified by biologics

Bilal Malik[1], Nathan W Bartlett[1], John W Upham[2], Kristy S Nichol[1], John Harrington[3], Peter A B Wark[1,3]

Affiliations expand

- PMID: 37114915

- DOI: 10.1111/resp.14506

**Free article**

## Abstract

**Background and objective:** Type 2 (T2) innate lymphoid cells (ILC2s) contribute to airway inflammation and disease in asthma. We hypothesize that ILC2s isolated from people with severe allergic and eosinophilic asthma would exhibit an enhanced T2 inflammatory activity that would be altered following treatment with mepolizumab and omalizumab. We compare peripheral blood (PB) isolated ILC2's proliferative capacity, IL-5 and IL-13 secretion and phenotype between healthy without asthma (HC), non-asthma allergic (NAA), mild asthma (MA) and severe allergic and eosinophilic asthma (SA) subjects. We then determined the impact of 6 months treatment with either mepolizumab or omalizumab on ILC2s physiology of SA subjects.

**Methods:** ILC2s were sorted and cultured in the presence of IL-2, IL-25, IL-33 and thymic stromal lymphopoietin (TSLP) for 14 days. ILC2s proliferation, phenotypes and functions were assessed using flowcytometry. The ILC2s response was then reassessed following clinically successful treatment of SA subjects with mepolizumab and omalizumab.

**Results:** SA ILC2s demonstrated increased proliferative capacity, TSLP receptor (TSLPR), GATA3 and NFATc1 protein expressions and increased IL-5 and IL-13 release. ILC2s were also capable of releasing IL-6 in response to stimulation. Mepolizumab treatment reduced

ILC2s proliferative capacity and expression of TSLPR, GATA3 and NFATc1. Both mepolizumab and omalizumab were associated with reduced ILC2s release of IL-5 and IL-13, only mepolizumab reduced IL-6.

**Conclusion:** ILC2s from severe allergic and eosinophilic asthma demonstrated an active phenotype typified by increased proliferation, TSLPR, GATA3 and NFATc1 expression and increased IL-5, IL-13 and IL-6 release. Mepolizumab reduced markers of ILC2s activation.

**Keywords:** ILC2; mepolizumab; omalizumab; proliferation; severe asthma; thymic stromal lymphopoietin receptor; type 2 cytokine; type 2 innate lymphoid cell.



# Comment in

- Mepolizumab attenuates ILC2s proliferation and activity in adults with severe eosinophilic asthma.
  Brusselle G, Riemann S, Maes T.Respirology. 2023 Aug;28(8):696-698. doi: 10.1111/resp.14517. Epub 2023 May 10.PMID: 37164907 No abstract available.

- 42 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS


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Editorial

Allergy

-

. 2023 Aug;78(8):2079-2080.

doi: 10.1111/all.15754. Epub 2023 Jun 14.

# The changing global prevalence of asthma and atopic dermatitis

Eve Denton[1], Robyn E O'Hehir[1,2], Mark Hew[1,3]

Affiliations expand

- PMID: 37102759

- DOI: 10.1111/all.15754

*No abstract available*

- 9 references

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS



Ann Allergy Asthma Immunol

. 2023 Aug;131(2):203-208.e1.

doi: 10.1016/j.anai.2023.04.022. Epub 2023 Apr 25.

# Targeting the interleukin-5 pathway improves cough hypersensitivity in patients with severe uncontrolled asthma

Keima Ito[1], Yoshihiro Kanemitsu[2], Kensuke Fukumitsu[1], Tomoko Tajiri[1], Hirono Nishiyama[1], Yuta Mori[1], Satoshi Fukuda[1], Takehiro Uemura[1], Hirotsugu Ohkubo[1], Ken Maeno[1], Yutaka Ito[1], Tetsuya Oguri[3], Masaya Takemura[3], Akio Niimi[1]

Affiliations expand

- PMID: 37100279

- DOI: 10.1016/j.anai.2023.04.022

## Abstract

**Background:** Capsaicin cough sensitivity (C-CS) reflects airway neuronal dysfunction and may be a significant biomarker of asthma. Although mepolizumab reduces cough in patients with severe uncontrolled asthma, it is unclear whether the cough reduction is associated with improved C-CS.

**Objective:** To clarify the effect of biologics on C-CS and cough-specific quality of life (QoL) in patients with severe uncontrolled asthma using our previous study cohort.

**Methods:** Overall, 52 consecutive patients who visited our hospital for severe uncontrolled asthma were included in the original study cohort, and 30 patients were eligible for this study. Changes in C-CS and cough-specific QoL were compared between patients treated with the anti-interleukin-5 (IL-5) pathway (n = 16) and those treated with other biologics (n = 14). The C-CS was measured as the concentration of capsaicin required to induce at least 5 coughs.

**Results:** Biologics significantly improved C-CS (P = .03). Anti-IL-5 pathway therapies significantly improved C-CS, whereas other biologics did not (P < .01 and P = .89, respectively). The C-CS improved significantly more in the anti-IL-5 pathway group than in the group treated with other biologics (P = .02). Changes in C-CS significantly correlated with improvements in cough-specific QoL in the anti-IL-5 pathway group (r = 0.58, P = .01) but not in the group treated with other biologics (r = 0.35, P = .22).

**Conclusion:** Anti-IL-5 pathway therapies improve C-CS and cough-specific QoL, and targeting the IL-5 pathway may be a therapeutic strategy for cough hypersensitivity in patients with severe uncontrolled asthma.





Ann Allergy Asthma Immunol

. 2023 Aug;131(2):270-271.

doi: 10.1016/j.anai.2023.04.025. Epub 2023 Apr 24.

# Electronic medical record-based machine learning predicts the relapse of asthma exacerbation

Ji-Hyang Lee[1], Chaelin Hong[2], Ji Seon Oh[3], Tae-Bum Kim[4]

Affiliations expand

- PMID: 37100278

- DOI: 10.1016/j.anai.2023.04.025

*No abstract available*

Scand J Med Sci Sports

. 2023 Aug;33(8):1509-1518.

doi: 10.1111/sms.14373. Epub 2023 Apr 20.

# A longitudinal study of exercise-induced bronchoconstriction and laryngeal obstruction in high school athletes

Karin Ersson[1,2], Elisabet Mallmin[3], Leif Nordang[3], Andrei Malinovschi[1], Henrik Johansson[1,2,4]

Affiliations expand

- PMID: 37082779

- DOI: 10.1111/sms.14373

## Abstract

**Background:** Exercise-induced bronchoconstriction (EIB) and exercise-induced laryngeal obstruction (EILO) are common in elite athletes. Knowledge of which factors are related to incident EIB and EILO is limited. The aim of this study was to explore the course of EIB and EILO in adolescent athletes over a 2 years period and baseline characteristics related to incident EIB.

**Methods:** Questionnaire data on respiratory symptoms, asthma, and aeroallergy and results of objective EIB and EILO tests were collected from 58 participants (27 tested for EILO) at baseline and after 2 years (follow-up). Associations between incident EIB and baseline asthma-like symptoms, exercise-induced symptoms, fractional exhaled nitric oxide (FeNO), aeroallergy, and sex were assessed using logistic regression models.

**Results:** Ten participants had incident EIB, and eight participants had persistent EIB. Five were EIB positive at baseline but negative at follow-up, while 35 participants were EIB negative at both time points. Having incident EIB was associated with reporting waking up with chest tightness (OR = 4.38; 95% CI: 1.06, 22.09). Reporting an increased number of asthma-like symptoms increased the likelihood of incident EIB (OR = 2.78; 95% CI: 1.16, 6.58). No associations were found between exercise-induced symptoms, FeNO, aeroallergy, or sex and incident EIB. Incident EILO was found in three and persistent EILO in two of the 27 participants tested.

**Conclusion:** Two in nine had incident EIB and one eighth had incident EILO, suggesting that recurrent testing for EIB and EILO may be relevant in young athletes. Particularly, EIB-negative athletes reporting multiple asthma-like symptoms could benefit from recurrent EIB testing.

**Keywords:** adolescent; athletes; bronchoconstriction; cohort; epidemiology; exercise-induced; laryngeal obstruction.



- 39 references

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

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Allergy

. 2023 Aug;78(8):2148-2156.

doi: 10.1111/all.15747. Epub 2023 May 21.

# Dupilumab improves long-term outcomes in patients with uncontrolled, moderate-to-severe GINA-based type 2 asthma, irrespective of allergic status

Klaus F Rabe[1,2], Ian D Pavord[3], William W Busse[4], Geoffrey L Chupp[5], Kenji Izuhara[6], Arman Altincatal[7], Rebecca Gall[8], Nami Pandit-Abid[9], Yamo Deniz[8], Paul J Rowe[9], Juby A Jacob-Nara[9], Amr Radwan[8]

Affiliations expand

- PMID: 37073882

- DOI: 10.1111/all.15747

## Abstract

**Background:** Previous research has shown greater efficacy of dupilumab in patients with uncontrolled asthma and type 2 inflammation. We analyzed dupilumab's efficacy in patients from the TRAVERSE study with or without evidence of allergic asthma and type 2 inflammation per current GINA guidelines (≥150 eosinophils/μL or FeNO ≥20 ppb).

**Methods:** All patients aged ≥12 years who rolled over from the placebo-controlled QUEST study (NCT02414854) to TRAVERSE (NCT02134028) received add-on dupilumab 300 mg every 2 weeks for up to 96 weeks. We assessed annualized severe asthma exacerbation rates (AERs) and changes from parent-study baseline (PSBL) in pre-bronchodilator $FEV_1$ and 5-item asthma control questionnaire (ACQ-5) score in patients with moderate-to-severe type 2 asthma with and without evidence of allergic asthma at PSBL.

**Results:** In TRAVERSE, dupilumab consistently reduced AER across all subgroups. By Week 96, dupilumab increased pre-bronchodilator $FEV_1$ from PSBL by 0.35-0.41 L in patients receiving placebo during QUEST (placebo/dupilumab) and 0.34-0.44 L in those receiving

dupilumab during QUEST (dupilumab/dupilumab) with an allergic phenotype at baseline. In patients without evidence of allergic asthma, pre-bronchodilator $FEV_1$ improved by 0.38-0.41 L and 0.33-0.37 L, respectively. By Week 48, ACQ-5 scores decreased from PSBL by 1.63-1.69 (placebo/dupilumab) and 1.74-1.81 (dupilumab/dupilumab) points across subgroups with allergic asthma, and 1.75-1.83 (placebo/dupilumab) and 1.78-1.86 (dupilumab/dupilumab) in those without.

**Conclusions:** Long-term treatment with dupilumab reduced exacerbation rates and improved lung function and asthma control in patients with asthma with type 2 inflammation as per current GINA guidance and irrespective of evidence of allergic asthma.



- 21 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated dataexpand

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60

Allergy

. 2023 Aug;78(8):2157-2167.

doi: 10.1111/all.15743. Epub 2023 May 25.

# Assessment of dupilumab in children with moderate-to-severe type 2 asthma

# with or without evidence of allergic asthma

Nikolaos G Papadopoulos[1], Stanley J Szefler[2], Leonard B Bacharier[3], Jorge F Maspero[4], Christian Domingo[5], Alessandro Fiocchi[6], Jason K Lee[7], Nadia Daizadeh[8], David J Lederer[9], Megan Hardin[8], Rebecca Gall[9], Michel Djandji[8], Shahid Siddiqui[9], Juby A Jacob-Nara[10], Yamo Deniz[9], Paul J Rowe[10]

Affiliations expand

- PMID: 37059696

- DOI: 10.1111/all.15743

## Abstract

**Background:** Cytokines, such as interleukins (IL)-4/5/13, play a key role in multiple type 2 inflammatory diseases, including allergic asthma. Dupilumab, a human monoclonal antibody, blocks the shared receptor component for IL-4/IL-13, inhibiting signaling. In this post hoc analysis of VOYAGE (NCT02948959), dupilumab efficacy was evaluated in patients aged 6-11 years with type 2 asthma with or without evidence of allergic asthma (baseline serum total IgE ≥30 IU/mL and ≥1 perennial aeroallergen-specific IgE ≥0.35kU/L).

**Methods:** Annualized severe exacerbation rates (AER) and changes in pre-bronchodilator (Pre-BD) forced expiratory volume in one second ($FEV_1$), percent-predicted pre-BD $FEV_1$ ($ppFEV_1$), and Asthma Control Score (ACQ)-7 were assessed during the treatment period.

**Results:** 350 children (261 with and 89 without evidence of allergic asthma) were included. Dupilumab versus placebo significantly reduced AER in patients with (0.24 vs. 0.62, relative risk reduction [RRR]: 62% [95% CI, 39-76], P < .0001) and without (0.39 vs. 0.80, RRR: 51% [95% CI, 0-76], P < .05) evidence of allergic asthma. Significant improvements in $ppFEV_1$, pre-bronchodilator $FEV_1$, and ACQ-7 scores were observed in dupilumab versus placebo throughout the treatment period in patients with evidence of allergic asthma. In patients without evidence of allergic asthma, numerical improvements in pre-bronchodilator $FEV_1$ and asthma control were observed by Week 52.

**Conclusion:** Dupilumab versus placebo reduced asthma exacerbations in children with type 2 asthma irrespective of evidence of allergic asthma; similar trends were observed in changes in lung function. Significant improvement in asthma control was observed in patients with evidence of allergic asthma, but not in those without.

**Keywords:** allergic; asthma; exacerbation; percentage predicted FEV1, dupilumab.



- 20 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated dataexpand

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61

J Investig Med

. 2023 Aug;71(6):613-622.

doi: 10.1177/10815589231167357. Epub 2023 Apr 13.

# E-cigarette use and prevalence of lung diseases among the U.S. population: a NHANES survey

Sudha Dirisanala[1], Srishti Laller[2], Naga Ganti[3], Shafaq Taj[4], Neel Patel[5], Kunwardeep Singh Arora[6], Inemesit Williams[7], Ayesha Hameed[8], Aasa Deepika Kuditipudi[9], Yadanar Win Lei[10], Raghavendra Tirupathi[3], Sachin Gupta[11], Urvish Patel[12], Vikramaditya Samala Venkata[13]

Affiliations expand

- PMID: 37052242

- DOI: 10.1177/10815589231167357

# Abstract

The primary aim of this study was to evaluate epidemiological characteristics and prevalence of lung disease among e-cigarettes users in the United States. A population-based, cross-sectional survey was performed using the National Health and Nutrition Examination Survey (NHANES) of 2015-2018. Adults using e-cigarettes (SMQ900), traditional smoking (SMQ020: > 100 cigarettes in lifetime or SMQ040: current cigarettes use), and dual smoking (e-cigarettes and traditional smoking) were identified and compared in their sociodemographic characteristics and prevalence of lung diseases (Asthma: MCQ010 and COPD: MCQ160O). We used the chi square test (categorical variables) and Mann-Whitney test and unpaired-student *t* test (continuous variables). p-value <0.05 was used as a reference. We excluded respondents <18 years and missing data on demographics and outcomes. Out of 178,157 respondents, 7745 (4.35%), 48,570 (27.26%), and 23,444 (13.16%) were e-cigarette smokers, traditional smokers, and dual smokers, respectively. Overall prevalence of asthma was 15.16% and COPD was 4.26%. E-cigarette smokers were younger in comparison to traditional smokers (median: 25 years vs 62 years; $p < 0.0001$). In females (49.34% vs 37.97%), Mexican (19.82% vs 13.35%), annual household income above $100,000 (23.97% vs 15.56%), prevalence of e-cigarette smoking was higher in comparison to traditional smoking ($p < 0.0001$). The prevalence of COPD was higher among dual smokers in comparison to e-cigarette and traditional smoking (10.14% vs 0.25% vs 8.11%; $p < 0.0001$). Prevalence of asthma was higher among dual and e-cigarette smokers in comparison with traditional smokers and non-smokers (22.44% vs 21.10% vs 14.46% vs 13.30%; $p < 0.0001$). Median age (Q1-Q3) was lower at which asthma (7 years (4-12) vs 25 years (8-50)) was diagnosed first among e-cigarettes smokers in comparison with traditional smokers. In a mixed effect multivariable logistic regression analysis, we found higher odds of asthma among e-cigarette users in comparison with non-smokers (Odds ratio (OR): 1.47; 95% Confidence Interval (CI): 1.21-1.78; $p = 0.0001$). Chronic Obstructive Pulmonary Disease (COPD) respondents were also associated with 11.28 higher odds of e-cigarette utilization (Oddsratio (OR): 11.28; 95% Confidence Interval (CI): 5.59-22.72; $p < 0.0001$). We conclude the higher prevalence of e-cigarette users is seen among the younger population, female, Mexican race, and annual income above $100,000 in comparison to traditional smokers. Chronic Obstructive Pulmonary Disease (COPD) and asthma were both more prevalent in dual smokers. As asthma was more prevalent and diagnosed at an early age in e-cigarette smokers, more prospective studies are needed to understand the effects of e-cigarette among the population at risk to mitigate the sudden rise in utilization and to create awareness.

**Keywords:** COPD; ENDS; National Health and Nutrition Examination Survey; asthma; e-cigarettes; smoking; vaping; vaping-associated lung injury.

SUPPLEMENTARY INFO

MeSH termsexpand

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62

Int J Epidemiol

. 2023 Aug 2;52(4):1231-1242.

doi: 10.1093/ije/dyad040.

# The influence of early-life animal exposure on the risk of childhood atopic dermatitis, asthma and allergic rhinoconjunctivitis: findings from the Danish National Birth Cohort

Angela Pinot De Moira[1,2], Neil Pearce[3], Marie Pedersen[1], Anne-Marie Nybo Andersen[1]

Affiliations expand

- PMID: 37018630

- PMCID: PMC10396419

- DOI: 10.1093/ije/dyad040

# Abstract

**Background:** Early-life animal exposure has been associated with both protective and harmful effects on asthma and allergic disease. We aimed to explore factors that may modify associations of early-life animal exposure with asthma and allergic disease, so as to better understand these differences in findings.

**Methods:** We used data from ≤84 478 children from the Danish National Birth Cohort recruited during pregnancy between 1996 and 2002, and linked registry data up to the child's 13th birthday. Adjusted Cox models were used to examine associations of early-life cat, dog, rabbit, rodent, bird and livestock exposure with atopic dermatitis, asthma and allergic rhinoconjunctivitis overall, and by source of exposure (domestic or occupation), parental history of asthma or allergy, maternal education level and timing of exposure.

**Results:** Overall, associations between animal exposure and the three outcomes of interest were weak. However, dog exposure was associated with marginally lower risk of atopic dermatitis and asthma [adjusted hazard ratio (aHR) = 0.81, 95% CI: 0.70-0.94 and 0.88, 95% CI: 0.82-0.94, respectively], whereas prenatal domestic bird exposure was associated with slightly increased risk of asthma (aHR = 1.18, 95% CI: 1.05-1.32). Source of exposure, parental history of asthma or allergy and timing of exposure modified associations. Early-life animal exposure did not appear to increase the risk of allergic rhinoconjunctivitis (aHR range = 0.88, 95% CI: 0.81-0.95 to 1.00, 95% CI: 0.91-1.10).

**Conclusions:** The overall weak associations observed between animal exposure and atopic dermatitis, asthma and allergic rhinoconjunctivitis were modified by type of animal, source of exposure, parental history of asthma or allergy and timing of exposure, suggesting that these factors should be considered when assessing the risks associated with early-life animal exposure.


**Keywords:** Danish National Birth Cohort; Lifecourse epidemiology; allergic disease; allergic rhinoconjunctivitis; animals; asthma; atopic dermatitis; children; pets.



# Conflict of interest statement

None declared.

- 56 references
- 2 figures

SUPPLEMENTARY INFO

Int J Epidemiol

. 2023 Aug 2;52(4):974-983.

doi: 10.1093/ije/dyad035.

# Why has epidemiology not (yet) succeeded in identifying the origin of the asthma epidemic?

Josep M Antó[1,2,3,4], Neil Pearce[5], Jeroen Douwes[6], Judith Garcia-Aymerich[1,3,4], Lucy Pembrey[7], Lorenzo Richiardi[8], Jordi Sunyer[1,2,3,4]

Affiliations expand

- PMID: 37004248
- PMCID: PMC10396414
- DOI: 10.1093/ije/dyad035

**Free PMC article**

*No abstract available*

## Conflict of interest statement

None declared.

- 109 references

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

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Review

Allergy

. 2023 Aug;78(8):2121-2147.

doi: 10.1111/all.15724. Epub 2023 Apr 10.

# Is exposure to pollen a risk factor for moderate and severe asthma exacerbations?

Isabella Annesi-Maesano[1], Lorenzo Cecchi[2,3], Benedetta Biagioni[4], Kian Fan Chung[5], Bernard Clot[6], Martine Collaud Coen[6], Gennaro D'Amato[7], Athanasios Damialis[8], Javier Dominguez-Ortega[9], Carmen Galàn[10,11], Stefanie Gilles[12], Stephen Holgate[13], Mohamed Jeebhay[14], Stelios Kazadzis[15], Nikolaos G Papadopoulos[16,17], Santiago Quirce[9], Joaquin Sastre[18], Fiona Tummon[6], Claudia Traidl-Hoffmann[12,19,20], Jolanta Walusiak-Skorupa[21], Pablo Alonso-

Coello[22,23], Carlos Canelo-Aybar[22,23], Yahveth Cantero-Fortiz[22,23], David Rigau[22,23], Josefina Salazar[22,23], Francisca Verdugo-Paiva[22,23], Marek Jutel[24], Cezmi A Akdis[25], Ioana Agache[26]

Affiliations expand

- PMID: 36961370

- DOI: 10.1111/all.15724

# Abstract

Limited number of studies have focused on the impact of pollen exposure on asthma. As a part of the EAACI Guidelines on Environment Science, this first systematic review on the relationship of pollen exposure to asthma exacerbations aimed to bridge this knowledge gap in view of implementing recommendations of prevention. We searched electronic iPubMed, Embase, and Web of Science databases using a set of MeSH terms and related synonyms and identified 73 eligible studies that were included for systemic review. When possible, meta-analyses were conducted. Overall meta-analysis suggests that outdoor pollen exposure may have an effect on asthma exacerbation, but caution is needed due to the low number of studies and their heterogeneity. The strongest associations were found between asthma attacks, asthma-related ED admissions or hospitalizations, and an increase in grass pollen concentration in the previous 2-day overall in children aged less than 18 years of age. Tree pollen may increase asthma-related ED visits or admissions lagged up to 7-day overall in individuals younger than 18 years. Rare data show that among subjects under 18 years of age, an exposure to grass pollen lagged up to 3 days may lower lung function. Further research considering effect modifiers of pollen sensitization, hay fever, asthma, air pollution, green spaces, and pre-existing medications is urgently warranted to better evaluate the impacts of pollen on asthma exacerbation. Preventive measures in relation to pollen exposure should be integrated in asthma control as pollen increase continues due to climate change.

**Keywords:** aerobiology; asthma; pollen.



- 146 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

Thorax

. 2023 Aug;78(8):775-783.

doi: 10.1136/thorax-2022-219651. Epub 2023 Mar 16.

# Activation of epithelial and inflammatory pathways in adolescent elite athletes exposed to intense exercise and air pollution

Janne Goossens[1], Anne-Charlotte Jonckheere[1], Sven F Seys[1], Ellen Dilissen[1], Tatjana Decaesteker[1], Camille Goossens[1], Koen Peers[2], Vincent Vanbelle[3], Jeroen Stappers[4], Sven Aertgeerts[5], Barbara De Wilde[6], Jasmine Leus[6 7], Sophie Verelst[7 8], Marc Raes[7 8], Lieven Dupont[9 10], Dominique M Bullens[11 7]

Affiliations expand

- PMID: 36927754

- PMCID: PMC10359548

- DOI: 10.1136/thorax-2022-219651

**Free PMC article**

## Abstract

**Rationale:** Participation in high-intensity exercise in early life might act as stressor to the airway barrier.

**Objectives:** To investigate the effect of intense exercise and associated exposure to air pollution on the airway barrier in adolescent elite athletes compared with healthy controls and to study exercise-induced bronchoconstriction (EIB) in this population.

**Methods:** Early-career elite athletes attending 'Flemish-Elite-Sports-Schools' (12-18 years) of 4 different sport disciplines (n=90) and control subjects (n=25) were recruited. Presence of EIB was tested by the eucapnic voluntary hyperventilation (EVH) test. Markers at mRNA and protein level; RNA-sequencing; carbon load in airway macrophages were studied on induced sputum samples.

**Results:** 444 genes were differentially expressed in sputum from athletes compared with controls, which were related to inflammation and epithelial cell damage and sputum samples of athletes contained significantly more carbon loaded airway macrophages compared with controls (24%, 95% CI 20% to 36%, p<0.0004). Athletes had significantly higher substance P (13.3 pg/mL, 95% CI 2.0 to 19.2) and calprotectin (1237 ng/mL, 95% CI 531 to 2490) levels as well as IL-6, IL-8 and TNF-α mRNA levels compared with controls (p<0.05). The incidence of EIB in athletes was 9%. The maximal fall in forced expiratory volume in 1 s (%) after EVH test in athletes was significantly associated with prior $PM_{10}$ and $PM_{2.5}$ exposure.

**Conclusion:** Early-career elite athletes showed increased markers of air pollution exposure, epithelial damage and airway inflammation compared with controls. Acute exposure to increased air pollution $PM_{10}$ levels was linked to increased airway hyper-reactivity.

**Trial registration number:** NCT03587675.

**Keywords:** airway epithelium; exercise.



# Conflict of interest statement

Competing interests: None declared.

- 57 references
- 5 figures

SUPPLEMENTARY INFO

MeSH terms, Associated dataexpand

Allergy

. 2023 Aug;78(8):2311-2314.

doi: 10.1111/all.15710. Epub 2023 Apr 11.

# Prescribing patterns of budesonide/formoterol maintenance and reliever therapy in patients with asthma in Sweden

Christer Janson[1], Erik Melén[2], Sofie de Fine Licht[3], Gunilla Telg[3], Ekaterina Maslova[4], Trung N Tran[5], Filip Surmont[4], Fredrik Wiklund[6], Urban Olsson[6], Bright I Nwaru[7,8], Magnus Ekström[9]

Affiliations expand

- PMID: 36919650

- DOI: 10.1111/all.15710

*No abstract available*

- 15 references

Editorial

Arch Bronconeumol

. 2023 Aug;59(8):473-475.

doi: 10.1016/j.arbres.2023.02.012. Epub 2023 Feb 25.

# Obese Asthma Syndrome: Much Work to Do

[Article in English, Spanish]

Ebymar Arismendi[1], Marina Bantulà[2], César Picado[3]

Affiliations expand

- PMID: 36894470

- DOI: 10.1016/j.arbres.2023.02.012

*No abstract available*

Am J Prev Med

. 2023 Aug;65(2):173-181.

doi: 10.1016/j.amepre.2023.01.038. Epub 2023 Mar 7.

# Cigarettes, ENDS Use, and Chronic Obstructive Pulmonary Disease Incidence: A Prospective Longitudinal Study

Steven F Cook[1], Jana L Hirschtick[1], Nancy L Fleischer[1], Douglas A Arenberg[2], Geoffrey D Barnes[3], David T Levy[4], Luz Maria Sanchez-Romero[4], Jihyoun Jeon[1], Rafael Meza[5]

Affiliations expand

- PMID: 36890083

- PMCID: PMC10363225 (available on 2024-08-01)

- DOI: 10.1016/j.amepre.2023.01.038

## Abstract

**Introduction:** Understanding the relationship between ENDS use and chronic obstructive pulmonary disease (COPD) and other respiratory conditions is critical. However, most previous studies have not fully adjusted for cigarette smoking history.

**Methods:** Using Waves 1-5 of the U.S. Population Assessment of Tobacco and Health study, the association between ENDS use and self-reported incident COPD was examined among adults aged 40+ years using discrete-time survival models. Current ENDS use was measured as a time-varying covariate, lagged by 1 wave, defined as established daily or some days of use. Multivariable models were adjusted for baseline demographics (age, sex, race/ethnicity, education), health characteristics (asthma, obesity, exposure to second-hand smoke), and smoking history (smoking status and cigarette pack years). Data were collected between 2013 and 2019, and the analysis was conducted in 2021-2022.

**Results:** Incident COPD was self-reported by 925 respondents during the 5-year follow-up. Before adjusting for other covariates, time-varying ENDS use appeared to double COPD incidence risk (hazard ratio=1.98, 95% CI=1.44, 2.74). However, ENDS use was no longer associated with COPD (adjusted hazard ratio=1.10, 95% CI=0.78, 1.57) after adjusting for current cigarette smoking and cigarette pack years.

**Conclusions:** ENDS use did not significantly increase the risk of self-reported incident COPD over a 5-year period once current smoking status and cigarette pack years were included. Cigarette pack years, by contrast, remained associated with a net increase in COPD incidence risk. These findings highlight the importance of using prospective longitudinal data and adequately controlling for cigarette smoking history to assess the independent health effects of ENDS.



SUPPLEMENTARY INFO

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Ann Allergy Asthma Immunol

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. 2023 Aug;131(2):217-223.e1.

doi: 10.1016/j.anai.2023.02.023. Epub 2023 Mar 3.

# Evaluating inhaler education interventions for hospitalized children with asthma: A randomized controlled trial

Anna Volerman[1], Uma Balachandran[2], Mengqi Zhu[2], Mary Akel[2], Ashley Hull[2], Michelle Siros[2], Viridiana Luna[2], Isabella Xu[2], Valerie G Press[3]

Affiliations expand

- PMID: 36870528

- DOI: 10.1016/j.anai.2023.02.023

## Abstract

**Background:** Most children with asthma have poor inhaler technique, with detrimental morbidity effects. Guidelines recommend clinicians provide inhaler education at every opportunity, yet resources are limited. A low-cost, technology-based intervention-Virtual Teach-to-Goal (V-TTG)-was developed to deliver tailored inhaler technique education with high fidelity.

**Objective:** To evaluate whether V-TTG leads to less inhaler misuse among children with asthma who are hospitalized vs brief intervention (BI, reading steps aloud).

**Methods:** A single-center randomized controlled trial of V-TTG vs BI was conducted with 5-to-10-year-old children with asthma hospitalized between January 2019 and February 2020. Inhaler technique was assessed pre- and post-education using 12-step validated checklists (misuse: < 10 steps correct).

**Results:** Among 70 children enrolled, mean age was 7.8 years (SD = 1.6). Most (86%) were Black. Most had an emergency department visit (94%) or hospitalization (90%) in the previous year. At baseline, nearly all children misused inhalers (96%). The proportion of children with inhaler misuse decreased significantly in V-TTG (100%→74%, P = .002) and BI (92%→69%, P = .04) groups, with no difference between groups at both time points (P = .2 and .9). On average, children performed 1.5 more steps correctly (SD = 2.0), with greater improvement with V-TTG (mean [SD] = 1.7 [1.6]) vs BI (mean [SD] = 1.4 [2.3]), though not

significant (P = .6). Concerning pre and post technique, older children were significantly more likely than younger children to show more correct steps (mean change = 1.9 vs 1.1, P = .002).

**Conclusion:** A technology-based intervention for tailored inhaler education led to improved technique among children, similarly to reading steps aloud. Older children saw greater benefits. Future studies should evaluate the V-TTG intervention across diverse populations and disease severities to identify the greatest impact.

**Clinical trial registration:** NCT04373499.





Allergy

. 2023 Aug;78(8):2305-2310.

doi: 10.1111/all.15693. Epub 2023 Mar 18.

# Factors associated with suboptimal response to monoclonal antibodies in severe asthma

Luis Pérez de Llano[1], Nuria Marina Malanda[2], Isabel Urrutia[3], Eva Martínez-Moragón[4], José Antonio Gullón-Blanco[5], Rocío Díaz-Campos[6], Mariana Muñoz Esquerre[7], Alicia Habernau Mena[8], Borja G Cosío[9], Carolina Cisneros[10], Francisco Javier Lázaro Polo[11], Daniel Laorden[12], David Dacal Rivas[1]

Affiliations expand

- PMID: 36866939

- DOI: 10.1111/all.15693

*No abstract available*

- 8 references

SUPPLEMENTARY INFO

Publication types, Grant supportexpand

FULL TEXT LINKS



Review

J Asthma

- 
- 
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. 2023 Aug;60(8):1503-1512.

doi: 10.1080/02770903.2023.2176775. Epub 2023 Feb 15.

# Scoping review: multiple stakeholders and child asthma management interventions

Samuel Adabla[1], Laura A Nabors[1], Olutosin Sanyaolu[1], Afolakemi Olaniyan[1], Jonathan A Bernstein[2]

Affiliations expand

- PMID: 36744817

- DOI: 10.1080/02770903.2023.2176775

## Abstract

**Objective:** This study reviewed research to identify interventions aimed at improving asthma management among children by educating parents and other professionals.

**Data sources:** PubMed, Medline, and Embase databases were utilized.

**Study selections:** Three databases were searched for child asthma management interventions published between 2012-2022 in English. Search terms included children, asthma, intervention(s), community pediatrics, coaches, schools, and stakeholders. Inclusion criteria were being an experimental study focused on children with asthma (birth-18 years), including stakeholder involvement, education, and a community focus. The search yielded 153 articles; nine were reviewed.

**Results:** In general, stakeholders developed programs that resulted in improvements in asthma symptoms, knowledge of asthma management, perceptions of health care, and decreased emergency health care visits. Successful interventions involved education about asthma management, providing medications, and partnerships with school staff, healthcare teams, and community members. Effective coordination and communication contributed to successful program implementation. Using technology for asthma management education was effective in tracking access to care and facilitated the delivery of medications.

**Conclusion:** The findings indicate that interventions were effective in improving child asthma management. Stakeholder partnerships were critical to the effectiveness of interventions. Marketing the intervention and encouraging communication with parents also fostered success. Being able to assess the home environment and staying in contact with parents were barriers to these interventions. Conducting randomized controlled trials using the interventions found effective in these studies to assess change in symptoms and

emergency care visits over time would yield important information about their long-term success and cost for implementation.

**Keywords:** Asthma; asthma management; children; stakeholder involvement.



Arch Dermatol Res

. 2023 Aug;315(6):1823-1826.

doi: 10.1007/s00403-023-02539-z. Epub 2023 Jan 28.

# Psoriasis associated with asthma and allergic rhinitis: a US-based cross-sectional study using the All of US Research Program

Marina Z Joel[1], Ryan Fan[2], William Damsky[3,4], Jeffrey M Cohen[5]

Affiliations expand

- PMID: 36707438

- DOI: 10.1007/s00403-023-02539-z

# Abstract

Psoriasis is a common chronic inflammatory disease with multiple known comorbidities. Increasing evidence suggests some mechanistic overlap in the immunopathogenesis of psoriasis and some cases of asthma and allergic rhinitis (AR), but the potential association between psoriasis and asthma and AR has not been thoroughly investigated. The study aimed to investigate the association between psoriasis and asthma and AR. We used data from the NIH All of US Research Program, a nationwide longitudinal cohort of US adults, collected from 2018 to present. The source population comprised a demographically and socioeconomically diverse cohort of over 300,000 Americans. We used multivariable logistic regression models to examine the association between psoriasis and asthma and AR, after adjusting for sociodemographic variables, body mass index, and smoking status. In total, 235,551 participants (mean [SD] age, 54.7 [16.6] years; 59.3% female), including 5165 individuals with psoriasis and 230,386 individuals without psoriasis, were included in our analysis. Participants with psoriasis had significantly higher prevalence of asthma (26.1% vs. 12.9%; P < 0.001) and AR (31.8% vs. 13.4%; P < 0.001) compared to participants without psoriasis. Psoriasis was significantly associated with both asthma [adjusted odds ratio (aOR) 2.22; 95% confidence interval (CI) 2.08-2.37] and AR (aOR, 2.57; 95% CI 2.42-2.73). In subgroup analyses, associations remained stable in multivariable analyses after stratification by age, sex, and income. Psoriasis is associated with both asthma and AR in our sample of US adults. Further research is needed to explore potentially unifying inflammatory pathways among psoriasis, asthma, and AR.



**Keywords:** Allergic rhinitis; Asthma; Cross-sectional; Epidemiology; Psoriasis.

Observational Study

J Asthma

. 2023 Aug;60(8):1622-1631.

doi: 10.1080/02770903.2023.2169932. Epub 2023 Jan 30.

# Does the severity of asthma affect exercise capacity and daily physical activity?

Rocco Francesco Rinaldo[1], Gianluca Imeri[2], Michele Mondoni[1], Elena Maria Parazzini[1], Beatrice Vigo[1], Alessandra Masseroni[1], Stefano Centanni[1], Fabiano Di Marco[2]

Affiliations expand

- PMID: 36650704

- DOI: 10.1080/02770903.2023.2169932

## Abstract

**Objective:** Exercise capacity, daily physical activity, and psychological profile are crucial aspects in the management of asthmatic patients. Whether these features are expressed in a different way in mild-moderate (MMA) and severe asthma (SA) is unknown.

**Methods:** In this observational cross-sectional study, patients matching the American Thoracic Society/European Respiratory Society (ATS/ERS) definition for SA underwent incremental cardiopulmonary exercise testing (CPET), full lung function testing, and an evaluation of daily step count and physical activity. Questionnaires on quality of life, general fatigue, and presence of anxiety and depression traits (Hospital Anxiety and Depression Scale - HADS) were administered. Patients were compared with a cohort of age- and gender-matched MMA patients.

**Results:** We enrolled 16 SA, 17 MMA patients, and 16 healthy subjects. Compared to MMA, SA subjects showed a median (interquartile range) reduced peak oxygen

consumption during CPET (20.4 (17.2-23.3) vs. 25.6 (18.5-30.3) ml/min/kg; $p = 0.019$), a reduced resting lung function (FEV1% of predicted 77 (67-84) vs. 96 (84-100); $p < 0.001$) and a pronounced anxiety trait at HADS (9.5 (3-11.7) vs. 4.0 (2.0-7.5); $p = 0.023$). In addition, SA patients showed a significantly higher reduction in inspiratory capacity from rest to peak (310 (160-520) vs. 110 (-65-325) ml; $p = 0.031$). We found no significant differences in mean daily step count or quality of life.

**Conclusions:** Compared to MMA, SA patients present a reduced exercise capacity and a more pronounced anxiety trait, but not worse daily physical activity or quality of life. These aspects should be considered in the clinical management and research development of SA.

**Keywords:** Severe asthma; cardiopulmonary exercise test; daily physical activity; exercise capacity; psychological profile; pulmonary function testing; quality of life.



1
J Asthma

. 2023 Aug;60(8):1608-1612.

doi: 10.1080/02770903.2023.2169930. Epub 2023 Feb 2.

# Can patients achieve sufficient peak inspiratory flow rate (PIFR) with Turbuhaler® during acute exacerbation of asthma?

Nur Azimah Mohd Rhazi[1], Jaya Muneswarao[2], Fatimatuzzahra' Abdul Aziz[1], Baharudin Ibrahim[3], Azlan Kamalludin[4], Shahrul Aiman Soelar[5]

Affiliations expand

- PMID: 36650693

- DOI: 10.1080/02770903.2023.2169930

# Abstract

**Introduction:** Anti-inflammatory reliever (AIR) with or without regular maintenance delivered through Turbuhaler® has been widely recommended in the GINA strategy document. These patients are not prescribed with additional reliever inhalers, but dependent on Turbuhaler® during acute asthma episodes. The peak inspiratory flow rate (PIFR) is crucial in drug delivery from a dry powder inhaler (DPI) such as Turbuhaler®. Despite its increasing usage, there are some concerns that patients on Turbuhaler® are not able to achieve adequate PIFR during acute exacerbation of asthma.

**Objective:** This study aimed to assess the PIFR at resistance settings that matched Turbuhaler® in patients with acute exacerbation of asthma.

**Methodology:** A six-month cross-sectional study was conducted at the Emergency Department (ED) of Hospital Sultanah Bahiyah and Hospital Kulim, Kedah, Malaysia. Adult patients diagnosed with mild to moderate acute exacerbations of asthma were recruited. The PIFRs were measured using the In-Check DIAL G16 that was set to simulate the resistance of Turbuhaler® (R3). The PIFRs were assessed before (pre) and after (post) the initial bronchodilator (BD) treatment at the ED. The minimal required PIFR was defined as flow rates ≥ 30 L/min while a PIFR of 60 L/min was considered as optimal.

**Results:** A total of 151 patients (81 females and 70 males) were recruited. The mean age was 37.5 years old with a range between 18 and 79 years old. The results showed that 98% ($n$ = 148) of patients managed to achieve the minimal PIFR required for pre-BD. The mean PIFR pre-BD was 60 ± 18.5 L/min and post-BD was 70 ± 18.5 L/min. Furthermore, more than half (54%, $n$ = 82) of the patients recorded PIFR ≥ 60 L/min during pre-BD, and about three-quarters (71%, $n$ = 92) achieved PIFR ≥ 60 L/min post-BD. The PIFR showed a moderate correlation with peak expiratory flow rate (PEFR) ($r$ = 0.55, 95% CI: 0.43-0.65, $p$ < 0.001).

**Conclusion:** The majority of patients with asthma in the present study were able to achieve sufficient PIFR from Turbuhaler® during mild to moderate acute exacerbations.

**Keywords:** Peak inspiratory flow rate; Turbuhaler; asthma; exacerbation.

J Asthma

. 2023 Aug;60(8):1601-1607.

doi: 10.1080/02770903.2023.2165445. Epub 2023 Feb 2.

# Changes in asthma emergency department visits in the United States during the COVID-19 pandemic

Dongni Ye[1,2], Abigail Gates[3], Lakshmi Radhakrishnan[3], Maria C Mirabelli[1], W Dana Flanders[1,4], Kanta Sircar[1,5]

Affiliations expand

- PMID: 36608267

- PMCID: PMC10293019 (available on 2024-08-01)

- DOI: 10.1080/02770903.2023.2165445

## Abstract

**Objective:** A better understanding of the impacts of the Coronavirus disease 2019 (COVID-19) pandemic on emergency department (ED) visits for asthma is needed to improve asthma control.

**Methods:** Using data from the National Syndromic Surveillance Program (NSSP), we assessed changes in average weekly asthma ED visits in the United States in 3 surveillance periods: 1) March 15, 2020-January 2, 2021; 2) January 3, 2021-January 1, 2022; and 3) January 2-March 5, 2022, relative to pre-pandemic comparison periods between December 30, 2018 and December 28, 2019. For each surveillance period, we assessed changes in asthma ED visits by age group and sex.

**Results:** For the surveillance period beginning March 15, 2020, average weekly asthma ED visits declined 31% relative to what was observed during the comparison period - that is, from 45,276 visits/week in 2019 to 31,374 visits/week in 2020. Declines of over 19% and 26% were observed for 2021 and 2022, respectively, relative to the comparison periods. In all surveillance periods, the largest declines occurred among children, especially those ages 0-4 (74%) and 5-11 (66%) years.

**Conclusions:** The COVID-19 pandemic impacted asthma ED visits in the United States. The impact was greater among children than adults, as ED visits among children were notably lower during all three pandemic surveillance periods than during the corresponding pre-pandemic periods. Additional information about the roles of behaviors of patients with asthma and changes in asthma care might improve our understanding of the reasons underlying these observed changes.

**Keywords:** Adults; children; epidemiology; pandemic; population-based; surveillance.

# Conflict of interest statement

Declaration of Interest Statement: The authors report there are no competing interests to declare.

. 2023 Aug;60(8):1584-1591.

doi: 10.1080/02770903.2022.2164200. Epub 2023 Feb 3.

# Primary health care utilization and hospital readmission in children with asthma: a multi-site linked data cohort study

Katherine Yh Chen[1,2,3], Renee Jones[1], Shaoke Lei[1], Shivanthan Shanthikumar[3,4,5], Lena Sanci[6], John Carlin[7], Harriet Hiscock[1,3,8]

Affiliations expand

- PMID: 36594684

- DOI: 10.1080/02770903.2022.2164200

## Abstract

**Objectives:** To (1) describe primary health care utilization and (2) estimate the effect of primary care early follow-up, continuity, regularity, frequency, and long consultations on asthma hospital readmission, including secondary outcomes of emergency (ED) presentations, asthma preventer adherence, and use of rescue oral corticosteroids within 12 months.

**Methods:** An Australian multi-site cohort study of 767 children aged 3-18 years admitted with asthma between 2017 and 2018, followed up for at least 12 months with outcome and primary care exposure data obtained through linked administrative datasets. We estimated the effect of primary care utilization through a modified Poisson regression adjusting for child age, asthma severity, socioeconomic status and self-reported GP characteristics.

**Results:** The median number of general practitioner (GP) consultations, unique GPs and clinics visited was 9, 5, and 4, respectively. GP care was irregular and lacked continuity, only 152 (19.8%) children visited their usual GP on more than 60% of occasions. After adjusting for confounders, there was overall weak indication of effects due to any of the exposures. Increased frequency of GP visits was associated with reduced readmissions (4-14 visits

associated with risk ratio of 0.71, 95% CI 0.50-1.00, $p$ = 0.05) and ED presentations (>14 visits associated risk ratio 0.62, 95% CI 0.42-0.91, $p$ = 0.02).

**Conclusions:** Our study demonstrates that primary care use by children with asthma is often irregular and lacking in continuity. This highlights the importance of improving accessibility, consistency in care, and streamlining discharge communication from acute health services.

**Keywords:** Asthma; child; linkage; primary care; readmission.



J Asthma

. 2023 Aug;60(8):1535-1544.

doi: 10.1080/02770903.2022.2158101. Epub 2023 Feb 2.

# The role of serum inflammatory in mycoplasma pneumonia infection with respiratory asthma

Xiaoju Zhou[1], Wei Jiang[1], Qianyi Zhou[1], Wenjie Yang[1]

Affiliations expand

- PMID: 36511625

- DOI: 10.1080/02770903.2022.2158101

# Abstract

**Objective:** With the growing frequency of *Mycoplasma pneumoniae* infections linked to respiratory asthma (MP-RA), particularly in children, the quest for novel diagnostic molecular markers has become critical. We examined the link between serum immunoglobulin, inflammatory variables, vitamin A, and vitamin D levels in MP-RA patients and then found markedly diagnostic indicators.

**Methods:** From January 2015 to March 2020, our hospital screened 55 cases of healthy control children (HC), 53 instances of mycoplasma pneumonia infection complicated with respiratory asthma (MP-RA), and 58 cases of non-respiratory asthma children for pneumonia mycoplasma infection (MP). Serum immunoglobulins, inflammatory markers, vitamin D, and vitamin A levels were analyzed, and a predictive model including the feature chosen in the least absolute shrinkage and selection operator regression model was developed.

**Results:** Serum TNF- and IL-1b levels were greater in MP-RA children than in MP children, but 25(OH)D, IgG, and IgA levels were lower. Our findings verified the link between IgA, TNF-a, 25(OH)D, and vitamin A with MP-RA. In addition, TNF-a, IL-1b, 25(OH)D (Vit-D), IgG, and IgA were the predictors in the prediction nomogram, showing the combined influence of serum inflammation in MP-RA. C-index of 0.985 (95% CI: -1.25 to 1.68) shows high scaling ability and the model exhibits good discriminative capacity. With range validation, the high C-index value of 0.96 is still possible.

**Conclusion:** TNF-a, IL-1b, 25(OH)D (Vit-D), IgG, and IgA were considered as predictors in children with MP-RA was investigated in this research.

**Keywords:** Serum immunoglobulin; asthma; inflammatory factors; mycoplasma pneumonia; vitamin A; vitamin D.

Meta-Analysis

J Asthma

. 2023 Aug;60(8):1481-1492.

doi: 10.1080/02770903.2022.2155189. Epub 2022 Dec 30.

# Dexamethasone versus prednisone/prednisolone in the management of pediatric patients with acute asthmatic exacerbations: a systematic review and meta-analysis

Elise Dahan[1,2], Nour El Ghazal[1,2], Hayato Nakanishi[1,2], Joe El Haddad[1,2], Reem H Matar[1,2,3], Danijel Tosovic[4], Azizullah Beran[5], Christian A Than[1,2,4], David Stiasny[6]

Affiliations expand

- PMID: 36461938

- DOI: 10.1080/02770903.2022.2155189

## Abstract

**Objective:** Acute asthmatic exacerbation is a common condition for pediatric emergency visits. Recently, dexamethasone has increasingly been used as an alternative to prednisone. This study aimed to evaluate the safety and efficacy of dexamethasone (DEX) against prednisone/prednisolone (PRED) in managing pediatric patients with acute asthmatic exacerbation.

**Data sources:** Cochrane, Embase, PubMed, Scopus, and Web of Science were searched for articles from their inception to August 2022 by two independent reviewers using the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) system. The review was registered prospectively with PROSPERO (CRD42022353462).

**Study selections:** From 316 studies screened, seventeen studies met the eligibility criteria, with 5967 pediatric patients experiencing an asthma exacerbation requiring treatment with either DEX (*n* = 2865) or PRED (*n* = 3102). Baseline patient characteristics (age, sex, PRAM (pediatric respiratory assessment measure), previous corticosteroid and beta-agonist inhaler) were comparable between groups.

**Results:** After treatment administration, the DEX group had fewer vomiting incidents (OR = 0.24, 95% CI: 0.11, 0.51, $I^2$ = 58%) and reduced noncompliance events (OR = 0.12, 95% CI: 0.04, 0.34, $I^2$ = 0%) when compared to the PRED group. Regarding emergency-department (ED)-related outcomes, there were no differences in hospital admission rates (OR = 0.83, 95% CI: 0.58, 1.19, $I^2$ = 15%), time spent in the ED (MD= -0.11 h, 95% CI: -0.52; 0.30, $I^2$ = 82%) or relapse occurrences (OR = 0.67, 95% CI: 0.30, 1.49, $I^2$ = 52%) between both groups.

**Conclusion:** Although there were no differences between the DEX and PRED groups in terms of hospital admission rates, time spent in the ED or relapse events, pediatric patients receiving DEX experienced lower noncompliance and vomiting rates.

**Keywords:** Meta-analysis; asthma; dexamethasone; pediatric; prednisolone; prednisone.



Ann Otol Rhinol Laryngol

. 2023 Aug;132(8):888-894.

doi: 10.1177/00034894221121407. Epub 2022 Sep 8.

# Radiofrequency Ablation for Inferior Turbinate Hypertrophy: Predictive Factors for Short and Long-Term Outcomes

Kristien Sleurs [1], Job Postelmans [2], Jasper V Smit [2]

Affiliations expand

- PMID: 36082420

- DOI: 10.1177/00034894221121407

## Abstract

**Objectives:** Radiofrequency Ablation (RFA) is a widely used technique for treatment of nasal obstruction due to inferior turbinate hypertrophy. This study aims to evaluate short and long-term outcome after RFA. Secondly, predictive factors for this outcome were evaluated.

**Methods:** A prospective clinical study was performed in 65 patients to evaluate short-term outcome and predictive factors (Study A). To evaluate long-term outcome and predictive factors we performed a second clinical study in 124 patients (Study B). Patients scored nasal symptoms on a 1 to 5 points visual analogue scale (VAS) and filled in questionnaires about their comorbidity, previous nasal surgery, and medication use.

**Results:** *Study A*: There was significant short-term (6-8 weeks after RFA) improvement in nasal obstruction (VAS -1.3, $P < .001$), trouble exercising (VAS -1.5, $P < .001$), trouble sleeping (VAS -0.9, $P < .001$), snoring (VAS -1.1, $P < .001$), and hyposmia (VAS -0.6, $P = .004$). Smoking ($R^2 = .065$, $P = .047$) was a predictor for less optimized and previous use of decongestive nasal spray ($R^2 = .135$, $P = .005$) for better short-term outcome. *Study B*: Nasal obstruction significantly decreased in the long term (1-5 years after RFA) compared to VAS before RFA (VAS -1.5, $P < .001$), but slightly increased compared to VAS 6 to 8 weeks after RFA (VAS +0.3, $P = .036$). Allergy ($R^2 = .066$, $P = .006$), asthma ($R^2 = .068$, $P = .005$), and previous use of corticosteroid nasal spray ($R^2 = .050$, $P = .016$) were associated with a less optimized and older age ($R^2 = .217$, $P < .001$) with better long-term outcome.

**Conclusion:** RFA is an efficient treatment for nasal obstruction, and improves sleeping, exercising, snoring, and hyposmia. Predictors for good short-term outcome were previous use of decongestive nasal spray and no smoking. Predictors for a less optimized long-term outcome were allergy, asthma, and previous use of corticosteroid nasal spray. Older age was associated with better long-term outcome.

**Keywords:** allergy; inferior turbinate; nasal obstruction; predictive factors; radiofrequency ablation.



Observational Study

Indian J Pediatr

. 2023 Aug;90(8):770-775.

doi: 10.1007/s12098-022-04162-8. Epub 2022 Jun 22.

# Comparison of Asthma Control among Children 5–18 Years of Age by Asthma Control Test Questionnaire of Global

# Initiative for Asthma 2017 (GINA-2017) Against Spirometry

Jahnavi M[1,2], Gowrishankar N C[3], Neduncheliyan K[4]

Affiliations expand

- PMID: 35731499

- DOI: 10.1007/s12098-022-04162-8

## Abstract

**Objective:** To compare asthma control by Asthma Control Test (ACT)/Childhood Asthma Control Test (cACT) Questionnaire of Global Initiative for Asthma 2017 (GINA-2017) against spirometry in children, 5-18 y of age, with asthma.

**Methods:** A prospective observational study was conducted between July 2017 and March 2019 in pulmonology OPD of a tertiary care center. Children with asthma aged 5-18 y, falling under the inclusion criteria had spirometry and cACT/ACT questionnaire before starting inhaled corticosteroids. After 12 wk, symptom control was reassessed by ACT/cACT and spirometry. Chi-square/Fischer exact test and paired t-test/Mann-Whitney U test used for qualitative and quantitative data, respectively.

**Results:** ACT/cACT pretreatment score was 12.76 (2.521), and at follow-up the score was 23.94 (1.941) ($p < 0.001$). Control by GINA increased from 2.04% to 91.84% at follow-up ($p < 0.001$). Significant improvement in forced expiratory volume in first second (FEV1), forced expiratory volume/forced vital capacity (FEV1/FVC), forced expiratory flow between 25 and 75% of FVC ($FEF_{25-75}$) and peak expiratory flow rate (PEFR) between pretreatment and follow-up seen were -71.86%, 106.84%, 101.82%, and 97.51% vs. 82.2%, 109.55%, 110.38%, and 107.00%, respectively. Positive correlation between ACT/cACT and FEV1 ($r = 0.26$, $p \leq 0.05$), PEFR ($r = 0.30$, $p \leq 0.05$).

**Conclusions:** There is a good correlation of symptom control between ACT/cACT and spirometry with significant positive correlation for FEV1, PEFR.

**Keywords:** Asthma; Asthma Control Test; Spirometry.



- 18 references

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Randomized Controlled Trial

J Pharm Pract

. 2023 Aug;36(4):803-809.

doi: 10.1177/08971900221076447. Epub 2022 Mar 26.

# A Randomized Controlled Study Addressing Dexamethasone Tolerability in the Treatment of Acute Asthma in Children: Mary Poppins on Trial!

Lyn Kathryn Sonnenberg[1], Douglas Sinclair[2]

Affiliations expand

- PMID: 35341362

- PMCID: PMC10350716

- DOI: 10.1177/08971900221076447

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# Abstract


AimEmesis of oral medications continues to be a problem in the management of acute pediatric asthma exacerbations; therefore, we set out to assess whether smaller volumes of oral dexamethasone resulted in better tolerability. **Methods:** Children aged 2-14 years, presenting to the emergency department with acute asthma exacerbation, were enrolled in this open, prospective randomized controlled trial. Participants received 0.3 mg/kg of dexamethasone in either its concentrated volume (10 mg/mL) or mixed with Ora Sweet (1 mg/mL). Tolerability was measured by vomiting within 45 minutes of receiving dexamethasone, with stratification, a priori, for prior vomiting. **Results:** 430 participants were enrolled. 23/213 (11%) in the 10 mg/mL group vomited dexamethasone compared to 16/217 (7%) in the 1 mg/mL group (P = .29). 11/179 (6%) in the 10 mg/mL group vomited compared to 8/183 (3%) in the 1 mg/mL group (.61). For those 68 stratified with prior vomiting, 12/34 (35%) in the 10 mg/mL group vomited compared to 8/34 (24%) in the 1 mg/mL group (P = .43). None of these results were statistically different. Prior vomiting increased the risk of vomiting, regardless of the formulation given (P < .001). **Conclusions:** Volume does not play a significant role in the tolerability of dexamethasone. Therefore, palatability should not be sacrificed for a smaller volume of dexamethasone to improve tolerability.



**Keywords:** asthma; dexamethasone; pediatrics; tolerability; vomiting.


# Conflict of interest statement


The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.


- 17 references
- 1 figure

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

1
Am J Rhinol Allergy
.
. 2023 Aug 3;19458924231193154.
doi: 10.1177/19458924231193154. Online ahead of print.

# TSLP Induces Epithelial-Mesenchymal Transition in Nasal Epithelial Cells From Allergic Rhinitis Patients Through TGF-β1/Smad2/3 Signaling

Hong Wei Yu[1], Wei Wei Wang[1], Qian Jing[1], Yong Liang Pan[1]

Affiliations expand

- PMID: 37537875

- DOI: 10.1177/19458924231193154

## Abstract

**Background:** Airway remodeling is demonstrated in Asian patients with allergic rhinitis (AR). The epithelial-mesenchymal transition (EMT) is one of the key mechanisms underlying airway remodeling. Thymic stromal lymphopoietin (TSLP) is an important contributor to airway remodeling. Although increased TSLP is found in AR, little is known about whether TSLP is involved in airway remodeling through induction of the EMT.

**Objective:** We investigated the effect of TSLP on the EMT in human nasal epithelial cells (HNECs) from AR patients.

**Methods:** Human nasal epithelial cells from AR patients were stimulated with TSLP in the absence or presence of the preincubation with a selective inhibitor of transforming growth factor beta 1 (TGF-β1) receptor (SB431542). The expression of TGF-β1 in the cells was evaluated by using real-time polymerase chain reaction, Western blotting, and immunocytochemistry. Western blotting and immunocytochemistry were used to assay EMT markers including vimentin, fibroblast-specific protein 1 (FSP1) and E-cadherin, small

mothers against decapentaplegic homolog2/3 (Smad2/3), and phosphorylated Smad2/3 in the cells. The levels of extracellular matrix components such as collagens I and III in supernatants were measured by enzyme-linked immunoassay. Morphological changes of the cells were observed under inverted phase-contrast microscope.

**Results:** A concentration-dependent increase of TGF-β1 mRNA and protein was observed following stimulation with TSLP. Furthermore, TSLP decreased the expression of E-cadherin protein, but upregulated the production of FSP1 and vimentin proteins along with increased levels of collagens I and III, and the morphology of the cells was transformed into fibroblast-like shape. Additionally, a significant increase was found in phosphorylation of Smad2/3 protein. However, these effects were reversed by SB431542 preincubation.

**Conclusion:** TSLP-induced HNECs to undergo the EMT process via TGF-β1-mediated Smad2/3 activation. TSLP is an activator of the EMT in HNECs and might be a potential target for inhibiting EMT and reducing airway remodeling in AR.

**Keywords:** allergic rhinitis; epithelial–mesenchymal transition; human nasal epithelial cells; small mothers against decapentaplegic homolog; thymic stromal lymphopoietin; transforming growth factor beta 1.



Minerva Med

. 2023 Aug 3.

doi: 10.23736/S0026-4806.23.08711-6. Online ahead of print.

# Clinical observation of leukotriene receptor antagonist montelukast

# sodium in the treatment of allergic rhinitis

Yanchun Chen[1], Gan Wang[1], Yaqin Liu[1], Xianwei Mei[2]

Affiliations expand

- PMID: 37534834

- DOI: 10.23736/S0026-4806.23.08711-6

*No abstract available*



PLoS One

. 2023 Aug 2;18(8):e0289407.

doi: 10.1371/journal.pone.0289407. eCollection 2023.

# Exploring Endotypes in Chronic Rhinosinusitis (ExpRess): Protocol for a cohort study

Shyam Ajay Gokani[1], Matthew Jefferson[2], Jelena Gavrilovic[2], Allan Clark[2], Falk Hildebrand[3], Tom Wileman[2 3], Claire Hopkins[4], Carl Philpott[1]

Affiliations expand


- PMID: 37531384

- PMCID: PMC10395813

- DOI: 10.1371/journal.pone.0289407

**Free PMC article**


# Abstract


**Background:** Chronic Rhinosinusitis (CRS) affects approximately 1 in 10 UK adults and impacts quality of life quality of life significantly. Response to treatment may be driven by individual CRS endotypes and therefore work to delineate biomarker clusters that may separate responders from non-responders is needed. The ongoing MACRO three-arm parallel-group trial randomises adult CRS patients to endoscopic sinus surgery, macrolide therapy or placebo.

**Aim:** This study aims to correlate CRS endotypes with clinical parameters from the ongoing MACRO trial, including olfactory function and outcomes in terms of response to treatment using core biomarkers sets.

**Methods:** Adult CRS patients enrolled into the MACRO trial will be recruited from participating UK otorhinolaryngology departments. Nasal tissue samples and swabs will be obtained in theatre or clinic from patients randomised to all three trial arms. Nasal tissue will be analysed with multiplex electrochemiluminescence for 32 cytokines including IL-5, IL-13, IgE and periostin. Bacterial swabs will be analysed using illumina miSeq 16S amplicon sequencing. Mean expression for each biomarker will be reported for treatment responder and non-responder groups. Correlation of biomarkers with MACRO trial outcome data such as endoscopic evaluation scores and quality-of-life improvement scores will be reported.

**Discussion:** Defining clear endotypes in CRS will contribute to refining patient pathways for the efficient use of clinical resources. This work may lay the groundwork for future studies to predict which patients might respond to medical or surgical therapy.




# Conflict of interest statement

The authors have declared that no competing interests exist.

- 10 references
- 1 figure

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grant supportexpand

FULL TEXT LINKS



Rhinology

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- 

. 2023 Aug 1;61(4):320-327.

doi: 10.4193/Rhin22.408.

# Efficacy and safety of switching between biologics in chronic rhinosinusitis with nasal polyps or N-ERD

F F Brkic[1], D T Liu[1], R Klimbacher[1], N J Campion[1], T J Bartosik[1], E Vyskocil[1], V Stanek[1], A Tu[1], T Arnoldner[2], C Bangert[2], K Gangl[1], J Eckl-Dorna[1], S Schneider[1]

Affiliations expand

- PMID: 37515811

- DOI: 10.4193/Rhin22.408

# Abstract

**Background and objective:** The effectiveness of biologics in chronic rhinosinusitis with nasal polyps (CRSwNP) is well-established. However, real-world experience on the effectiveness of transitioning between two monoclonal antibodies is scarce. Therefore, we aimed to analyze the safety and efficacy of antibody switching in treatment of chronic rhinosinusitis.

**Methods:** All patients with CRSwNP or nonsteroidal anti-inflammatory drugs-exacerbated respiratory disease (N-ERD) requiring a switch between biologics were retrospectively studied. Analysis included changes in polyp size, quality of life parameters, asthma control, and side effects.

**Results:** Out of 195 patients treated with biologics for CRSwNP or N-ERD in our center, 23 (11.8%) required transition to a different monoclonal antibody. The majority switched from omalizumab to dupilumab (17/23, 73.9%), mostly due to inadequate symptom control. Nine out of these 17 patients (52.9%) were switched without a washout period. All patients showed significant improvement in nasal polyp score, asthma control test and sino-nasal outcome test-22 after changing to dupilumab. Keratoconjunctivitis sicca was the side-effect (4.3%) reported after the switch from omalizumab to dupilumab, which lead to termination of therapy in one patient. Due to limited sample size, other antibody transitions were reported in a descriptive manner.

**Conclusion:** The transition to dupilumab is an effective option in patients with inadequate treatment response or side-effects of omalizumab in nasal polyposis. Our preliminary results indicate that a wash-out period may not be necessary when switching between biologics, however, these findings require further investigations. Other monoclonal antibody transitions also show promising results, but warrant validations in larger cohorts due to small patient samples in our study.

Pediatrics

. 2023 Aug 1;152(2):e2022060531.

doi: 10.1542/peds.2022-060531.

# Patterns in the Development of Pediatric Allergy

Stanislaw J Gabryszewski[1], Jesse Dudley[2], Di Shu[2,3], Jennifer A Faerber[2], Robert W Grundmeier[2], Alexander G Fiks[2], David A Hill[1,4]

Affiliations expand

- PMID: 37489286

- PMCID: PMC10389774 (available on 2024-08-01)

- DOI: 10.1542/peds.2022-060531

## Abstract

**Objectives:** Describe clinical and epidemiologic patterns of pediatric allergy using longitudinal electronic health records (EHRs) from a multistate consortium of US practices.

**Methods:** Using the multistate Comparative Effectiveness Research through Collaborative Electronic Reporting EHR database, we defined a cohort of 218 485 children (0-18 years) who were observed for ≥5 years between 1999 and 2020. Children with atopic dermatitis (AD), immunoglobulin E-mediated food allergy (IgE-FA), asthma, allergic rhinitis (AR), and eosinophilic esophagitis (EoE) were identified using a combination of diagnosis codes and medication prescriptions. We determined age at diagnosis, cumulative incidence, and allergic comorbidity.

**Results:** Allergic disease cumulative (and peak age of) incidence was 10.3% (4 months) for AD, 4.0% (13 months) for IgE-FA, 20.1% (13 months) for asthma, 19.7% (26 months) for AR,

and 0.11% (35 months) for EoE. The most diagnosed IgE-FAs were peanut (1.9%), egg (0.8%), and shellfish (0.6%). A total of 13.4% of children had ≥2 allergic conditions, and respiratory allergies (ie, asthma, AR) were commonly comorbid with each other, and with other allergic conditions.

**Conclusions:** We detail pediatric allergy patterns using longitudinal, health care provider-based data from EHR systems across multiple US states and varied pediatric practice types. Our results support the population-level allergic march progression and indicate high rates of comorbidity among children with food and respiratory allergies.



## Conflict of interest statement

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



Allergy

. 2023 Aug;78(8):2232-2254.

doi: 10.1111/all.15807. Epub 2023 Jul 11.

# Global, regional, and national burden of allergic disorders and their risk factors

# in 204 countries and territories, from 1990 to 2019: A systematic analysis for the Global Burden of Disease Study 2019

Youn Ho Shin[1,2], Jimin Hwang[3,4], Rosie Kwon[5], Seung Won Lee[6], Min Seo Kim[7,8]; GBD 2019 Allergic Disorders Collaborators; Jae Il Shin[9], Dong Keon Yon[5,10]

Collaborators, Affiliations expand

- PMID: 37431853

- DOI: 10.1111/all.15807

## Abstract

**Background:** Asthma and atopic dermatitis (AD) are chronic allergic conditions, along with allergic rhinitis and food allergy and cause high morbidity and mortality both in children and adults. This study aims to evaluate the global, regional, national, and temporal trends of the burden of asthma and AD from 1990 to 2019 and analyze their associations with geographic, demographic, social, and clinical factors.

**Methods:** Using data from the Global Burden of Diseases (GBD), Injuries, and Risk Factors Study 2019, we assessed the age-standardized prevalence, incidence, mortality, and disability-adjusted life years (DALYs) of both asthma and AD from 1990 to 2019, stratified by geographic region, age, sex, and socio-demographic index (SDI). DALYs were calculated as the sum of years lived with disability and years of life lost to premature mortality. Additionally, the disease burden of asthma attributable to high body mass index, occupational asthmagens, and smoking was described.

**Results:** In 2019, there were a total of 262 million [95% uncertainty interval (UI): 224-309 million] cases of asthma and 171 million [95% UI: 165-178 million] total cases of AD globally; age-standardized prevalence rates were 3416 [95% UI: 2899-4066] and 2277 [95% UI: 2192-2369] per 100,000 population for asthma and AD, respectively, a 24.1% [95% UI: -27.2 to -20.8] decrease for asthma and a 4.3% [95% UI: 3.8-4.8] decrease for AD compared to baseline in 1990. Both asthma and AD had similar trends according to age, with age-specific prevalence rates peaking at age 5-9 years and rising again in adulthood. The prevalence and incidence of asthma and AD were both higher for individuals with higher SDI; however, mortality and DALYs rates of individuals with asthma had a reverse trend, with higher mortality and DALYs rates in those in the lower SDI quintiles. Of the three risk factors, high body mass index contributed to the highest DALYs and deaths due to asthma,

accounting for a total of 3.65 million [95% UI: 2.14-5.60 million] asthma DALYs and 75,377 [95% UI: 40,615-122,841] asthma deaths.

**Conclusions:** Asthma and AD continue to cause significant morbidity worldwide, having increased in total prevalence and incidence cases worldwide, but having decreased in age-standardized prevalence rates from 1990 to 2019. Although both are more frequent at younger ages and more prevalent in high-SDI countries, each condition has distinct temporal and regional characteristics. Understanding the temporospatial trends in the disease burden of asthma and AD could guide future policies and interventions to better manage these diseases worldwide and achieve equity in prevention, diagnosis, and treatment.

**Keywords:** asthma; atopic dermatitis; disability-adjusted life years; eczema; epidemiology; global burden; mortality.



- 41 references

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS


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Cite

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7

Int Immunopharmacol

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. 2023 Aug;121:110559.

doi: 10.1016/j.intimp.2023.110559. Epub 2023 Jun 24.

# Hypoxia induces the production of epithelial-derived cytokines in eosinophilic chronic rhinosinusitis with nasal polyps

Meiping Zhang[1], Binxiang Tang[1], Ligui Huang[2], Yishan Xiong[3], Junhao Tu[3], Yizhen Jia[3], Fan Jiang[3], Li Shen[3], Qing Luo[3], Jing Ye[4]

Affiliations expand

- PMID: 37364325

- DOI: 10.1016/j.intimp.2023.110559

**Free article**

## Abstract

**Background:** Hypoxia plays a significant role in the pathogenesis of chronic rhinosinusitis (CRS). However, the role and mechanism of hypoxia in the type 2 immune response in eosinophilic chronic rhinosinusitis with nasal polyps (ECRSwNP) remain unclear.

**Methods:** The expression of hypoxia-inducible factor-1α (HIF-1α) and epithelial-derived cytokines (EDCs), including interleukin (IL)-25, IL-33, and thymic stromal lymphopoietin (TSLP), was detected in nasal polyps via immunohistochemical analysis. The relationship between HIF-1α and EDCs was also elucidated using Pearson's correlation. Moreover, primary human nasal epithelial cells (HNECs) and a mouse model of ECRSwNP were employed to elucidate the role and mechanism of hypoxia in type 2 immune responses.

**Results:** HIF-1α, IL-25, IL-33, and TSLP expression levels were upregulated in the non-ECRSwNP and ECRSwNP groups compared with the control group, with the ECRSwNP group having the highest HIF-1α and EDC expression levels. Additionally, HIF-1α was positively correlated with IL-25 and IL-33 in the ECRSwNP group. Meanwhile, treatment with a HIF-1α inhibitor, PX-478, inhibited the hypoxia-induced increase in the mRNA and protein expression of EDCs and type 2 cytokines in HNECs. Similarly, in vivo, PX-478 inhibited EDC expression in the sinonasal mucosa of mice with ECRSwNP.

**Conclusions:** Hypoxia induces EDC expression by upregulating HIF-1α levels, thereby promoting type 2 immune responses and the development of ECRSwNP. Hence, targeting HIF-1α may represent an effective therapeutic strategy for ECRSwNP.

**Keywords:** Eosinophilic chronic rhinosinusitis with nasal polyps; Epithelial-derived cytokines; Hypoxia; Hypoxia-inducible factor-1α; Type 2 immune response.



## Conflict of interest statement

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

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS


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8

Review

Curr Opin Allergy Clin Immunol

. 2023 Aug 1;23(4):341-345.

doi: 10.1097/ACI.0000000000000925. Epub 2023 Jun 19.

# Clinical outcomes of AIT in the elderly population

Andrzej Bożek[1]

Affiliations expand

- PMID: 37357782

- DOI: 10.1097/ACI.0000000000000925


# Abstract


**Purpose of review:** This review aims to present the current knowledge on the effectiveness and safety of allergen immunotherapy (AIT) in patients over 60 years of age with inhalant allergies.

**Recent findings:** Over the last 10 years, the problem of immunoglobulin E allergy in seniors has been noticed by many authors. At the same time, in the 1990s, trials of desensitization to selected inhalant allergens were started, obtaining evidence of the effectiveness of AIT, both with the use of sublingual immunotherapy (SLIT) and injection immunotherapy (SCIT), in patients over 60 years of age with allergic rhinitis. Such data have been confirmed for AITs for grasses, birch, and house dust mites. Currently, these patients are being monitored to assess the long-term effect of AIT. All available observations confirm the high safety of AIT in seniors.

**Summary:** Seniors with allergic rhinitis or asthma may qualify for AIT if they do not have contraindications. These patients can experience a sustained clinical benefit even after completing AIT treatment. Studies indicate that injectable and sublingual routes of administration may be effective in this age group, provided the suspect allergen is accurately diagnosed.





- 37 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS


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9

Int Immunopharmacol

. 2023 Aug;121:110449.

doi: 10.1016/j.intimp.2023.110449. Epub 2023 Jun 9.

# Overexpression of AXL on macrophages associates with disease severity and recurrence in chronic rhinosinusitis with nasal polyps

Tiansheng Wang[1], Yu Chen[1], Ru Gao[1], Jian Shui[2], Bin Xie[3]

Affiliations expand

- PMID: 37302367

- DOI: 10.1016/j.intimp.2023.110449

## Abstract

**Background:** Chronic rhinosinusitis with nasal polyps (CRSwNP) is characterized by high tissue heterogeneity and risk of postoperative recurrence, but the underlying mechanisms are poorly elucidated. This study aims to explore the expressions of AXL on macrophages and their roles in the pathogenesis of CRSwNP, and evaluate their associations with disease severity and recurrence.

**Methods:** Healthy controls (HCs), chronic rhinosinusitis without nasal polyps (CRSsNP) and CRSwNP patients were recruited in this study. Protein and mRNA levels of AXL and macrophage markers were detected in tissue samples, and their relationships with clinical variables and risk of postoperative recurrence were assessed. Immunofluorescence staining was conducted to confirm the location of AXL and its co-expression with macrophages. Regulated AXL in THP-1 and peripheral blood mononuclear cells (PBMC)-derived macrophages, and evaluated their polarization and cytokine secretion.

**Results:** We found that AXL was enhanced in the mucosa and serum samples of CRSwNP patients, especially in recurrent cases. Tissue AXL levels were positively correlated with

peripheral eosinophil count and percentage, Lund-Mackay score, Lund-Kennedy score, and macrophage M2 markers levels. Immunofluorescence staining results demonstrated that AXL was augmented and predominantly expressed on M2 macrophages in the tissues of CRSwNP, particularly in recurrent cases. In vitro experiment, overexpression of AXL promoted the M2 polarization of THP-1 and PBMC-derived macrophages, and facilitated the production of TGF-β1 and CCL-24.

**Conclusions:** AXL driving the M2 macrophage polarization exacerbated the disease severity and contributed to the postoperative recurrence in CRSwNP patients. Our findings supported AXL-targeted prevention and treatment of recurrent CRSwNP.

**Keywords:** AXL; Chronic rhinosinusitis with nasal polyps; Disease severity; Macrophages; Recurrence.



# Conflict of interest statement

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

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS


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10

Biomed Pharmacother

. 2023 Aug;164:114959.

doi: 10.1016/j.biopha.2023.114959. Epub 2023 May 31.

# Bergapten ameliorates combined allergic rhinitis and asthma syndrome after PM2.5 exposure by balancing Treg/Th17 expression and suppressing STAT3 and MAPK activation in a mouse model

Yuna Jiang[1], Thi Van Nguyen[1], Juan Jin[1], Zhen Nan Yu[1], Chang Ho Song[2], Ok Hee Chai[3]

Affiliations expand

- PMID: 37267637

- DOI: 10.1016/j.biopha.2023.114959

**Free article**

## Abstract

Combined allergic rhinitis and asthma syndrome (CARAS) causes chronic respiratory inflammation in allergic individuals. Long-term exposure to particulate matter 2.5 (PM2.5; particles 2.5 μm or less in diameter) can aggravate respiratory damage. Bergapten (5-methoxysporalen) is a furocoumarin mostly found in bergamot essential oil and has significant antioxidant, anticancer, and anti-inflammatory activity. This study created a model in which CARAS was exacerbated by PM2.5 exposure, in BALB/c mice and explored the potential of bergapten as a therapeutic agent. The bergapten medication increased ovalbumin (OVA)-specific immunoglobulin (Ig) G2a level in serum and decreased OVA-specific IgE and IgG1 expression. Clinical nasal symptoms diminished significantly, with weakened inflammatory reaction in both the nasal mucosa and lungs. Furthermore, bergapten controlled the T helper (Th)1 to Th2 ratio by increasing cytokines associated with Th1-like interleukin (IL)-12 and interferon gamma and decreasing the Th2 cytokines IL-4, IL-5, and IL-13. Factors closely related to the balance between regulatory T cells and Th17 (such as IL-10, IL-17, Forkhead box protein P3, and retinoic-related orphan receptor gamma) were also regulated. Notably, pro-inflammatory cytokines IL-6, IL-1β, and tumor necrosis factor-alpha were reduced by bergapten, which suppressed the activation of both the signal transducer and activator of transcription 3 signaling pathway and the mitogen-activated protein kinase signaling pathway. Therefore, bergapten might have potential as a therapeutic agent for CARAS.

**Keywords:** Bergapten; CARAS; MAPK pathway; PM2.5; STAT3; Treg/Th17 balance.



## Conflict of interest statement

Declaration of Competing Interest The authors affirm that this paper is free of any conflicts of interest.



Multicenter Study

Respir Med

. 2023 Aug-Sep;215:107299.

doi: 10.1016/j.rmed.2023.107299. Epub 2023 May 29.

# Development of a diagnostic score using FeNO and symptoms to predict asthma

Benjamin Brunn[1], Alexander Hapfelmeier[2], Rudolf A Jörres[3], Konrad Schultz[4], Antonius Schneider[5]

Affiliations expand

- PMID: 37257788

- DOI: 10.1016/j.rmed.2023.107299

# Abstract

**Background:** Fractional exhaled nitric oxide (FeNO) is known as effective for ruling-in asthma. The diagnostic value might be increased in combination with clinical signs and symptoms (CSS). The aim was to develop a new model for ruling-in and ruling-out asthma.

**Methods:** Diagnostic multi-centre study in three practices of pneumologists in Germany. Whole-body plethysmography was combined with bronchodilation tests or bronchial provocation as diagnostic reference standard. Follow-up was performed after 3 months. An expert committee evaluated test results, symptoms, and course of disease for the final diagnosis. Relevant CSS known from guidelines were used to enable combinatorial development of decision rules. Outcomes of multiple logistic regression modeling were translated into a diagnostic score and internally validated by ten-fold cross validation.

**Results:** 308 patients with complete follow-up were included. 186 (60.4%) were female, average age was 44.7 years and 161 (52.5%) had asthma. The average area under the receiver operating curve (AUC) of the diagnostic score was 0.755 (interquartile range 0.721-0.814). Allergic rhinitis, wheezing, dyspnea on exertion, coughing attacks at night, and awakening by shortness of breath were leading symptoms for ruling-in asthma. Frequent coughing and frequent respiratory infections were leading symptoms for ruling-out. The combination of FeNO and CSS allowed ruling-in asthma with a probability of up to 99%, and ruling-out with a post-test probability down to 9%.

**Conclusion:** The diagnostic scoring model increased the diagnostic value of FeNO in combination with CSS. The new decision rule allowed to rule-in asthma with high certainty, and also to rule-out with acceptable certainty.

**Keywords:** Asthma; Clinical decision rule; Diagnostic study; Fractional exhaled nitric oxide; Primary health care; Symptoms.



# Conflict of interest statement

Declaration of competing interest AS is an external expert for the Federal Joint Committee (Gemeinsamer Bundesausschuss) with regard to the development of the disease management programs for asthma and COPD; he received regular remuneration for taking part in the sessions. AS and KS are members of the National Asthma Guideline Board

(Nationale Versorgungsleitlinie Asthma). The other authors declare that no conflicts of interest exist.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS



Acta Otorhinolaryngol Ital

. 2023 Aug;43(4):252-261.

doi: 10.14639/0392-100X-N2212. Epub 2023 May 23.

# Italian version of the Brief Questionnaire of Olfactory Disorders (Brief-IT-QOD)

Arianna Cardella[1,2], Giuseppe Riva[3], Andrea Preti[1], Andrea Albera[3], Livio Luzi[2,4], Roberto Albera[3], Davide Cadei[1], Gian Marco Motatto[3], Filippo Omenetti[1], Giancarlo Pecorari[3], Francesco Ottaviani[1,5], Francesco Mozzanica[1,5]

Affiliations expand

- PMID: 37224170

- PMCID: PMC10366567

- DOI: 10.14639/0392-100X-N2212

**Free PMC article**


# Abstract

## in English, Italian


**Objective:** To evaluate the reliability and validity of the Italian version of the Brief Questionnaire of Olfactory Disorders (Brief-IT-QOD).

**Methods:** The study consisted of six phases: item generation, reliability analysis (112 dysosmic patients for internal consistency analysis and 61 for test-retest reliability analysis), normative data generation (303 normosmic subjects), validity analysis (comparison of Brief-IT-QOD scores of healthy and dysosmic subjects and scores correlation with psychophysical olfactory testing TDI and SNOT-22 scores), responsiveness analysis (10 dysosmic chronic rhinosinusitis with nasal polyps patients before and after biologic therapy), and cut-off value determination (ROC curve analysis of Brief-IT-QOD sensitivity and specificity).

**Results:** All subjects completed the Brief-IT-QOD. Internal consistency ($\alpha > 0.70$) and test-retest reliability (ICC > 0.7) were acceptable and satisfactory for both questionnaire subscales. A significant difference between dysosmic and control subjects was found in both subscales ($p < 0.05$). Significant correlations between subscales scores and TDI and SNOT-22 scores were observed. Brief-IT-QOD scores before treatment were significantly higher than after biological therapy.

**Conclusions:** Brief-IT-QOD is reliable, valid, responsive to changes in QoL, and recommended for clinical practice and outcome research.



**Keywords:** olfaction disorders; quality of life; questionnaire.




# Conflict of interest statement

The authors declare no conflict of interest.

- 25 references
- 5 figures

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

Editorial

Int Forum Allergy Rhinol

. 2023 Aug;13(8):1489-1491.

doi: 10.1002/alr.23186. Epub 2023 Jun 2.

# Allergies, depression, and anxiety: The role of the rhinologist

David A Gudis[1], Rodney J Schlosser[2], Claire Hopkins[3], Claus Bachert[4,5], Elina Toskala[6], Sarah K Wise[7]

Affiliations expand

- PMID: 37208976

- DOI: 10.1002/alr.23186

*No abstract available*

**Keywords:** allergic rhinitis; allergies; anxiety; depression; mood disorders.

Sci Total Environ

. 2023 Aug 1;884:163802.

doi: 10.1016/j.scitotenv.2023.163802. Epub 2023 Apr 29.

# Long-term residential exposure to air pollution and risk of chronic respiratory diseases in Italy: The BIGEPI study

Pierpaolo Marchetti[1], Jessica Miotti[1], Francesca Locatelli[1], Leonardo Antonicelli[2], Sandra Baldacci[3], Salvatore Battaglia[4], Roberto Bono[5], Angelo Corsico[6], Claudio Gariazzo[7], Sara Maio[3], Nicola Murgia[8], Pietro Pirina[9], Camillo Silibello[10], Massimo Stafoggia[11], Lorena Torroni[1], Giovanni Viegi[3], Giuseppe Verlato[1], Alessandro Marcon[12]; BIGEPI group

Affiliations expand

- PMID: 37127163

- DOI: 10.1016/j.scitotenv.2023.163802

**Free article**

## Abstract

Long-term exposure to air pollution has adverse respiratory health effects. We investigated the cross-sectional relationship between residential exposure to air pollutants and the risk of suffering from chronic respiratory diseases in some Italian cities. In the BIGEPI project, we harmonised questionnaire data from two population-based studies conducted in 2007-2014. By combining self-reported diagnoses, symptoms and medication use, we identified cases of rhinitis (n = 965), asthma (n = 328), chronic bronchitis/chronic obstructive pulmonary disease (CB/COPD, n = 469), and controls (n = 2380) belonging to 13 cohorts from 8 Italian cities (Pavia, Turin, Verona, Terni, Pisa, Ancona, Palermo, Sassari). We derived mean residential concentrations of fine particulate matter ($PM_{10}$, $PM_{2.5}$), nitrogen dioxide ($NO_2$), and summer ozone ($O_3$) for the period 2013-2015 using spatiotemporal models at a 1 km resolution. We fitted logistic regression models with controls as reference category, a random-intercept for cohort, and adjusting for sex, age, education, BMI, smoking, and climate. Mean ± SD exposures were 28.7 ± 6.0 μg/m$^3$ ($PM_{10}$), 20.1 ± 5.6 μg/m$^3$ ($PM_{2.5}$), 27.2 ± 9.7 μg/m$^3$ ($NO_2$), and 70.8 ± 4.2 μg/m$^3$ (summer $O_3$). The concentrations of $PM_{10}$, $PM_{2.5}$, and $NO_2$ were higher in Northern Italian cities. We found associations between PM exposure and rhinitis ($PM_{10}$: OR 1.62, 95%CI: 1.19-2.20 and $PM_{2.5}$: OR 1.80, 95%CI: 1.16-2.81, per 10 μg/m$^3$) and between $NO_2$ exposure and CB/COPD (OR 1.22, 95%CI: 1.07-1.38 per 10 μg/m$^3$), whereas asthma was not related to environmental exposures. Results remained consistent using different adjustment sets, including bi-pollutant models, and after excluding subjects who had changed residential address in the last 5 years. We found novel evidence of association between long-term PM exposure and increased risk of rhinitis, the chronic respiratory disease with the highest prevalence in the general population. Exposure to $NO_2$, a pollutant characterised by strong oxidative properties, seems to affect mainly CB/COPD.

**Keywords:** Air quality; Asthma; Chronic bronchitis; Epidemiology; Public health; Rhinitis.



# Conflict of interest statement

Declaration of competing interest Sara Maio reports financial support was provided by National Institute for Insurance against Accidents at Work.

Meta-Analysis

Rhinology

. 2023 Aug 1;61(4):290-296.

doi: 10.4193/Rhin21.380.

# Intranasal antihistamines in the treatment of idiopathic non-allergic rhinitis: a systematic review and meta-analysis

N Khoueir[1], M G Khalaf[1], R Assily[1], S Rassi[1], W A Hamad[1]

Affiliations expand

- PMID: 37083127

- DOI: 10.4193/Rhin21.380

## Abstract

**Background:** Idiopathic rhinitis (IR), previously known as vasomotor rhinitis (VMR), is the most common type of non-allergic rhinitis (NAR) which affects around 100 million people worldwide. The treatment of patients with IR is not standardized. Intranasal antihistamines (INAH) are potent drugs in the treatment of allergic rhinitis but are frequently prescribed in the treatment of IR. This systematic review of the literature and meta-analysis aims to assess the effects of INAH on IR.

**Methodology:** A comprehensive review of the literature was conducted on Medline, Embase and Cochrane library. Randomized, controlled trials and non-randomized comparative parallel group trials comparing INAH to placebo or different INAHs were included. The primary outcome was the change in disease specific quality of life questionnaires, total nasal symptom score (TNSS). The secondary outcomes were other reported nasal symptom scores, individual symptom scores and adverse events.

**Results:** Six trials out of 987 assessing a total of 675 participants were deemed relevant for inclusion. Compared to placebo, INAH decreased total nasal symptom scores. One study also reported reduction of symptoms recorded on a visual analogue scale. There was no difference between the INAHs in terms of efficacy. Bitter taste sensation was the most frequently reported adverse event.

**Conclusions:** INAHs seem to have benefit over placebo on nasal symptoms improvement in the treatment of NAR. No superiority between INAHs was identified.



J Clin Sleep Med

. 2023 Aug 1;19(8):1545-1552.

doi: 10.5664/jcsm.10608. Online ahead of print.

# A sleep clinician's guide to runny noses: evaluation and management of chronic

# rhinosinusitis to improve sleep apnea care in adults

Mir M Ali[1], Matthew Ellison[2], Onyinye I Iweala[3], Andrew R Spector[1]

Affiliations expand

- PMID: 37082825

- PMCID: PMC10394352 (available on 2024-08-01)

- DOI: 10.5664/jcsm.10608

## Abstract

**Study objectives:** The treatment of obstructive sleep apnea is often impeded by intolerance of positive airway pressure therapy, which is frequently attributed to the inability to breathe through the nose. Providers caring for patients with sleep apnea need a working knowledge of nasal passage disease and available treatments to better manage this common comorbidity.

**Methods:** This review examines the literature connecting rhinosinusitis to adverse sleep and sleep apnea outcomes. It explores the different types of nasal and sinus diseases a sleep apnea provider might encounter, focusing on the medications used to treat them and indications for referral to otolaryngology.

**Results:** Chronic rhinosinusitis can be either allergic or nonallergic. Both types can interfere with sleep and sleep apnea therapy. The successful management of chronic rhinosinusitis can improve positive airway pressure tolerance and adherence. A wide range of over-the-counter and prescription pharmacotherapy is available, with data supporting intranasal over oral treatment. Surgical treatment for chronic rhinosinusitis in obstructive sleep apnea addresses nasal obstruction, often with inferior turbinate reduction and septoplasty.

**Conclusions:** Sleep specialists should have a working knowledge of the available options to treat chronic rhinosinusitis. These options are often safe, effective, and readily accessible. Otolaryngologists and allergists/immunologists provide additional treatment options for more complicated patients. Providing treatment for chronic rhinosinusitis should be included as part of comprehensive sleep apnea care.

**Citation:** Ali MM, Ellison M, Iweala OI, Spector AR. A sleep clinician's guide to runny noses: evaluation and management of chronic rhinosinusitis to improve sleep apnea care in adults. *J Clin Sleep Med*. 2023;19(8):1545-1552.

**Keywords:** allergic rhinitis; obstructive sleep apnea; rhinosinusitis; sinus disease.



## Conflict of interest statement

All authors have seen and approved the manuscript. The authors report no conflicts of interest.



Randomized Controlled Trial

Rhinology

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. 2023 Aug 1;61(4):328-337.

doi: 10.4193/Rhin22.328.

# Blood eosinophils to direct oral corticosteroid treatment for patients with nasal polyps â€" an open label,

# non-inferiority, randomized control trial

J Deng[1], Z Wang[2], Z Xu[1], Y Lai[1], R Zheng[1], W Gao[1], J Shi[1], Y Sun[3]

Affiliations expand

- PMID: 37066680

- DOI: 10.4193/Rhin22.328

## Abstract

**Background:** Chronic rhinosinusitis with nasal polyps (CRSwNP) is a heterogeneous disorder. We aimed to evaluate the value of blood eosinophil count (BEC) for guiding oral corticosteroid therapy for CRSwNP.

**Methods:** Subjects with CRSwNP were entered into a 2:1 randomized biomarker-directed corticosteroid versus standard therapy study base on the principle of potential benefits to patients. Subjects in the standard arm received oral prednisone (30mg/day) alone for 7 days, whereas in the biomarker-directed arm, prednisone (30mg/day), or nasal steroid spray (budesonide 256ug/day) was given according to the BEC which was measured to define eosinophil-high and -low CRSwNP (BEC > and < 0.37x109/L, respectively). The primary outcome was the total nasal symptom scores (TNSS) of the two arms with the non-inferiority margin of 1.8. Secondary outcomes included nasal polyp size scores (NPSS) and SNOT-22. Patients were followed up the day after last dose of treatment.

**Results:** A total of 105 subjects with CRSwNP were randomized into the biomarker-directed therapy group or the standard care group. The biomarker therapy demonstrated non-inferiority compared to standard care. There were no between-group differences for TNSS, NPSS and SNOT-22 improvements after treatment. Comparisons of TNSS, SNOT-22 and NPSS revealed no significant difference in terms of the effectiveness ratios of the biomarker-directed therapy and the standard care.

**Conclusion:** A biomarker-directed strategy using the BEC can be used to direct corticosteroid therapy without increasing treatment failure or worsening of symptoms in patients with CRSwNP.

- Cited by 1 article

SUPPLEMENTARY INFO

Review

Otolaryngol Head Neck Surg

. 2023 Aug;169(2):221-226.

doi: 10.1002/ohn.297. Epub 2023 Feb 17.

# Minimal Radiographic Mucosal Thickness or Opacification Criterion for Sinus-Specific Endoscopic Sinus Surgery for Chronic Rhinosinusitis

Zoe A Walters[1], Katie M Phillips[1], Melissa J Previtera[2], Stacey T Gray[3], Ahmad R Sedaghat[1]

Affiliations expand

- PMID: 36807128

- DOI: 10.1002/ohn.297

## Abstract

**Objective:** Primary chronic rhinosinusitis (CRS) is typically a diffuse process and the extent of endoscopic sinus surgery (ESS) performed for medically recalcitrant CRS is impacted by many factors. However, some third-party payors have implemented policies to authorize coverage for ESS in a sinus-by-sinus manner based on a minimal measurement of millimeters of mucosal thickening or sinus opacification in the corresponding sinus that is being surgically addressed. Our objective was to determine whether such policies are based on scientific evidence that in patients with medically recalcitrant CRS, a minimum measurement of mucosal thickening or sinus opacification is a predictor of CRS in that sinus or improved outcomes after ESS on a sinus-by-sinus basis.

**Data sources:** Medline, Embase, Scopus, and Web of Science databases, from inception through May 2022.

**Review methods:** A systematic review was performed. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines were followed.

**Results:** We identified 6070 abstracts which were screened and from which 112 studies ultimately underwent a full-text review. From these studies, we found that none investigated (or provided evidence of) whether any minimal degree of radiographic mucosal thickening or sinus opacification predicted CRS or better outcomes after ESS in a sinus-specific manner.

**Conclusion:** We were unable to find evidence supporting a minimum millimeter measurement of mucosal thickening or sinus opacification as predictors of CRS or better post-ESS outcomes in a sinus-specific manner in patients with medically recalcitrant CRS. The extent of ESS for CRS should be determined through personalized medical decision-making that considers all patient-specific factors.

**Keywords:** coverage; endoscopic sinus surgery; insurance; millimeters; minimum mucosal thickening; payor; reimbursement; sinus opacification.



- 41 references

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

Arch Dermatol Res

. 2023 Aug;315(6):1823-1826.

doi: 10.1007/s00403-023-02539-z. Epub 2023 Jan 28.

# Psoriasis associated with asthma and allergic rhinitis: a US-based cross-sectional study using the All of US Research Program

Marina Z Joel [1], Ryan Fan [2], William Damsky [3 4], Jeffrey M Cohen [5]

Affiliations expand

- PMID: 36707438

- DOI: 10.1007/s00403-023-02539-z

## Abstract

Psoriasis is a common chronic inflammatory disease with multiple known comorbidities. Increasing evidence suggests some mechanistic overlap in the immunopathogenesis of psoriasis and some cases of asthma and allergic rhinitis (AR), but the potential association between psoriasis and asthma and AR has not been thoroughly investigated. The study aimed to investigate the association between psoriasis and asthma and AR. We used data from the NIH All of US Research Program, a nationwide longitudinal cohort of US adults, collected from 2018 to present. The source population comprised a demographically and socioeconomically diverse cohort of over 300,000 Americans. We used multivariable logistic regression models to examine the association between psoriasis and asthma and

AR, after adjusting for sociodemographic variables, body mass index, and smoking status. In total, 235,551 participants (mean [SD] age, 54.7 [16.6] years; 59.3% female), including 5165 individuals with psoriasis and 230,386 individuals without psoriasis, were included in our analysis. Participants with psoriasis had significantly higher prevalence of asthma (26.1% vs. 12.9%; P < 0.001) and AR (31.8% vs. 13.4%; P < 0.001) compared to participants without psoriasis. Psoriasis was significantly associated with both asthma [adjusted odds ratio (aOR) 2.22; 95% confidence interval (CI) 2.08-2.37] and AR (aOR, 2.57; 95% CI 2.42-2.73). In subgroup analyses, associations remained stable in multivariable analyses after stratification by age, sex, and income. Psoriasis is associated with both asthma and AR in our sample of US adults. Further research is needed to explore potentially unifying inflammatory pathways among psoriasis, asthma, and AR.

**Keywords:** Allergic rhinitis; Asthma; Cross-sectional; Epidemiology; Psoriasis.



- 15 references

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

SpringerLink FULL-TEXT ARTICLE UNIMORE

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Int Forum Allergy Rhinol

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. 2023 Aug;13(8):1561-1563.

doi: 10.1002/alr.23110. Epub 2022 Nov 29.

# Effect of dupilumab on Eustachian tube dysfunction in patients with chronic rhinosinusitis with nasal polyposis

Michael T Chang[1], Pooya Roozdar[1], Yi-Tsen Lin[2], Jennifer Y Lee[1], Jayakar V Nayak[1], Zara M Patel[1], Peter H Hwang[1]

Affiliations expand

- PMID: 36399364

- DOI: 10.1002/alr.23110

*No abstract available*

**Keywords:** chronic rhinosinusitis; quality of life; therapeutics.

- 6 references

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS

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Int Forum Allergy Rhinol

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. 2023 Aug;13(8):1542-1545.

doi: 10.1002/alr.23108. Epub 2022 Nov 29.

# Dupilumab-related adverse events among patients with chronic rhinosinusitis with nasal polyposis

Daniel J Lee[1], Hannah B Cramer[1], Rijul S Kshirsagar[2], Jennifer E Douglas[1], Michael A Kohanski[1], James N Palmer[1], Nithin D Adappa[1], John V Bosso[1]

Affiliations expand

- PMID: 36394542

- DOI: 10.1002/alr.23108

*No abstract available*

**Keywords:** adverse; autoimmune reaction; dupilumab; event; severe.

- 8 references

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS




1
Heart Lung

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. 2023 Aug 2;62:168-174.

doi: 10.1016/j.hrtlng.2023.07.008. Online ahead of print.

# Relationship between nighttime symptoms and clinical features in COPD patients: A cross-sectional multicenter study in China

Jiankang Wu[1], Weiwei Meng[1], Huihui Zeng[1], Yiming Ma[1], Yan Chen[2]

Affiliations expand

- PMID: 37541136

- DOI: 10.1016/j.hrtlng.2023.07.008

## Abstract

**Background:** Chronic obstructive pulmonary disease (COPD) is a chronic respiratory disease that causes breathing difficulties, coughing, and other symptoms. Nighttime symptoms, such as coughing, wheezing, and shortness of breath, can significantly impact the quality of life for people with COPD.

**Objective:** To investigate the relationship between nighttime symptoms and other clinical features in patients with COPD, and identify potential risk factors associated with nighttime symptoms.

**Methods:** This cross-sectional study was conducted from October 1, 2022 to November 30, 2022 in 24 hospital outpatient departments in different cities of Hunan Province, China. The COPD Nighttime Symptom Instrument (NiSCI) was used to measure the severity of night time symptoms in COPD patients. Descriptive and inferential statistics were used to express patient socio-demographics and factors influencing nighttime symptoms.

**Results:** The study included 2219 COPD patients. The results showed that nighttime symptom scores differed significantly based on gender, whether the patient had experienced acute exacerbation in the past year, mMRC and CAT scores, the duration of home oxygen therapy and home non-invasive ventilation (all $P < 0.0001$). Multiple linear regression analysis revealed that CAT score ($P < 0.0001$) was significantly associated with nighttime symptom scores.

**Conclusion:** Nighttime symptoms are prevalent in Chinese COPD patients and correlate with disease severity. The assessment and management of nighttime symptoms in COPD patients must take into account gender, CAT and mMRC scores, history of acute exacerbations, and duration of home oxygen therapy and home non-invasive ventilation to enable tailoring of treatment strategies to individual needs.

**Keywords:** COPD; Clinical features; Nighttime symptoms; Related factors.

## Conflict of interest statement

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



EClinicalMedicine

. 2023 Jul 20;62:102100.

doi: 10.1016/j.eclinm.2023.102100. eCollection 2023 Aug.

# Efficacy and safety of pharmacotherapy for refractory or unexplained chronic cough: a systematic review and network meta-analysis

Ziwen Zheng[1,2,3], Junfeng Huang[1,3], Ziyuan Xiang[1,3], Tong Wu[1,2,3], Xiaoqing Lan[1,2,3], Shuojia Xie[1,2,3], Zikai Lin[1,2,3], Kailun Tang[1,4,3], Alyn Morice[5], Shiyue Li[1,3], Woo-Jung Song[6], Ruchong Chen[1,3]

Affiliations expand

- PMID: 37538538

- PMCID: PMC10393600

- DOI: 10.1016/j.eclinm.2023.102100

# Abstract

**Background:** Refractory chronic cough (RCC) has a significant impact on patient's health-related quality of life and represents a challenge in clinical management. However, the optimal treatment for RCC remains controversial. This study aimed to investigate and compare the efficacy and safety of the current pharmacological therapeutic options for RCC.

**Methods:** A systematic review was performed by searching PubMed, Web of Science, Embase, and Ovid databases from January 1, 2008 to March 1, 2023. All randomised control trials (RCTs) reporting outcomes of efficacy or/and safety were included in the Bayesian network meta-analysis. Here, we compared the effects on Leicester Cough Questionnaire (LCQ), Visual Analogue Scale (VAS), and objective cough frequency of patients with RCC. Besides, we also compared the incidence of adverse events (AEs) for analysis of safety. PROSPERO registration: CRD42022345940.

**Findings:** 19 eligible RCTs included 3326 patients and 7 medication categories: P2X3 antagonist, GABA modulator, Transient Receptor Potential (TRP) modulator, NK-1 agonist, opioid analgesic, macrolide, and sodium cromoglicate. Compared with placebo, mean difference (MD) of LCQ and 24 h cough frequency for P2X3 antagonist relief were 1.637 (95% CI: 0.887-2.387) and -11.042 (P = 0.035). Compared with placebo, effect sizes (MD for LCQ and cough severity VAS) for GABA modulator were 1.347 (P = 0.003) and -7.843 (P = 0.003). In the network meta-analysis, gefapixant is the most effective treatment for patients with RCC (The Surface Under the Cumulative Ranking Curves (SUCRA) is 0.711 in LCQ, 0.983 in 24 h cough frequency, and 0.786 in cough severity VAS). Lesogaberan had better efficacy than placebo (SUCRA: 0.632 vs. 0.472) in 24 h cough frequency. Eliapixant and lesogaberan had better efficacy than placebo in cough severity VAS. However, TRP modulator had worse efficacy than placebo. In the meta-analysis of AEs, the present study found P2X3 antagonist had a significant correlation to AEs (RR: 1.129, 95% CI: 1.012-1.259), especially taste-related AEs (RR: 6.216, P < 0.05).

**Interpretation:** In this network meta-analysis, P2X3 antagonist showing advantages in terms of efficacy is currently the most promising medication for treatment of RCC. GABA modulator also showed potential efficacy for RCC but with AEs of the central system. Nevertheless, the role of TRP modulator needed to be revisited. Further research is needed to determine the potential beneficiary population for optimizing the pharmacological management of chronic cough.

**Funding:** National Natural Science Foundation of China (81870079), Guangdong Science and Technology Project (2021A050520012), Incubation Program of National Science Foundation for Distinguished Young Scholars (GMU2020-207).

**Keywords:** Efficacy; Network meta-analysis; Pharmacotherapy; Refractory chronic cough.



# Conflict of interest statement

All authors declare that they have no conflict of interest.

- 56 references
- 3 figures

Ann Allergy Asthma Immunol

. 2023 Aug;131(2):275.

doi: 10.1016/j.anai.2023.03.035.

# Chronic cough is complicated

Miles Weinberger[1]

Affiliations expand

- PMID: 37536874

- DOI: 10.1016/j.anai.2023.03.035

*No abstract available*

Review

Clin Transl Med

. 2023 Aug;13(8):e1343.

doi: 10.1002/ctm2.1343.

# From bench to bedside: The role of cough hypersensitivity in chronic cough

Matthew G Drake[1], Lorcan P McGarvey[2], Alyn H Morice[3]

Affiliations expand

- PMID: 37501282
- PMCID: PMC10374883
- DOI: 10.1002/ctm2.1343

**Free PMC article**

## Abstract

**Background:** Chronic cough is a burdensome condition characterized by persistent cough lasting longer than 8 weeks. Chronic cough can significantly affect quality of life, physical function and productivity, with many people troubled with a cough that lasts for months or even years. People with chronic cough commonly report a persistent urge to cough with frequent bouts of coughing triggered by innocuous stimuli, which has led to the concept of cough hypersensitivity.

**Main body:** Both central and peripheral neural pathways regulate cough, and although mechanisms driving development of cough hypersensitivity are not fully known, sensitization of these neural pathways contributes to excessive cough triggering in cough hypersensitivity. Effective therapies that control chronic cough are currently lacking. Recent therapeutic development has focused on

several ion channels and receptors involved in peripheral activation of cough (e.g., transient receptor potential channels, P2 × 3 receptors and voltage-gated sodium channels) or central cough processing (e.g., neurokinin-1 [NK-1] receptors and nicotinic acetylcholine receptors).

**Conclusion:** These targeted therapies provide novel insights into mechanisms underlying cough hypersensitivity and may offer new treatment options for people with chronic cough. In this review, we explore preclinical and clinical studies that have improved our understanding of the mechanisms responsible for chronic cough and discuss the most promising targeted approaches to date, including trials of P2 × 3-receptor antagonists and NK-1-receptor antagonists.

**Keywords:** antitussives; cough sensitization; refractory chronic cough; unexplained chronic cough.



# Conflict of interest statement

Matthew G. Drake reports receiving consultancy fees from AstraZeneca, Chiesi, GSK and MSD. Lorcan P. McGarvey reports receiving consultancy fees from Applied Clinical Intelligence, Bayer, Bellus Health, Bionorica, Chiesi, MSD, Nocion Therapeutics and Shionogi; receiving an investigator-initiated grant from MSD; participating on a data safety-monitoring/advisory board for AstraZeneca, Bayer, Bellus Health, Chiesi, MSD, Nocion Therapeutics, Shionogi and Trevi; and serving as cochair of ERS NEuroCOUGH Clinical Research Consortium. Alyn H. Morice reports receiving consultancy fees from Bayer, Bellus Health, Boehringer Ingelheim, MSD, Pfizer, Procter & Gamble and Shionogi; receiving payment or honoraria for lectures, presentations, or speakers bureaus from AstraZeneca, Boehringer Ingelheim and MSD; receiving grant support from Afferent, Infirst, MSD and Procter & Gamble; and serving as chair of the Hull University Teaching Hospitals Drug and Therapeutics Committee.

Respirology

. 2023 Aug;28(8):807-816.

doi: 10.1111/resp.14548. Epub 2023 Jul 11.

# Towards regional progress: APSR 2022 Big Five Lung Diseases Workshop

Paul N Reynolds[1], Sameera Ansari[2,3], Rosalyn Hernandez-Sebastian[4], Watchara Boonsawat[5], Shih-Yu Chen[6], Landy Lan[7,8], Dawei Yang[8], G M Monsur Habib[9], Jennifer Ann Mendoza-Wi[10], Hung-Ling Huang[11,12,13], Le Thi Tuyet Lan[14], Nguyen Nhu Vinh[14], Maria Lowella F De Leon[15], Anne B Chang[16,17]

Affiliations expand

- PMID: 37433568

- DOI: 10.1111/resp.14548

*No abstract available*

**Keywords:** COPD; COVID-19; asthma; lung cancer; respiratory infections; tuberculosis.

. 2023 Aug;29(8):927-937.

doi: 10.18553/jmcp.2023.22417. Epub 2023 May 27.

# Identifying potentially undiagnosed nontuberculous mycobacterial lung disease among patients with chronic obstructive pulmonary disease: Development of a predictive algorithm using claims data

Ping Wang[1], Theodore K Marras[2], Paul D Allison[3], Mariam Hassan[1], Anjan Chatterjee[1]

Affiliations expand

- PMID: 37243674

- PMCID: PMC10397327

- DOI: 10.18553/jmcp.2023.22417

**Free PMC article**

## Abstract

**BACKGROUND:** Nontuberculous mycobacterial lung disease (NTMLD) is a debilitating disease. Chronic obstructive pulmonary disease (COPD) is the leading comorbidity associated with NTMLD in the United States. Their similarities in symptoms and overlapping radiological findings may delay NTMLD diagnosis in patients with COPD. **OBJECTIVE:** To develop a predictive model that identifies potentially undiagnosed NTMLD among patients with COPD. **METHODS:** This retrospective cohort study developed a predictive model of NTMLD using US Medicare beneficiary claims data (2006 - 2017). Patients with COPD with NTMLD were matched 1:3 to patients with COPD without NTMLD by age, sex, and year of COPD diagnosis. The predictive model was developed using logistic regression modeling risk factors such as pulmonary symptoms, comorbidities, and health care resource utilization. The final model was based on model fit statistics and clinical inputs. Model performance was evaluated for both discrimination and generalizability with c-statistics and receiver operating characteristic curves. **RESULTS:** There were 3,756 patients

with COPD with NTMLD identified and matched to 11,268 patients with COPD without NTMLD. A higher proportion of patients with COPD with NTMLD, compared with those with COPD without NTMLD, had claims for pulmonary symptoms and conditions, including hemoptysis (12.6% vs 1.4%), cough (63.4% vs 24.7%), dyspnea (72.5% vs 38.2%), pneumonia (59.2% vs 13.4%), chronic bronchitis (40.5% vs 16.3%), emphysema, (36.7% vs 11.1%), and lung cancer (15.7% vs 3.5%). A higher proportion of patients with COPD with NTMLD had pulmonologist and infectious disease (ID) specialist visits than patients with COPD without NTMLD (≥ 1 pulmonologist visit: 81.3% vs 23.6%, respectively; ≥ 1 ID visit: 28.3% vs 4.1%, respectively, $P < 0.0001$). The final model consists of 10 risk factors (≥ 2 ID specialist visits; ≥ 4 pulmonologist visits; the presence of hemoptysis, cough, emphysema, pneumonia, tuberculosis, lung cancer, or idiopathic interstitial lung disease; and being underweight during a 1-year pre-NTMLD period) predicting NTMLD with high sensitivity and specificity (c-statistic, 0.9). The validation of the model on new testing data demonstrated similar discrimination and showed the model was able to predict NTMLD earlier than the receipt of the first diagnostic claim for NTMLD. **CONCLUSIONS:** This predictive algorithm uses a set of criteria comprising patterns of health care use, respiratory symptoms, and comorbidities to identify patients with COPD and possibly undiagnosed NTMLD with high sensitivity and specificity. It has potential application in raising timely clinical suspicion of patients with possibly undiagnosed NTMLD, thereby reducing the period of undiagnosed NTMLD. **DISCLOSURES:** Dr Wang and Dr Hassan are employees of Insmed, Inc. Dr Chatterjee was an employee of Insmed, Inc, at the time of this study. Dr Marras is participating in multicenter clinical trials sponsored by Insmed, Inc, has consulted for RedHill Biopharma, and has received a speaker's honorarium from AstraZeneca. Dr Allison is an employee of Statistical Horizons, LLC. This study was funded by Insmed Inc.

- 2 figures

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

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Review

Neurosci Biobehav Rev

-
-

. 2023 Aug;151:105227.

doi: 10.1016/j.neubiorev.2023.105227. Epub 2023 May 10.

# Multiple chemical sensitivity: It's time to catch up to the science

John Molot[1], Margaret Sears[2], Hymie Anisman[3]

Affiliations expand

- PMID: 37172924

- DOI: 10.1016/j.neubiorev.2023.105227

**Free article**

## Abstract

Multiple chemical sensitivity (MCS) is a complex medical condition associated with low dose chemical exposures. MCS is characterized by diverse features and common comorbidities, including fibromyalgia, cough hypersensitivity, asthma, and migraine, and stress/anxiety, with which the syndrome shares numerous neurobiological processes and altered functioning within diverse brain regions. Predictive factors linked to MCS comprise genetic influences, gene-environment interactions, oxidative stress, systemic inflammation, cell dysfunction, and psychosocial influences. The development of MCS may be attributed to the sensitization of transient receptor potential (TRP) receptors, notably TRPV1 and TRPA1. Capsaicin inhalation challenge studies demonstrated that TRPV1 sensitization is manifested in MCS, and functional brain imaging studies revealed that TRPV1 and TRPA1 agonists promote brain-region specific neuronal variations. Unfortunately, MCS has often been inappropriately viewed as stemming exclusively from psychological disturbances, which has fostered patients being stigmatized and ostracized, and often being denied accommodation for their disability. Evidence-based education is essential to provide appropriate support and advocacy. Greater recognition of receptor-mediated biological mechanisms should be incorporated in laws, and regulation of environmental exposures.

**Keywords:** Asthma; Chronic migraine; Multiple chemical sensitivity; TRPA1 receptors; TRPV1 receptors.



SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

Eur J Intern Med

. 2023 Aug;114:141-142.

doi: 10.1016/j.ejim.2023.05.008. Epub 2023 May 9.

# Chronic cough in very old patients on long-term therapy with angiotensin converting enzyme inhibitors and new-onset cancer

Antonella Gallo[1], Maria Grazia Massaro[2], Sara Camilli[2], Elena Verrecchia[2], Massimo Montalto[3]

Affiliations expand

- PMID: 37164886

- DOI: 10.1016/j.ejim.2023.05.008

*No abstract available*

**Keywords:** Angiotensin converting enzyme inhibitors (ACEi); Cancer bradykinin; Chronic cough; Elderly.

## Conflict of interest statement

Declaration of Competing Interest The authors have no conflict of interest relating to this study.

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

UNIMORE

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

1
Inflamm Res

.
. 2023 Aug 4.

doi: 10.1007/s00011-023-01774-4. Online ahead of print.

# BI 1291583: a novel selective inhibitor of cathepsin C with superior in vivo profile for the treatment of bronchiectasis

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Affiliations expand

- PMID: 37542002

- DOI: 10.1007/s00011-023-01774-4

## Abstract

**Background:** Airway inflammation in chronic inflammatory lung diseases (e.g. bronchiectasis) is partly mediated by neutrophil-derived serine protease (NSP)/antiprotease imbalance. NSPs are activated during neutrophil myelopoiesis in bone marrow by cathepsin C (CatC; DPP1). CatC is therefore an attractive target to reduce NSP

activity in the lungs of patients with bronchiectasis, restoring the protease/antiprotease balance. We report results from the preclinical pharmacological assessment of the novel CatC inhibitor BI 1291583.

**Methods:** Binding kinetics of BI 1291583 to human CatC were determined by surface plasmon resonance. In vitro inhibition of human CatC activity was determined by CatC-specific fluorescent assay, and selectivity was assessed against related cathepsins and unrelated proteases. Inhibition of NSP neutrophil elastase (NE) production was assessed in a human neutrophil progenitor cell line. In vivo inhibition of NE and NSP proteinase 3 (PR3) in bronchoalveolar lavage fluid (BALF) neutrophils after lipopolysaccharide (LPS) challenge and distribution of BI 1291583 was determined in a mouse model.

**Results:** BI 1291583 bound human CatC in a covalent, reversible manner, selectively and fully inhibiting CatC enzymatic activity. This inhibition translated to concentration-dependent inhibition of NE activation in U937 cells and dose-dependent, almost-complete inhibition of NE and PR3 activity in BALF neutrophils in an in vivo LPS-challenge model in mice. BI 1291583 exhibited up to 100 times the exposure in the target tissue bone marrow compared with plasma.

**Conclusion:** BI 1291583-mediated inhibition of CatC is expected to restore the protease-antiprotease balance in the lungs of patients with chronic airway inflammatory diseases such as bronchiectasis.

**Keywords:** Bronchiectasis; Cathepsin C inhibitor; Neutrophil-derived serine protease activity; Preclinical.



- 34 references

. 2023 Aug 2;23(1):281.

doi: 10.1186/s12890-023-02565-7.

# Idiopathic pulmonary fibrosis in the United States: time to diagnosis and treatment

Michelle B Herberts[1], Taylor T Teague[1], Viengneesee Thao[2], Lindsey R Sangaralingham[2], Henry J Henk[3], Kevin T Hovde[2], Timothy M Dempsey[1 4], Andrew H Limper[5 6]

Affiliations expand

- PMID: 37532984

- PMCID: PMC10398946

- DOI: 10.1186/s12890-023-02565-7

**Free PMC article**

## Abstract

**Objective:** Create a timeline of diagnosis and treatment for IPF in the US.

**Design, setting, and participants:** A retrospective analysis was performed in collaboration with the OptumLabs Data Warehouse using an administrative claims database of Medicare Fee for Service beneficiaries. Adults 50 and over with IPF were included (2014 to 2019).

**Exposure:** To focus on IPF, the following diagnoses were excluded: post-inflammatory fibrosis, hypersensitivity pneumonitis, rheumatoid arthritis, sarcoidosis, scleroderma, and connective tissue disease.

**Main outcomes and measures:** Data were collected from periods prior, during, and following initial clinical diagnosis of IPF. This included prior respiratory diagnoses, number of respiratory-related hospitalizations, anti-fibrotic and oxygen use, and survival.

**Results:** A total of 44,891 with IPF were identified. The most common diagnoses prior to diagnosis of IPF were upper respiratory infections (47%), acute bronchitis (13%), other respiratory disease (10%), chronic obstructive pulmonary disease and bronchiectasis (7%),

and pneumonia (6%). The average time to a diagnosis of IPF was 2.7 years after initial respiratory diagnosis. Half of patients had two or more respiratory-related hospitalizations prior to IPF diagnosis. Also, 37% of patients were prescribed oxygen prior to diagnosis of IPF. These observations suggest delayed diagnosis. We also observed only 10.4% were treated with anti-fibrotics. Overall survival declined each year after diagnosis with median survival of 2.80 years.

**Conclusions and relevance:** Our retrospective cohort demonstrates that IPF is often diagnosed late, usually preceded by other respiratory diagnoses and hospitalizations. Use of available therapies is low and outcomes remain poor.

**Keywords:** Diagnosis; Idiopathic pulmonary fibrosis; Mortality; Oxygen; Treatment.



# Conflict of interest statement

The authors declare no competing interests.

- 25 references
- 5 figures

SUPPLEMENTARY INFO

MeSH terms, Substances, Grant supportexpand

FULL TEXT LINKS



Lancet Respir Med

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. 2023 Aug;11(8):669-670.

doi: 10.1016/S2213-2600(23)00258-8.

# Developments and priorities in bronchiectasis research

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Affiliations expand

- PMID: 37532394

- DOI: 10.1016/S2213-2600(23)00258-8

*No abstract available*

## Conflict of interest statement

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ERJ Open Res

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. 2023 Jul 31;9(4):00158-2023.

doi: 10.1183/23120541.00158-2023. eCollection 2023 Jul.

# Healthcare costs and resource utilisation in bronchiectasis, asthma and COPD

Raffaella Ronco[1,2], Giovanni Franco[3], Matteo Monzio Compagnoni[1,2], Stefano Aliberti[4,5], Fabrizio Luppi[3], Giovani Corrao[1,2], Paola Faverio[3]

Affiliations expand

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- PMCID: PMC10388176
- DOI: 10.1183/23120541.00158-2023

**Free PMC article**

## Abstract

**Direct healthcare costs for patients with asthma are less than half (-52%) and for patients with COPD are 41% higher if compared to those of patients with bronchiectasis. The leading expense items in bronchiectasis are hospitalisations and antibiotics.** https://bit.ly/3Iq8AUP.



## Conflict of interest statement

Conflict of interest: G. Corrao received research support from the European Community, the Italian Medicines Agency (AIFA), and the Italian Ministry of Education, Universities and Research. He took part in a variety of projects that were funded by pharmaceutical companies (Novartis, GSK, Roche, AMGEN and BMS). He also received honoraria as a member of the Advisory Board of Roche. S. Aliberti received consulting fees, honoraria for lectures, presentations or educational events and participation on a data safety monitoring board or advisory board from Insmed, Zambon, AstraZeneca, CLS Behring, Grifols, Fondazione Internazionale Menarini, MSD, Brahms, Physioassist SAS, GlaxoSmithKline Spa and Thermofisher Scientific. He also received royalties from McGraw-Hill. No other potential conflicts of interest were declared for the other authors.

- 11 references

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Editorial

J Hum Genet

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. 2023 Aug;68(8):571-575.

doi: 10.1038/s10038-023-01166-w. Epub 2023 Jun 5.

# The challenge of diagnosing primary ciliary dyskinesia: a commentary on various causative genes and their pathogenic variants

Naoto Keicho[1], Kozo Morimoto[2], Minako Hijikata[3]

Affiliations expand

- PMID: 37277434

- DOI: 10.1038/s10038-023-01166-w

*No abstract available*

- 10 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

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Respirology

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. 2023 Aug;28(8):804-806.

doi: 10.1111/resp.14527. Epub 2023 May 30.

# Bronchiectasis is associated with coronary artery calcification even in never smokers

Lewis Holmes[1], Isaac Lui[2], Paul Lilburn[1 3], Christopher Naoum[4], Leonard Kritharides[4 5], Lloyd Ridley[2 5], Lucy Morgan[1 5]

Affiliations expand

- PMID: 37253637

- DOI: 10.1111/resp.14527

**Free article**

*No abstract available*

**Keywords:** CT chest; atherosclerosis; bronchiectasis; cardiovascular disease; coronary artery calcification.

- 4 references

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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7

Meta-Analysis

Pulm Pharmacol Ther

. 2023 Aug;81:102226.

doi: 10.1016/j.pupt.2023.102226. Epub 2023 May 23.

# Nebulized amphotericin B for preventing exacerbations in allergic bronchopulmonary aspergillosis: A systematic review and meta-analysis

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Affiliations expand

- PMID: 37230237

- DOI: 10.1016/j.pupt.2023.102226


# Abstract


**Background:** Allergic bronchopulmonary aspergillosis (ABPA) is complicated by exacerbations in more than one-third of the subjects. Whether nebulized amphotericin B (NAB) therapy prevents ABPA exacerbations remains unclear.

**Objectives:** The primary objective of this systematic review and meta-analysis was to determine the frequency of subjects remaining exacerbation-free, one year after initiating NAB. The key secondary objectives were the time to first exacerbation and the safety of NAB therapy.

**Methods:** We searched the PubMed and Embase databases for studies evaluating ≥5 subjects of ABPA managed with NAB. We report the pooled proportion of ABPA subjects remaining exacerbation free after one year. For the randomized controlled trials (RCTs), we estimate the pooled risk difference (RD) of exacerbation-free status at one year with NAB versus the control arm.

**Results:** We included five studies for our analysis; three were observational (n = 28) and two RCTs (n = 160). The pooled proportion (95% confidence interval [CI]) of subjects remaining exacerbation free with NAB at one year was 76% (62-88). The pooled RD (95% CI) of an exacerbation-free status at one year was 0.33 (-0.12 to 0.78) and was not significantly different between the NAB and control arms. The time to first exacerbation was longer with NAB than with the standard therapy. No serious adverse events were reported with NAB.

**Conclusion:** NAB does not improve exacerbation-free status at one year; however, weak evidence suggests it delays ABPA exacerbations. More research using different dosing regimens is required.



**Keywords:** ABPM; Asthma; Bronchiectasis; Inhaled amphotericin B; Itraconazole; Relapse.




# Conflict of interest statement

Declaration of competing interest None.

SUPPLEMENTARY INFO

Pediatr Pulmonol

. 2023 Aug;58(8):2308-2316.

doi: 10.1002/ppul.26485. Epub 2023 May 24.

# Impact of Elexacaftor-Tezacaftor-Ivacaftor on lung disease in cystic fibrosis

Courtney Gushue[1,2,3], Mariah Eisner[3,4], Shasha Bai[4], Terri Johnson[1,3], Melissa Holtzlander[1,2,3], Karen McCoy[1,2,3], Shahid Sheikh[1,2,3]

Affiliations expand

- PMID: 37222417

- DOI: 10.1002/ppul.26485

## Abstract

**Background:** In people with cystic fibrosis (pwCF), the impact of cystic fibrosis transmembrane conductance regulator (CFTR) modulator therapies, such as Elexacaftor-Tezacaftor-Ivacaftor (ETI), on structural changes in the lungs is unclear.

**Objective:** To determine the impact of ETI on clinical parameters and on structural lung disease as measured by the changes in the chest computed tomography (CT) scans in pwCF.

**Methods:** Percent predicted forced expiratory volume in one second (ppFEV1), body mass index (BMI), and microbiologic data were collected at initiation and 3-month intervals for 1 year. Chest CT scans before starting ETI therapy (baseline) and at 1-year on ETI therapy were compared by two pulmonologists independently.

**Results:** The sample size was 67 pwCF, 30 (44.8%) males, median age of 25 (16, 33.5) years. Significant increases in ppFEV1 and BMI observed by 3 months of ETI therapy persisted throughout 1 year of ETI therapy ($p < 0.001$ at all-time points for both). After 1 year on ETI, pwCF had significant reductions in Pseudomonas aeruginosa (-42%) and MRSA (-42%) positivity. None of the pwCF had worsening of chest CT parameters during 1 year of ETI therapy. Comparing chest CT findings at baseline and at 1-year follow-up, bronchiectasis was present in 65 (97%) pwCF and at 1-year follow-up decreased in 7 (11%). Bronchial wall thickening 64 (97%), decreased in 53 (79%). Mucous plugging in 63 (96%), absent in 11 (17%), and decreased in 50 (77%). Hyperinflation/air trapping in 44 (67%), decreased in 11 (18%), absent in 27 (44%) CONCLUSIONS: ETI significantly improved clinical outcomes and lung disease as documented by improvement in chest CT scans.

**Keywords:** bronchiectasis; chest computed tomography; cystic fibrosis.



- 19 references

SUPPLEMENTARY INFO

MeSH terms, Substances, Grant supportexpand

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9

Thorax

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. 2023 Aug;78(8):835-839.

doi: 10.1136/thorax-2022-219943. Epub 2023 May 19.

# Effect of elexacaftor/tezacaftor/ivacaftor on airway and systemic inflammation in cystic fibrosis

Michelle Casey[1,2], Claudie Gabillard-Lefort[1], Oisín F McElvaney[1], Oliver J McElvaney[1,3], Tomás Carroll[1], Ronan C Heeney[1], Cedric Gunaratnam[1,2], Emer P Reeves[1], Mark P Murphy[4], Noel G McElvaney[1,2]

Affiliations expand

- PMID: 37208188

- DOI: 10.1136/thorax-2022-219943

## Abstract

Treatment with elexacaftor/tezacaftor/ivacaftor (ETI) has been shown to improve lung function in people with cystic fibrosis (PWCF). However, its biological effects remain incompletely understood. Here we describe alterations in pulmonary and systemic inflammation in PWCF following initiation of ETI. To address this, we collected spontaneously expectorated sputum and matching plasma from PWCF (n=30) immediately prior to ETI therapy, then again at 3 and 12 months. Within 3 months, PWCF demonstrated reduced activity of neutrophil elastase, proteinase three and cathepsin G, and decreased concentrations of interleukin (IL)-1β and IL-8 in sputum, accompanied by decreased *Pseudomonas* burden and restoration of secretory leukoprotease inhibitor levels. Once treated with ETI, all airway inflammatory markers studied in PWCF had reduced to levels found in matched non-CF bronchiectasis controls. In PWCF with advanced disease, ETI resulted in decreased plasma concentrations of IL-6, C-reactive protein and soluble TNF receptor one as well as normalisation of levels of the acute phase protein, alpha-1 antitrypsin. These data clarify the immunomodulatory effects of ETI and underscore its role as a disease modifier.

**Keywords:** cystic fibrosis; innate immunity; lung proteases.

## Conflict of interest statement

Competing interests: NGM reports consulting fees from Vertex, Inhibrx and Intellia unrelated to the submitted work.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS



Editorial

Pediatr Pulmonol

. 2023 Aug;58(8):2183-2186.

doi: 10.1002/ppul.26467. Epub 2023 May 12.

# World Bronchiectasis Day: It is time for global action to promote equity of care

Oleksandr Mazulov[1], Zena Powell[2], Ed Powell[2], Andrew Bush[3], Anne B Chang[4,5], Ahmad Kantar[6], Keith Grimwood[7,8], Bulent Karadag[9]; Child-BEAR-Net*

Affiliations expand

- PMID: 37171114

- DOI: 10.1002/ppul.26467

*No abstract available*

**Keywords:** QoL; bronchiectasis; children; cystic fibrosis.

- 16 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Eur Radiol

. 2023 Aug;33(8):5528-5539.

doi: 10.1007/s00330-023-09616-x. Epub 2023 Apr 18.

# Ultra-high resolution CT imaging of interstitial lung disease: impact of photon-counting CT in 112 patients

Yann Gaillandre[1], Alain Duhamel[1,2], Thomas Flohr[3], Jean-Baptiste Faivre[1], Suonita Khung[1], Antoine Hutt[1], Paul Felloni[1], Jacques Remy[1], Martine Remy-Jardin[4,5]

Affiliations expand

- PMID: 37071165

- DOI: 10.1007/s00330-023-09616-x

# Abstract

**Objectives:** To compare lung parenchyma analysis on ultra-high resolution (UHR) images of a photon-counting CT (PCCT) scanner with that of high-resolution (HR) images of an energy-integrating detector CT (EID-CT).

**Methods:** A total of 112 patients with stable interstitial lung disease (ILD) were investigated (a) at T0 with HRCT on a 3rd-generation dual-source CT scanner; (b) at T1 with UHR on a PCCT scanner; (c) with a comparison of 1-mm-thick lung images.

**Results:** Despite a higher level of objective noise at T1 (74.1 ± 14.1 UH vs 38.1 ± 8.7 UH; $p < 0.0001$), higher qualitative scores were observed at T1 with (a) visualization of more distal bronchial divisions (median order; Q1-Q3) (T1: 10th division [9-10]; T0: 9th division [8-9]; $p < 0.0001$); (b) greater scores of sharpness of bronchial walls ($p < 0.0001$) and right major fissure ($p < 0.0001$). The scores of visualization of CT features of ILD were significantly superior at T1 (micronodules: $p = 0.03$; linear opacities, intralobular reticulation, bronchiectasis, bronchiolectasis, and honeycombing: $p < 0.0001$), leading to the reclassification of 4 patients with non-fibrotic ILD at T0, recognized with fibrotic ILD at T1. At T1, the mean (± SD) radiation dose ($CTDI_{vol}$: 2.7 ± 0.5 mGy; DLP: 88.5 ± 21 mGy.cm) was significantly lower than that delivered at T0 ($CTDI_{vol}$: 3.6 ± 0.9 mGy; DLP: 129.8 ± 31.7 mGy.cm) ($p < 0.0001$), corresponding to a mean reduction of 27% and 32% for the $CTDI_{vol}$ and DLP, respectively.

**Conclusions:** The UHR scanning mode of PCCT allowed a more precise depiction of CT features of ILDs and reclassification of ILD patterns with significant radiation dose reduction.

**Clinical relevance statement:** Evaluation of lung parenchymal structures with ultra-high-resolution makes subtle changes at the level of the secondary pulmonary lobules and lung microcirculation becoming visually accessible, opening new options for synergistic collaborations between highly-detailed morphology and artificial intelligence.

**Key points:** • Photon-counting CT (PCCT) provides a more precise analysis of lung parenchymal structures and CT features of interstitial lung diseases (ILDs). • The UHR mode ensures a more precise delineation of fine fibrotic abnormalities with the potential of modifying the categorization of ILD patterns. • Better image quality at a lower radiation dose with PCCT opens new horizons for further dose reduction in noncontrast UHR examinations.

**Keywords:** Computed tomography; Humans; Lung; Lung diseases, interstitial; Thorax.

## Comment in

- Photon-counting detector CT: improving interstitial lung disease classification using ultra-high resolution at a fraction of the radiation dose?
  Rajendran K, Koo CW.Eur Radiol. 2023 Aug;33(8):5526-5527. doi: 10.1007/s00330-023-09617-w. Epub 2023 Apr 18.PMID: 37071170 **Free PMC article.** No abstract available.

- Cited by 1 article
- 11 references

SUPPLEMENTARY INFO

MeSH termsexpand

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Physiother Theory Pract

. 2023 Aug 3;39(8):1574-1581.

doi: 10.1080/09593985.2022.2043965. Epub 2022 Feb 21.

# Gait and functional balance in non-CF bronchiectasis

Naciye Vardar-Yagli[1], Melda Saglam[1], Merve Firat[1], Aslihan Cakmak[1], Deniz Inal-Ince[1], Ebru Calik Kutukcu[1], Lutfi Coplu[2]

Affiliations expand

- PMID: 35189785

- DOI: 10.1080/09593985.2022.2043965


# Abstract


**Background:** The decline in ambulatory activities and negative alterations in gait characteristics may impair balance and increase fall risk in obstructive lung diseases. Few studies have evaluated balance and gait parameters in individuals with bronchiectasis.

**Purpose:** This study aimed to compare the gait parameters and functional balance in individuals with non-cystic fibrosis (CF) bronchiectasis and healthy subjects.

**Methods:** This cross-sectional and retrospective study analyzed data from 22 individuals with non-CF bronchiectasis and 32 healthy controls recorded between July 2019 and July 2020. Functional balance was assessed using the Timed Up and Go (TUG) test. Gait parameters were evaluated using the Biodex Gait Trainer. Step cycle (s), gait speed (m/s), the number of steps per minute, and ambulation index were measured for 6 min.

Results The TUG time (s) was significantly longer ($p = .019$, effect size = 0.66), and gait speed (m/s) ($p < 0.001$, effect size = 2.47), step cycle (s) ($p < 0.001$, effect size = 2.23), and ambulation index ($p < 0.001$, effect size = 2.56) were significantly reduced in individuals with non-CF bronchiectasis compared with healthy controls.

**Conclusion:** Non-CF bronchiectasis is related to unfavorable changes in gait characteristics, such as slower gait speed and the decreased average step cycle. In addition, impairment in functional balance and mobility exists in a small percentage of adults with non-CF bronchiectasis. In comprehensive pulmonary rehabilitation, balance and gait evaluations should be included to prevent falls in adults with non-CF bronchiectasis.



**Keywords:** Bronchiectasis; Timed Up And Go test; gait analysis; gait speed; posture.