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

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. 2023 Jul 28;13(1):12245.

doi: 10.1038/s41598-023-39001-z.

### Examining changes in vascular function, arterial stiffness and systemic inflammation during hospitalization and recovery from an acute exacerbation of chronic obstructive pulmonary disease

[Desi P Fuhr](#)<sup>1</sup>, [Andrew R Brotto](#)<sup>1,2</sup>, [Brian H Rowe](#)<sup>3</sup>, [Mohit Bhutani](#)<sup>1</sup>, [Rhonda J Rosychuk](#)<sup>4</sup>, [Michael K Stickland](#)<sup>5,6</sup>

Affiliations expand

- PMID: 37507427
- DOI: [10.1038/s41598-023-39001-z](https://doi.org/10.1038/s41598-023-39001-z)

## Abstract

An acute exacerbation of COPD (AECOPD) is associated with increased risk of cardiovascular (CV) events. The elevated risk during an AECOPD may be related to changes in vascular function, arterial stiffness, and systemic inflammation; the time course of these measures and their corresponding recovery are poorly understood. Further, physical activity is reduced during an AECOPD, and physical activity may influence the cardiovascular responses to an AECOPD. The purpose of the study was to examine the acute impact of an AECOPD requiring hospitalization on vascular function, arterial stiffness, and systemic inflammation and examine whether physical activity modulates these variables during recovery. Patients hospitalized for an AECOPD were prospectively recruited and compared to control patients with stable COPD. Vascular function, arterial stiffness, and systemic inflammation (CRP, IL-6) were measured at hospital admission, hospital discharge and within 14 days of discharge. Physical activity was electronically tracked daily while in hospital and for 7 days following discharge using a Fitbit. One hundred and twenty-one patients with an AECOPD requiring hospitalization and 33 control patients with stable COPD were enrolled in the study. Vascular function was significantly lower, and systemic inflammation higher at hospital admission in patients with an AECOPD compared to stable COPD. Significant improvements in vascular function and inflammation were observed within 14 days of hospital discharge; however, vascular function remained lower than stable COPD. Physical activity was low at admission and increased following discharge; however, physical activity was unrelated to measures of vascular function or inflammation at any time point. An AECOPD requiring hospitalization is associated with impaired vascular function that persists during recovery. These findings provide a mechanistic link to help explain the enduring increase in CV risk and mortality following a severe AECOPD event. Clinical trial registration: ClinicalTrials.gov [#NCT01949727](#); Registered: 09/20/2013.

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- [50 references](#)

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Chest



. 2023 Jul 26;S0012-3692(23)01054-1.

doi: 10.1016/j.chest.2023.07.019. Online ahead of print.

# Race-specific spirometry equations do not improve models of dyspnea and quantitative chest CT phenotypes

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Affiliations expand

- PMID: 37507005
- DOI: [10.1016/j.chest.2023.07.019](https://doi.org/10.1016/j.chest.2023.07.019)

## Abstract

**Background:** Race-specific spirometry reference equations are used globally to interpret lung function for clinical, research, and social purposes, but inclusion of race is under scrutiny.

**Research question:** Does including self-identified race in spirometric reference equation formation improve the ability of predicted FEV<sub>1</sub> values to explain quantitative chest CT abnormalities, dyspnea or GOLD classification?

**Study design and methods:** Using data from healthy never-smoking adults in both the National Health and Nutrition Survey (NHANES, 2007-12) and COPD Genetic Epidemiology study (COPDGene) cohorts, we generated race-neutral, race-free and race-specific prediction equations for FEV<sub>1</sub>. Using sensitivity/specificity, multivariable logistic regression, and random forest models, we applied these equations in a cross-sectional analysis to populations of smokers and former smokers to determine how they affected Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification and the fit of models predicting quantitative chest CT phenotypes or dyspnea.

**Results:** Race-specific equations showed no advantage relative to race-neutral or race-free equations in models of quantitative chest CT phenotypes or dyspnea. Race-neutral reference equations reclassified up to 19% of Black participants into more severe GOLD classes, and race-neutral/free equations may improve model fit for dyspnea symptoms relative to race-specific equations.

**Interpretation:** Race-specific equations offered no advantage over race-neutral/free ppFEV<sub>1</sub> values in three distinct explanatory models of dyspnea and chest CT abnormalities. Race-neutral/free reference equations may improve pulmonary disease diagnoses and treatment in populations highly vulnerable to lung disease.

**Keywords:** Ethnicity; Pulmonary Function Test; Race; Reference Equations; Spirometry.

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Eur J Clin Pharmacol

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. 2023 Jul 29.

doi: 10.1007/s00228-023-03543-y. Online ahead of print.

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

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Affiliations expand

- PMID: 37507595
- DOI: [10.1007/s00228-023-03543-y](https://doi.org/10.1007/s00228-023-03543-y)

## Abstract

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

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

**Results:** Twenty studies including 23,955 participants were included. The proportion of participants with a history of COPD exacerbation (%) in the previous year and the postbronchodilator forced expiratory volume in the first second (FEV<sub>1</sub>) (%predicted) were important factors affecting drug efficacy. After adjusting the above factors to median levels of 100% and 45.5%, respectively, the moderate or severe exacerbation rates at 52 weeks for olodaterol/tiotropium, formoterol/budesonide, indacaterol/glycopyrronium, formoterol/glycopyrronium, vilanterol/fluticasone, salmeterol/fluticasone, and vilanterol/umeclidinium were 38.3%, 41.0%, 42.6%, 47.0%, 47.5%, 47.9%, and 53.0%, respectively. In terms of safety, significant differences were observed among drugs containing different LABA/LAMA FDCs.

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

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

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PLoS One



. 2023 Jul 28;18(7):e0288783.

doi: 10.1371/journal.pone.0288783. eCollection 2023.

# [Application of mendelian randomization to study the causal relationship between smoking and the risk of chronic obstructive pulmonary disease](#)

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Affiliations [expand](#)

- PMID: 37506114
- DOI: [10.1371/journal.pone.0288783](https://doi.org/10.1371/journal.pone.0288783)

## **Abstract**

**Background:** Smoking is a risk factor for chronic obstructive pulmonary disease (COPD). Few studies have assessed the causal relationship between smoking and COPD using Mendelian randomization.

**Methods:** Exposure and outcome datasets were obtained from the IEU Open GWAS project (<https://gwas.mrcieu.ac.uk/>). The exposure data set includes smoking (ever smoke, smoking/smokers in household, exposure to tobacco smoke at home). The outcome data

set includes COPD susceptibility and acute COPD admissions. The main methods of Mendelian randomization analysis are weighted median method and MR-Egger method. Heterogeneity and polymorphism analyses were performed to ensure the accuracy of the results.

**Resluts:** ever smoke increased the risk of COPD prevalence, and ever smoke and smoking/smokers in household increased the risk of acute COPD admission. Conclusion Therefore, we should enhance the management of nonpharmacological prescription of COPD to reduce the individual incidence.

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## Conflict of interest statement

The authors declare that there are no competing interests.

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JMIR Res Protoc



. 2023 Jul 28;12:e48235.

doi: 10.2196/48235.

## Cognitive Interventions in Individuals With Chronic Respiratory Diseases: Protocol for a Systematic Review

[Danielle Ryzer](#)<sup>1</sup>, [Bushra Bhatti](#)<sup>1</sup>, [Alana Streicher](#)<sup>1</sup>, [Paula Weinberg](#)<sup>1</sup>, [Fady Hanna](#)<sup>1</sup>, [Jessica Moretto](#)<sup>1</sup>, [Dina Brooks](#)<sup>1,2,3</sup>, [Shirley Quach](#)<sup>1,2</sup>, [Ana Oliveira](#)<sup>1,4,5</sup>

Affiliations expand

- PMID: 37505801
- DOI: [10.2196/48235](#)

## Abstract

**Background:** Chronic respiratory diseases (CRDs) may cause reduced oxygen availability to organs and body tissues, leading to an increased risk for ischemic damage, which can result in brain tissue injury. This damage can lead to a myriad of neurological symptoms contributing to cognitive decline. Cognitive interventions may attenuate cognitive deficits in people with CRDs; however, the effects have not yet been systematically summarized in the literature.

**Objective:** The purpose of this systematic review is to assess the effects of cognitive interventions (including cognitive behavioral therapy and transcranial brain stimulation) on cognitive function (primary outcome), HRQL, self-management, symptoms, physical activity, physical function, ability to complete activities of daily living (ADLs), hospital admissions, functional capacity, functional performance, psychological and social outcomes, exacerbations, healthcare utilization, and survival in individuals with CRDs.

**Methods:** This review will be conducted in accordance with the Cochrane handbook for systematic reviews of interventions and reported following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Searches will be performed in MEDLINE, Embase, Emcare, PsycINFO, Scopus, and CINAHL. Articles will be included if they focus on the effects of cognitive interventions on adults with CRDs, are published in peer-reviewed journals, and are written in English, French, or Portuguese. Risk of bias will be evaluated with the Cochrane Risk of Bias 2 tool for randomized controlled trials, and the Risk of Bias in Non-randomized Studies of Interventions tool for nonrandomized studies. Meta-analyses will be performed if at least 2 studies provided sufficient data for a specific outcome. The GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) assessment will be used to evaluate the overall quality of the evidence.

**Results:** This systematic review was initiated in November 2022 and registered with PROSPERO in February 2023, prior to title and abstract screening. Full-text screening of articles will be completed in June 2023. Data extraction and drafting of the manuscript will occur from July 2023 to August 2023, with expected publication in February 2024.

**Conclusions:** This systematic review will summarize the effects of cognitive interventions on cognitive function in people with CRDs. It will guide health care professionals in



selecting evidence-based strategies to enhance cognitive well-being and overall health outcomes for individuals with CRDs. Additionally, it will identify research gaps and highlight areas for future exploration, supporting researchers in advancing knowledge in this field.

**Trial registration:** PROSPERO CRD42023396234; <https://tinyurl.com/mwjrfbxv>.

**International registered report identifier (irrid):** PRR1-10.2196/48235.

**Keywords:** COPD; CRD; brain exercise; chronic pulmonary disease; cognition; cognitive; cognitive function; cognitive therapy; lung; memory; memory training; pulmonary; respiratory; review methodology; systematic review.

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Membranes (Basel)

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. 2023 Jul 24;13(7):686.

doi: 10.3390/membranes13070686.

## [Safety and Effectiveness of Carbon Dioxide Removal CO2RESET Device in Critically Ill Patients](#)

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Affiliations expand

- PMID: 37505051
- DOI: [10.3390/membranes13070686](https://doi.org/10.3390/membranes13070686)

## Abstract

**Background:** In this retrospective study, we report the effectiveness and safety of a dedicated extracorporeal carbon dioxide removal (ECCO<sub>2</sub>R) device in critically ill patients.

**Methods:** Adult patients on mechanical ventilation due to acute respiratory distress syndrome (ARDS) or decompensated chronic obstructive pulmonary disease (dCOPD), who were treated with a dedicated ECCO<sub>2</sub>R device (CO2RESET, Eurosets, Medolla, Italy) in case of hypercapnic acidemia, were included. Repeated measurements of CO<sub>2</sub> removal (VCO<sub>2</sub>) at baseline and 1, 12, and 24 h after the initiation of therapy were recorded.

**Results:** Over a three-year period, 11 patients received ECCO<sub>2</sub>R (median age 60 [43-72] years) 3 (2-39) days after ICU admission; nine patients had ARDS and two had dCOPD. Median baseline pH and PaCO<sub>2</sub> levels were 7.27 (7.12-7.33) and 65 (50-84) mmHg, respectively. With a median ECCO<sub>2</sub>R blood flow of 800 (500-800) mL/min and maximum gas flow of 6 (2-14) L/min, the VCO<sub>2</sub> at 12 h after ECCO<sub>2</sub>R initiation was 157 (58-183) mL/min. Tidal volume, respiratory rate, and driving pressure were significantly reduced over time. Few side effects were reported.

**Conclusions:** In this study, a dedicated ECCO<sub>2</sub>R device provided a high VCO<sub>2</sub> with a favorable risk profile.

**Keywords:** ARDS; CO<sub>2</sub> removal; complications; extracorporeal; high blood flow; respiratory failure.

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## Review

Nat Rev Dis Primers

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. 2023 Jul 27;9(1):39.

doi: 10.1038/s41572-023-00450-5.

# HIV-associated lung disease

[Ioannis Konstantinidis<sup>1</sup>](#), [Kristina Crothers<sup>2</sup>](#), [Ken M Kunisaki<sup>3</sup>](#), [M Bradley Drummond<sup>4</sup>](#), [Thomas Benfield<sup>5</sup>](#), [Heather J Zar<sup>6,7</sup>](#), [Laurence Huang<sup>8,9</sup>](#), [Alison Morris<sup>10</sup>](#)

Affiliations expand

- PMID: 37500684
- DOI: [10.1038/s41572-023-00450-5](https://doi.org/10.1038/s41572-023-00450-5)

## Abstract

Lung disease encompasses acute, infectious processes and chronic, non-infectious processes such as chronic obstructive pulmonary disease, asthma and lung cancer. People living with HIV are at increased risk of both acute and chronic lung diseases. Although the use of effective antiretroviral therapy has diminished the burden of infectious lung disease, people living with HIV experience growing morbidity and mortality from chronic lung diseases. A key risk factor for HIV-associated lung disease is cigarette smoking, which is more prevalent in people living with HIV than in uninfected people. Other risk factors include older age, history of bacterial pneumonia, *Pneumocystis pneumonia*, pulmonary tuberculosis and immunosuppression. Mechanistic investigations support roles for aberrant innate and adaptive immunity, local and systemic inflammation, oxidative stress, altered lung and gut microbiota, and environmental exposures such as biomass fuel burning in the development of HIV-associated lung disease. Assessment, prevention and treatment strategies are largely extrapolated from data from HIV-uninfected people. Smoking cessation is essential. Data on the long-term consequences of HIV-associated lung disease are limited. Efforts to continue quantifying the effects of HIV infection on the lung, especially in low-income and middle-income countries, are essential to advance our knowledge and optimize respiratory care in people living with HIV.

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[Chest](#)

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. 2023 Jul 25;S0012-3692(23)01055-3.

doi: 10.1016/j.chest.2023.07.020. Online ahead of print.

# **Preserved ratio impaired spirometry and chronic obstructive pulmonary disease accelerate frailty progression: evidence from a prospective cohort study**

[Di He](#)<sup>1</sup>, [Mengsha Yan](#)<sup>1</sup>, [Yong Zhou](#)<sup>2</sup>, [Huiqing Ge](#)<sup>2</sup>, [Xuhui Zhang](#)<sup>3</sup>, [Yuying Xu](#)<sup>1</sup>, [Chengguo Liu](#)<sup>4</sup>, [Kejing Ying](#)<sup>5</sup>, [Yimin Zhu](#)<sup>6</sup>

[Affiliations](#) [expand](#)

- PMID: 37499976
- DOI: [10.1016/j.chest.2023.07.020](https://doi.org/10.1016/j.chest.2023.07.020)

## Abstract

**Background:** Chronic obstructive pulmonary disease (COPD) was found to associate with frailty. However, there is inadequate longitudinal evidence for associations of COPD with frailty progression. Furthermore, recent studies revealed a new phenotype of lung function impairment: preserved ratio impaired spirometry (PRISm). Associations of PRISm and its transitions with frailty progression are unclear.

**Research question:** What are the associations of PRISm, transitions of PRISm, and COPD with frailty progression?

**Study design and methods:** To analyze the associations of PRISm and COPD with frailty progression, 5,901 subjects were included from the English Longitudinal Study of Ageing. Subjects were classified into three lung function patterns of normal spirometry, PRISm, and COPD. Frailty progression was assessed by repeated measurements of the frailty index (FI) during follow-up. Among these 5,901 subjects, 3,765 subjects were included to analyze the associations of PRISm transitions with frailty progression. PRISm transitions were assessed based on the changes of lung function patterns after a four-year interval. Linear mixed-effect models were used for statistical analyses.

**Results:** The median follow-up periods were 9.5 years for the analyses of PRISm and COPD with frailty progression and 5.8 years for PRISm transitions with frailty progression. When compared with normal spirometry, subjects with PRISm and COPD presented accelerated FI progression with additional annual increases of 0.301(95%CI: 0.211 to 0.392,  $P<0.001$ ) and 0.172(95%CI: 0.102 to 0.242,  $P<0.001$ ), respectively. Subjects who transitioned from normal spirometry to PRISm also presented accelerated FI progression when compared with stable normal spirometry ( $\beta=0.242$ , 95%CI: 0.008 to 0.476,  $P=0.042$ ). However, no accelerated FI progression was found in PRISm subjects who transitioned to normal spirometry ( $\beta=0.119$ , 95%CI: -0.181 to 0.418,  $P=0.438$ ).

**Interpretation:** Our findings indicate that PRISm and COPD are associated with accelerated frailty progression. Further studies are needed to elucidate the causality of PRISm and COPD with frailty.

**Keywords:** COPD; PRISm; epidemiology; frailty; transition.

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Ann Am Thorac Soc

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doi: 10.1513/AnnalsATS.202304-384CME. Online ahead of print.

## Personalizing Selection of Inhaled Delivery Systems in COPD

[Donald A Mahler](#)<sup>1</sup>, [David M G Halpin](#)<sup>2,3</sup>

Affiliations expand

- PMID: 37499210
- DOI: [10.1513/AnnalsATS.202304-384CME](https://doi.org/10.1513/AnnalsATS.202304-384CME)

### **Abstract**

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

to determine whether the inhaled medication-delivery system is providing benefits. Continued and repeated education on device features and correct technique is warranted to optimize efficacy.

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PLoS One



. 2023 Jul 27;18(7):e0280613.

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## Using machine learning to design a short test from a full-length test of functional health literacy in adults-The development of a short form of the Danish TOFHLA

[Lisa Korsbakke Emtækær Hæsum](#)<sup>1,2</sup>, [Simon Lebech Cichosz](#)<sup>2</sup>, [Ole Kristian Hejlesen](#)<sup>2</sup>

Affiliations expand

- PMID: 37498890
- PMCID: [PMC10373996](#)
- DOI: [10.1371/journal.pone.0280613](#)

**Abstract**

**Introduction:** Patients are compelled to become more involved in shared decision making with healthcare professionals in the self-management of chronic disease and general adherence to treatment. Therefore, it is valuable to be able to identify patients with low functional health literacy so they can be given special instructions about the management of chronic disease and medications. However, time spent by both patients and clinicians is a concern when introducing a screening instrument in the clinical setting, which raises the need for short instruments for assessing health literacy that can be used by patients without the involvement of healthcare personnel. This paper describes the development of a short version of the full-length Danish TOFHLA (DS-TOFHLA) that is easily applicable in the clinical context and where the use does not require a trained interviewer.

**Materials and methods:** Data were collected as a part of a large-scale telehomecare project (TeleCare North), which was a randomized controlled trial that included 1225 patients with chronic obstructive pulmonary disease. The DS-TOFHLA was developed solely using an algorithm-based selection of variables and multiple linear regression. A multiple linear regression model was developed using an exhaustive search strategy.

**Results:** The exhaustive search showed that the number of items in the full-length TOFHLA could be reduced from 17 numeracy items and 50 reading comprehension items to 20 reading comprehension items while maintaining a correlation of  $r = 0.90$  between the scores from full-length and short versions. A generic model-based approach was developed, which is suitable for development of short versions of the TOFHLA in other languages, including the original American version.

**Conclusions:** This study demonstrated how a generic model-based approach could be applied in the development of a short version of the TOFHLA, thereby reducing the 67 items to 20 items in the short version. Furthermore, this study showed that the inclusion of numeracy items was not necessary. The development of the DS-TOFHLA presents an opportunity to reliably identify patients with inadequate functional health literacy in approximately 5 minutes without involvement of healthcare personnel. The approach may be used in the development of short versions of any scaling questionnaire.

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## Conflict of interest statement

The authors have declared that no competing interests exist.

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**Review**

Eur Respir Rev

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

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

## Regenerative and translational medicine in COPD: hype and hope

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

Affiliations expand

- PMID: 37495247
- PMCID: [PMC10369169](#)
- DOI: [10.1183/16000617.0223-2022](#)

**Free PMC article**

**Abstract**

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

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## Conflict of interest statement

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

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. 2023 Jul 24;S0012-3692(23)01052-8.

doi: 10.1016/j.chest.2023.07.017. Online ahead of print.

# Association between regular moderate-to-vigorous physical activity initiation after COPD diagnosis and mortality: an emulated target trial using nationwide cohort data

[Taeyun Kim](#)<sup>1</sup>, [Hyunsoo Kim](#)<sup>2</sup>, [Sunga Kong](#)<sup>3</sup>, [Sun Hye Shin](#)<sup>1</sup>, [Juhee Cho](#)<sup>4</sup>, [Danbee Kang](#)<sup>5</sup>, [Hye Yun Park](#)<sup>6</sup>

Affiliations expand

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- DOI: [10.1016/j.chest.2023.07.017](https://doi.org/10.1016/j.chest.2023.07.017)

## Abstract

**Background:** Moderate-to-vigorous physical activity (MVPA) in patients with chronic obstructive pulmonary disease (COPD) affects their overall health outcomes, including symptom relief and improved quality of life. However, the magnitude of the effect of MVPA initiation on real-world clinical outcomes has not been well investigated.

**Research question:** How does MVPA initiation impact mortality and severe exacerbation rates in patients who have not engaged in MVPA before COPD diagnosis?

**Study design and methods:** We included patients with COPD aged  $\geq 40$  years who were not performing MVPA before COPD diagnosis and had at least one health screening visit before and after their COPD diagnosis between January 1, 2010, and December 31, 2018. The main exposure was MVPA, defined as vigorous aerobic exercise over 20 minutes per day on  $\geq 3$  days per week or moderate aerobic exercise over 30 minutes per day on  $\geq 5$  days per week. The primary endpoint was the all-cause mortality rate, and the secondary endpoint was the initial severe exacerbation as the time to event after COPD diagnosis.

**Results:** In total, 110,097 person-trials were included (27,564 MVPA increases and 82,533 control groups). No differences were observed between the covariates after matching. The

adjusted hazards ratio (HR) of all-cause mortality for the MVPA group compared to the control was 0.84 (95% confidence interval (CI): 0.79, 0.89). In subgroup analysis, patients aged >65, women, never smokers, and the higher Charlson comorbidity index (CCI) group showed a stronger effect of MVPA on reducing mortality than younger men, ever smokers, and the lower CCI group (p for interaction <0.05). The fully adjusted HR for the risk of severe exacerbation (MVPA group vs. control) was 0.90 (95% CI: 0.87, 0.94).

**Interpretation:** MVPA initiation can potentially reduce mortality and severe exacerbations in patients with COPD, although personalized interventions and further clinical trials are necessary.

**Keywords:** COPD; exacerbation; mortality; physical activity.

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. 2023 Jul 26;18(7):e0288759.

doi: 10.1371/journal.pone.0288759. eCollection 2023.

## [Incidence of chronic disease following smoking cessation treatment: A matched cohort study using linked administrative healthcare data in Ontario, Canada](#)

[Dolly Baliunas](#)<sup>1 2 3 4</sup>, [Sabrina Voci](#)<sup>5</sup>, [Peter Selby](#)<sup>3 5 6 7 8</sup>, [Claire de Oliveira](#)<sup>6 9 10 11</sup>, [Paul Kurdyak](#)<sup>6 8 11 12</sup>, [Laura Rosella](#)<sup>3 11</sup>, [Laurie Zawertailo](#)<sup>5 6 13</sup>, [Longdi Fu](#)<sup>11</sup>, [Rinku Sutradhar](#)<sup>3 10 11</sup>

Affiliations expand

- PMID: 37494345
- PMCID: [PMC10370896](#)
- DOI: [10.1371/journal.pone.0288759](#)

**Free PMC article**

## **Abstract**

Scarce evidence is available on the impact of real-world smoking cessation treatment on subsequent health outcomes, such as incidence of chronic disease. This study compared two cohorts of people that smoke-those that enrolled in a smoking cessation program, and a matched control that had not accessed the program-to assess the incidence of cancer, chronic obstructive pulmonary disease, diabetes, hypertension, and major cardiovascular events over a 5-year follow-up period. We selected five sub-cohorts with matched treatment-control pairs in which both individuals were at risk of the five chronic diseases. Incident chronic disease from index date until December 31, 2017, was determined through linkage with routinely collected healthcare data. The cumulative incidence of each chronic disease was estimated using the cumulative incidence function with death as a competing risk. Gray's test was used to test for a difference between matched treatment and control groups in the chronic disease-specific cumulative incidence function over follow-up. Analyses were stratified by sex. Among females, cumulative incidence of diabetes was higher over follow-up for the treatment group (5-year cumulative incidence 5.8% vs 4.2%,  $p = 0.004$ ), but did not differ for the four other chronic diseases. Among males, cumulative incidence of chronic obstructive pulmonary disease (12.2% vs 9.1%,  $p < 0.001$ ) and diabetes (6.7% vs 4.8%,  $p < 0.001$ ) both had higher 5-year cumulative incidence for the treated versus control groups but did not differ for the other three chronic diseases. We conclude that accessing primary-care based smoking cessation treatment is associated with increased incidence of diabetes for both sexes, and chronic obstructive pulmonary disease for males (possibly due to under diagnosis prior to treatment), within 5 years of treatment. The associations detected require further research to understand causal relationships.

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## **Conflict of interest statement**

I have read the journal's policy and the authors of this manuscript have the following competing interests: DB has received investigator-initiated grant support from Pfizer Canada, Ontario Ministry of Health and Long-Term Care, and the Canadian Institutes of

Health Research (CIHR). CdO reports receiving grant funding from CIHR, University of Toronto, Medical Research Council, National Institutes of Health, Centre for Addiction and Mental Health (CAMH), Ontario Ministry of Health and Long-Term Care, Canadian Centre for Applied Research in Cancer Control and Ontario Mental Health Foundation. PS reports receiving funding from CCSRI, CIHR, Canadian Partnership Against Cancer, Centre for Addiction and Mental Health (CAMH), Health Canada, Medical Psychiatry Alliance, Ontario Ministry of Health and Long-Term Care, Ontario Neurotrauma Foundation and the Public Health Agency of Canada. PS also reports funding from the following commercial organizations: Patient-Centred Outcome Research Institute and Pfizer. PS has received honoraria in the past 3 years from University of Ottawa Heart Institute, Royal College of Physicians and Surgeons of Canada, Royal Victoria Regional Health Centre, Department of Family and Community Medicine at the University of Toronto, Northern Ontario School of Medicine, Canadian Partnership Against Cancer, Battle River Treaty 6 Healthcare, Lung Association of Nova Scotia, Exchange Summit, Toronto Public Health, Ontario Association of Public Health Dentistry and ECHO. PS has been retained as an expert witness by the Ontario and New Brunswick provincial governments in litigation against the tobacco industry. PS was a member and co-chaired the Ministry of Health's Ontario Smoke Free Strategy cessation subcommittee. Through an open tender process, Johnson & Johnson, Novartis and Pfizer are vendors of record for providing free/discounted smoking cessation pharmacotherapy for research studies in which PS and LZ are principal or co-investigator. PK reports receiving grant funding from CIHR and the Ontario Ministry of Health and Long-Term Care. LR reports receiving grant funding from CIHR, SSHRC, New Frontiers in Research Fund, Canada Research Chairs and the Connaught Foundation. LZ reports receiving grant funding from Pfizer, Ontario Ministry of Health and Long-Term Care, Health Canada, CIHR and CCSRI. LZ also received honoraria and travel funds from Pfizer and University of Ottawa Heart Institute. RS reports receiving funding from CIHR, Terry Fox Research Institute, Garron Family Cancer Centre and Sick Kids Foundation, Canadian Society of Colon and Rectal Surgeons, Sunnybrook Foundation, Pediatric Oncology Group of Ontario, Ontario Institute for Cancer Research, PSI Foundation, C17 Research Network, Cancer Care Ontario, Canadian Centre for Applied Research in Cancer Control, Canadian Breast Cancer Foundation, Sunnybrook AFP Innovation Fund, CCSRI, Ministry of Health and Long-Term Care and the Ontario Medical Association. No other disclosures were reported. This does not alter our adherence to PLOS ONE policies on sharing data and materials.

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. 2023 Jul 26;12:RP85875.

doi: 10.7554/eLife.85875.

# Short-range interactions between fibrocytes and CD8<sup>+</sup> T cells in COPD bronchial inflammatory response

[Edmée Eyraud](#)<sup>1,2</sup>, [Elise Maurat](#)<sup>1,2</sup>, [Jean-Marc Sac-Epée](#)<sup>3</sup>, [Pauline Henrot](#)<sup>1,2,4</sup>, [Maeva Zysman](#)<sup>1,2,4</sup>, [Pauline Esteves](#)<sup>1,2</sup>, [Thomas Trian](#)<sup>1,2</sup>, [Jean-William Dupuy](#)<sup>1</sup>, [Alexander Leipold](#)<sup>4</sup>, [Antoine-Emmanuel Saliba](#)<sup>4</sup>, [Hugues Bequeret](#)<sup>1,2,5</sup>, [Pierre-Olivier Girodet](#)<sup>1,2,5</sup>, [Matthieu Thumerel](#)<sup>1,2,5</sup>, [Romain Hustache-Castaing](#)<sup>1,2,5</sup>, [Roger Marthan](#)<sup>1,2,5</sup>, [Florian Levet](#)<sup>6,7</sup>, [Pierre Vallois](#)<sup>3</sup>, [Cécile Contin-Bordes](#)<sup>8,9</sup>, [Patrick Berger](#)<sup>1,2,5</sup>, [Isabelle Dupin](#)<sup>2</sup>

Affiliations expand

- PMID: 37494277
- PMCID: [PMC10371228](#)
- DOI: [10.7554/eLife.85875](#)

**Free PMC article**

## **Abstract**

Bronchi of chronic obstructive pulmonary disease (COPD) are the site of extensive cell infiltration, allowing persistent contact between resident cells and immune cells. Tissue fibrocytes interaction with CD8<sup>+</sup> T cells and its consequences were investigated using a combination of *in situ*, *in vitro* experiments and mathematical modeling. We show that

fibrocytes and CD8<sup>+</sup> T cells are found in the vicinity of distal airways and that potential interactions are more frequent in tissues from COPD patients compared to those of control subjects. Increased proximity and clusterization between CD8<sup>+</sup> T cells and fibrocytes are associated with altered lung function. Tissue CD8<sup>+</sup> T cells from COPD patients promote fibrocyte chemotaxis via the CXCL8-CXCR1/2 axis. Live imaging shows that CD8<sup>+</sup> T cells establish short-term interactions with fibrocytes, that trigger CD8<sup>+</sup> T cell proliferation in a CD54- and CD86-dependent manner, pro-inflammatory cytokines production, CD8<sup>+</sup> T cell cytotoxic activity against bronchial epithelial cells and fibrocyte immunomodulatory properties. We defined a computational model describing these intercellular interactions and calibrated the parameters based on our experimental measurements. We show the model's ability to reproduce histological ex vivo characteristics, and observe an important contribution of fibrocyte-mediated CD8<sup>+</sup> T cell proliferation in COPD development. Using the model to test therapeutic scenarios, we predict a recovery time of several years, and the failure of targeting chemotaxis or interacting processes. Altogether, our study reveals that local interactions between fibrocytes and CD8<sup>+</sup> T cells could jeopardize the balance between protective immunity and chronic inflammation in the bronchi of COPD patients.

**Keywords:** cellular interactions; chronic respiratory diseases; computational biology; human; immunological synapse; immunology; inflammation; lung function; probabilistic cellular automata; systems biology.

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## Conflict of interest statement

EE, EM, JS, PH, PE, TT, JD, AL, AS, HB, MT, RH, RM, FL, PV, CC No competing interests declared, MZ MZ reports personal fees from AstraZeneca, Boehringer Ingelheim, Novartis, Chiesi, GlaxoSmithKline and non-financial support Lilly outside the submitted work, PG POG has a patent (EP 3050574: Use of plerixafor for treating and/or preventing acute exacerbations of chronic obstructive pulmonary disease) granted. POG reports grants, personal fees and non-financial support from AstraZeneca, personal fees and non-financial support from Chiesi, personal fees and non-financial support from GlaxoSmithKline, personal fees and non-financial support from Novartis, personal fees and non-financial support from Sanofi, outside the submitted work, PB PB has a patent (EP N3050574: Use of plerixafor for treating and/or preventing acute exacerbations of chronic obstructive pulmonary disease) granted. PB reports grants from AstraZeneca, Glaxo-Smith-Kline, Novartis, Chiesi, which support COBRA during the conduct of the study; grants and personal fees from AstraZeneca, BoehringerIngelheim, Novartis, personal fees and non-financial support from Chiesi, Sanofi, Menarini, outside the submitted work, ID ID has a patent (EP 3050574: Use of plerixafor for treating and/or preventing acute exacerbations of chronic obstructive pulmonary disease) granted

## Update of



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- doi: 10.7554/eLife.85875.2
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. 2023 Jul 28;1-8.

doi: 10.1080/17476348.2023.2239708. Online ahead of print.

# **Up-to-date guidance towards improving medication adherence in patients with chronic obstructive pulmonary disease**

[Meredith A Case](#)<sup>1</sup>, [Michelle N Eakin](#)<sup>1</sup>

Affiliations expand

- PMID: 37494126
- DOI: [10.1080/17476348.2023.2239708](https://doi.org/10.1080/17476348.2023.2239708)

## Abstract

**Introduction:** Despite efficacious treatment for chronic obstructive pulmonary disease (COPD), medication adherence remains quite poor, with most estimates based on electronic monitoring devices ranging from 20-30%. This degree of nonadherence represents a significant missed opportunity to realize the benefits of treatment of this disease.

**Areas covered:** In this article, we review research on the prevalence of nonadherence among patients with COPD, the association of nonadherence with health outcomes, barriers to adherence in this patient population, and potential interventions.

**Expert opinion:** Integrating research into practice involves assessing patients' adherence, identifying modifiable barriers to adherence, open discussion of these barriers with patients, and tailored interventions to address them. These interventions may include treatment of previously unrecognized comorbid disease, providing educational or behavioral interventions, optimizing prescribing strategies, use of adherence aids, or addressing cost and other access barriers. Electronic inhaler monitors are promising interventions for both monitoring and improving adherence. However, remaining concerns about integration into patient care, data management, cost, acceptability, and ethical and privacy issues must be overcome prior to their implementation in clinical practice.

**Keywords:** Chronic obstructive pulmonary disease; digital health; electronic monitors; medication adherence; medication compliance.

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. 2023 Jul 24;49(3):e20230171.

doi: 10.36416/1806-3756/e20230171.

# Using the pulmonary function laboratory to assist in disease management: COPD

[Article in English, Portuguese]

[José Alberto Neder](#)<sup>1</sup>, [Danilo Cortozi Berton](#)<sup>2</sup>, [Denis E O'Donnell](#)<sup>1</sup>

Affiliations expand

- PMID: 37493791
- DOI: [10.36416/1806-3756/e20230171](https://doi.org/10.36416/1806-3756/e20230171)

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. 2023 Jul 25;13(7):e071550.

doi: 10.1136/bmjopen-2022-071550.

# Discharge prescription patterns for antiplatelet and statin therapy following carotid endarterectomy: an analysis of the vascular quality initiative

[Michael Eppler](#)<sup>1</sup>, [Nikhil Singh](#)<sup>2</sup>, [Li Ding](#)<sup>1</sup>, [Gregory Magee](#)<sup>1</sup>, [Parveen Garg](#)<sup>3</sup>

Affiliations expand

- PMID: 37491096
- PMCID: [PMC10373683](#)
- DOI: [10.1136/bmjopen-2022-071550](#)

**Free PMC article**

## **Abstract**

**Objectives:** Despite guidelines endorsing statin and single antiplatelet therapy (SAPT) therapy post-carotid endarterectomy (CEA), these medications may be either under or inappropriately prescribed. We determined rates of new statin prescriptions as well as change in antiplatelet therapy (APT) regimen at discharge. We identified characteristics associated with these occurrences.

**Design:** We performed a retrospective Vascular Quality Initiative registry analysis of more than 125 000 patients who underwent CEA from 2013 to 2021.

**Setting:** The Vascular Quality Initiative is a multicentre registry database including academic and community-based hospitals throughout the USA.

**Participants:** Patients age ≥ 18 years undergoing CEA with available statin and APT data (preprocedure and postprocedure) were included.

**Primary and secondary outcome measures:** We determined overall rates of statin and APT prescription at discharge. Multivariate logistic regression was used to determine clinical and demographic characteristics that were mostly associated with new statin prescription or changes in APT regimen at discharge.

**Results:** Study participants were predominantly male (61%) and White (90%), with a mean age of 70.6 ± 9.1. 13.1% of participants were not on statin therapy pre-CEA, and 48% of these individuals were newly prescribed one. Statin rates steadily increased throughout the study period: 36.2% in 2013 to 62% in 2021. A higher likelihood of new statin prescription

was associated with non-race, diabetes, coronary heart disease, stroke, TIA and a non-elective indication. Older age, female gender, chronic obstructive pulmonary disease and prior carotid revascularisation were associated with a lower likelihood of new statin prescription. Nearly all participants were discharged on APT (63% SAPT and 37% dual antiplatelet therapy, DAPT). Among these individuals, 16% were discharged on a regimen that was different from the one on admission (11 947 (10.7%) of patients were upgraded to DAPT and 5813 (5.2%) were downgraded to SAPT).

**Conclusions:** Although statin use has substantially improved following CEA, more than half of individuals not on a statin preprocedure remained this way at discharge. In addition, DAPT at discharge was frequent, a quarter of whom were on SAPT preprocedure. Further efforts are needed to improve rates of new statin prescriptions, ensure appropriate APT intensity at discharge and determine how different discharge APT regimens impact outcomes.

**Keywords:** Adult cardiology; Cardiology; PREVENTIVE MEDICINE; Stroke medicine; Thromboembolism; Vascular medicine.

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## Conflict of interest statement

Competing interests: None declared.

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. 2023 Jul 24;23(1):1417.

doi: 10.1186/s12889-023-16308-0.

# Short-term effect of particulate matter on lung function and impulse oscillometry system (IOS) parameters of chronic obstructive pulmonary disease (COPD) in Beijing, China

[Rui-Xia Zhu](#)<sup>1</sup>, [Xiu-Hong Nie](#)<sup>2</sup>, [Xiao-Fang Liu](#)<sup>3</sup>, [Yong-Xiang Zhang](#)<sup>4</sup>, [Jin Chen](#)<sup>5</sup>, [Xue-Jiao Liu](#)<sup>6</sup>, [Xin-Jie Hui](#)<sup>1</sup>

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- PMID: 37488590
- PMCID: [PMC10367330](#)
- DOI: [10.1186/s12889-023-16308-0](#)

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## **Abstract**

**Objective:** This study aimed to evaluate the associations between particulate matter (PM), lung function and Impulse Oscillometry System (IOS) parameters in chronic obstructive pulmonary disease (COPD) patients and identify effects between different regions in Beijing, China.

**Methods:** In this retrospective study, we recruited 1348 outpatients who visited hospitals between January 2016 and December 2019. Ambient air pollutant data were obtained from the central monitoring stations nearest the participants' residential addresses. We analyzed the effect of particulate matter with aerodynamic diameter  $\leq 2.5 \mu\text{m}$  (PM<sub>2.5</sub>) exposure on lung function and IOS parameters using a multiple linear regression model, adjusting for sex, smoking history, education level, age, body mass index (BMI), mean temperature, and relative humidity .

**Results:** The results showed a relationship between PM<sub>2.5</sub>, lung function and IOS parameters. An increase of 10 µg/m<sup>3</sup> in PM<sub>2.5</sub> was associated with a decline of 2.083% (95% CI: -3.047 to - 1.103) in forced expiratory volume in one second /predict (FEV<sub>1</sub>%pred), a decline of 193 ml/s (95% CI: -258 to - 43) in peak expiratory flow (PEF), a decline of 0.932% (95% CI: -1.518 to - 0.342) in maximal mid-expiratory flow (MMEF); an increase of 0.732 Hz (95% CI: 0.313 to 1.148) in resonant frequency (F<sub>res</sub>), an increase of 36 kpa/(ml/s) (95% CI: 14 to 57) in impedance at 5 Hz (Z<sub>5</sub>) and an increase of 31 kpa/(ml/s) (95% CI: 2 to 54) in respiratory impedance at 5 Hz (R<sub>5</sub>). Compared to patients in the central district, those in the southern district had lower FEV<sub>1</sub>/FVC, FEV<sub>1</sub>%pred, PEF, FEF<sub>75%</sub>, MMEF, X<sub>5</sub>, and higher F<sub>res</sub>, Z<sub>5</sub> and R<sub>5</sub> (p < 0.05).

**Conclusion:** Short-term exposure to PM<sub>2.5</sub> was associated with reductions in lung function indices and an increase in IOS results in patients with COPD. The heavier the PM<sub>2.5</sub>, the more severe of COPD.

**Keywords:** Chronic obstructive pulmonary disease (COPD); Impulse Oscillometry System (IOS); Lung function; Particulate matter.

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## Conflict of interest statement

No part of the research was funded by tobacco industry sources.  
The authors declare no financial or other potential conflict of interest.

- [52 references](#)
- [8 figures](#)

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. 2023 Jul 24;33(1):27.

doi: 10.1038/s41533-023-00347-6.

## **Rational use of inhaled corticosteroids for the treatment of COPD**

[Jennifer K Quint](#)<sup>1</sup>, [Amnon Ariel](#)<sup>2</sup>, [Peter J Barnes](#)<sup>3</sup>

Affiliations expand

- PMID: 37488104
- PMCID: [PMC10366209](#)
- DOI: [10.1038/s41533-023-00347-6](#)

**Free PMC article**

### **Abstract**

Inhaled corticosteroids (ICS) are the mainstay of treatment for asthma, but their role in chronic obstructive pulmonary disease (COPD) is debated. Recent randomised controlled trials (RCTs) conducted in patients with COPD and frequent or severe exacerbations demonstrated a significant reduction (~25%) in exacerbations with ICS in combination with dual bronchodilator therapy (triple therapy). However, the suggestion of a mortality benefit associated with ICS in these trials has since been rejected by the European Medicines Agency and US Food and Drug Administration. Observational evidence from routine clinical practice demonstrates that dual bronchodilation is associated with better clinical outcomes than triple therapy in a broad population of patients with COPD and infrequent exacerbations. This reinforces guideline recommendations that ICS-containing maintenance therapy should be reserved for patients with frequent or severe exacerbations and high blood eosinophils (~10% of the COPD population), or those with concomitant asthma. However, data from routine clinical practice indicate ICS overuse, with up to 50-80% of patients prescribed ICS. Prescription of ICS in patients not fulfilling guideline criteria puts patients at unnecessary risk of pneumonia and other long-term adverse events and also has cost implications, without any clear benefit in disease control. In this article,



we review the benefits and risks of ICS use in COPD, drawing on evidence from RCTs and observational studies conducted in primary care. We also provide a practical guide to prescribing ICS, based on the latest global treatment guidelines, to help primary care providers identify patients for whom the benefits of ICS outweigh the risks.

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# Conflict of interest statement

J.K.Q. declares personal fees for advisory board participation or speaking fees from GlaxoSmithKline, Boehringer Ingelheim, AstraZeneca and Chiesi, but declares no non-financial competing interests. A.A. declares personal fees from AstraZeneca, and personal fees and non-financial support from Boehringer Ingelheim, outside the submitted work. P.J.B. declares research funding from AstraZeneca and Boehringer Ingelheim; consulting fees from AstraZeneca, Boehringer Ingelheim and Teva; and payment or honoraria for lectures, presentations, speaker bureaus, manuscript writing or educational events from AstraZeneca, Boehringer Ingelheim, Novartis and Teva. P.J.B. declares no non-financial competing interests.

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. 2023 Jul 24;thorax-2022-219463.

# Admission blood eosinophil count, inpatient death and death at 1 year in exacerbating patients with COPD

[Carlos Echevarria](#)<sup>1,2</sup>, [John Steer](#)<sup>2,3</sup>, [Arun Prasad](#)<sup>3</sup>, [Jennifer K Quint](#)<sup>4</sup>, [Stephen C Bourke](#)<sup>2,5</sup>

Affiliations expand

- PMID: 37487711
- DOI: [10.1136/thorax-2022-219463](https://doi.org/10.1136/thorax-2022-219463)

## Abstract

**Background:** Blood eosinophil counts have been studied in patients with stable chronic obstructive pulmonary disease (COPD) and are a useful biomarker to guide inhaled corticosteroid use. Less is known about eosinophil counts during severe exacerbation.

**Methods:** In this retrospective study, 2645 patients admitted consecutively with COPD exacerbation across six UK hospitals were included in the study, and the clinical diagnosis was confirmed by a respiratory specialist. The relationship between admission eosinophil count, inpatient death and 1-year death was assessed. In a backward elimination, Poisson regression analysis using the log-link function with robust estimates, patients' markers of acute illness and stable-state characteristics were assessed in terms of their association with eosinopenia.

**Results:** 1369 of 2645 (52%) patients had eosinopenia at admission. Those with eosinopenia had a 2.5-fold increased risk of inpatient death compared with those without eosinopenia (12.1% vs 4.9%, RR=2.50, 95% CI 1.88 to 3.31,  $p<0.001$ ). The same mortality risk with eosinopenia was seen among the subgroup with pneumonic exacerbation ( $n=788$ , 21.3% vs 8.5%, RR=2.5, 95% CI 1.67 to 2.24,  $p<0.001$ ). In a regression analysis, eosinopenia was significantly associated with: older age and male sex; a higher pulse rate, temperature, neutrophil count, urea and C reactive protein level; a higher proportion of patients with chest X-ray consolidation and a reduced Glasgow Coma Score; and lower systolic and diastolic blood pressure measurements and lower oxygen saturation, albumin, platelet and previous admission counts.

**Discussion:** During severe COPD exacerbation, eosinopenia is common and associated with inpatient death and several markers of acute illness. Clinicians should be cautious about using eosinophil results obtained during severe exacerbation to guide treatment decisions regarding inhaled corticosteroid use.

**Keywords:** COPD Exacerbations; COPD epidemiology; COPD exacerbations mechanisms; Eosinophil Biology.

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## Conflict of interest statement

Competing interests: CE has received grants from GlaxoSmithKline. JS and AP have nil to declare. JKQ has received grants from The Health Foundation, MRC, GSK, Bayer, BI, AUK-BLF, HDR UK, Chiesi and AZ and personal fees for advisory board participation or speaking fees from GlaxoSmithKline, Boehringer Ingelheim, AstraZeneca, Chiesi, Insmmed and Bayer. SJB has received grants from GSK, and personal fees for advisory board participation or speaking fees from Philips, AstraZeneca, Chiesi and Boehringer Ingelheim.

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Semin Respir Crit Care Med

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. 2023 Jul 24.

doi: 10.1055/s-0043-1770121. Online ahead of print.

## Management of Pulmonary Hypertension Associated with Chronic Lung Disease

[Isabel Blanco](#)<sup>1 2 3</sup>, [Fernanda Hernández-González](#)<sup>1 2 3</sup>, [Agustín García](#)<sup>1 2 3</sup>, [Rodrigo Torres-Castro](#)<sup>1 2 3</sup>, [Joan A Barberà](#)<sup>1 2 3</sup>

Affiliations expand

- PMID: 37487524

- DOI: [10.1055/s-0043-1770121](https://doi.org/10.1055/s-0043-1770121)

## Abstract

Pulmonary hypertension (PH) is a common complication of chronic lung diseases, particularly in chronic obstructive pulmonary disease (COPD) and interstitial lung diseases (ILD) and especially in advanced disease. It is associated with greater mortality and worse clinical course. Given the high prevalence of some respiratory disorders and because lung parenchymal abnormalities might be present in other PH groups, the appropriate diagnosis of PH associated with respiratory disease represents a clinical challenge. Patients with chronic lung disease presenting symptoms that exceed those expected by the pulmonary disease should be further evaluated by echocardiography. Confirmatory right heart catheterization is indicated in candidates to surgical treatments, suspected severe PH potentially amenable with targeted therapy, and, in general, in those conditions where the result of the hemodynamic assessment will determine treatment options. The treatment of choice for these patients who are hypoxemic is long-term oxygen therapy and pulmonary rehabilitation to improve symptoms. Lung transplant is the only curative therapy and can be considered in appropriate cases. Conventional vasodilators or drugs approved for pulmonary arterial hypertension (PAH) are not recommended in patients with mild-to-moderate PH because they may impair gas exchange and their lack of efficacy shown in randomized controlled trials. Patients with severe PH (as defined by pulmonary vascular resistance  $>5$  Wood units) should be referred to a center with expertise in PH and lung diseases and ideally included in randomized controlled trials. Targeted PAH therapy might be considered in this subset of patients, with careful monitoring of gas exchange. In patients with ILD, inhaled treprostinil has been shown to improve functional ability and to delay clinical worsening.

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## Conflict of interest statement

None declared.

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. 2023 Jul 24;e232309.

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# Association of Early-, Middle-, and Late-Life Depression With Incident Dementia in a Danish Cohort

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## Abstract

**Importance:** Late-life depressive symptoms are associated with subsequent dementia diagnosis and may be an early symptom or response to preclinical disease. Evaluating associations with early- and middle-life depression will help clarify whether depression influences dementia risk.

**Objective:** To examine associations of early-, middle-, and late-life depression with incident dementia.

**Design, setting, and participants:** This was a nationwide, population-based, cohort study conducted from April 2020 to March 2023. Participants included Danish citizens from the general population with depression diagnoses who were matched by sex and birth year to individuals with no depression diagnosis. Participants were followed up from 1977 to 2018. Excluded from analyses were individuals followed for less than 1 year, those younger than 18 years, or those with baseline dementia.

**Exposure:** Depression was defined using diagnostic codes from the International Classification of Diseases (ICD) within the Danish National Patient Registry (DNPR) and Danish Psychiatric Central Research Register (DPCRR).

**Main outcomes and measure:** Incident dementia was defined using ICD diagnostic codes within the DPCRR and DNPR. Cox proportional hazards regression was used to examine associations between depression and dementia adjusting for education, income, cardiovascular disease, chronic obstructive pulmonary disease, diabetes, anxiety disorders, stress disorders, substance use disorders, and bipolar disorder. Analyses were stratified by age at depression diagnosis, years since index date, and sex.

**Results:** There were 246 499 individuals (median [IQR] age, 50.8 [34.7-70.7] years; 159 421 women [64.7%]) with diagnosed depression and 1 190 302 individuals (median [IQR] age, 50.4 [34.6-70.0] years; 768 876 women [64.6%]) without depression. Approximately two-thirds of those diagnosed with depression were diagnosed before the age of 60 years (684 974 [67.7%]). The hazard of dementia among those diagnosed with depression was 2.41 times that of the comparison cohort (95% CI, 2.35-2.47). This association persisted when the time elapsed from the index date was longer than 20 to 39 years (hazard ratio [HR], 1.79; 95% CI, 1.58-2.04) and among those diagnosed with depression in early, middle, or late life (18-44 years: HR, 3.08; 95% CI, 2.64-3.58; 45-59 years: HR, 2.95; 95% CI, 2.75-3.17; ≥60 years: HR, 2.31; 95% CI, 2.25-2.38). The overall HR was greater for men (HR, 2.98; 95% CI, 2.84-3.12) than for women (HR, 2.21; 95% CI, 2.15-2.27).

**Conclusions and relevance:** Results suggest that the risk of dementia was more than doubled for both men and women with diagnosed depression. The persistent association between dementia and depression diagnosed in early and middle life suggests that depression may increase dementia risk.

## Conflict of interest statement

Conflict of Interest Disclosures: Dr Gradus reported receiving personal fees from Peabody Arnold and having patent for use of glecaprevir/pibrentasvir for the treatment of posttraumatic stress disorder pending. Dr Smith reported receiving personal fees from US Food and Drug Administration outside the submitted work. Dr Lash reported receiving grants from the National Institutes of Health during the conduct of the study and personal fees from Amgen outside the submitted work. Dr Glymour reported receiving grants from the National Institutes of Health/National Institute on Aging outside the submitted work. Dr Henderson reported receiving grants from the National Institutes of Health and reviewer honoraria from Institute for Clinical and Economic Review on dementia topics outside the submitted work. No other disclosures were reported.

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# Structured Evaluation and Management of Patients with COPD in an Accredited Program

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## **Abstract**

**Background:** Chronic obstructive pulmonary disease (COPD) is an ambulatory care-sensitive condition.

**Methods:** We compared the impact of care received by patients with COPD at Joint Commission-accredited, disease-specific clinics and primary care clinics at an academic health care system from April 2014 to March 2018. Patients with COPD  $\geq 40$  years old with  $\geq 2$  outpatient visits 30 days apart were identified. Baseline demographics, disease-specific performance measures, and health care utilization were compared between groups. Propensity matching was conducted and time to the first emergency department (ED) visit and hospitalization was performed using Cox regression analysis.

**Results:** Of 4646 unique patients with COPD, 1114 were treated at disease-specific clinics and 3532 at primary care clinics. The entire group was predominantly female (58.8 %), non-Hispanic White (74.2 %) with a mean age of  $65.4 \pm 11.4$  years consisting of current (47.6 %) or former smokers (38.4 %). In the disease-specific group, performance measures were performed more frequently, and lower rates of ED visits (hazard ratio [HR]=0.31, 95%

confidence interval [CI] 0.18-0.54) and hospitalizations (HR 0.41, 95% CI 0.21-0.79) noted in comparison to the primary care group.

**Conclusions:** In this observational study, the implementation of achronic disease management program through accredited disease-specific clinics for patients with COPD was associated with reduced all-cause ED visits and hospitalizations.

**Keywords:** COPD; Joint Commission; accreditation; chronic disease management; emergency department use; health care utilization; hospitalizations.

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## [Augmentation Therapy Modulates Systemic Inflammation in Individuals with Alpha-1 Antitrypsin Deficiency and Chronic Obstructive Pulmonary Disease](#)

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## Free article

## Abstract

**Background:** Alpha-1 antitrypsin (AAT) deficiency is a genetic disorder that leads to chronic obstructive pulmonary disease (COPD) and lower circulating levels of AAT, which is a protease inhibitor with potent anti-inflammatory effects. In order to better understand the presence of systemic inflammation in AAT-deficient individuals with COPD, we investigated the plasma levels of C-reactive protein (CRP).

**Methods:** AAT-deficient individuals and a matched cohort with a normal AAT genotype were recruited from the Alpha-1 Foundation DNA and Tissue Bank. AAT genotypes were determined by a combination of a Taqman-based assay. AAT and CRP levels were determined by nephelometry. Comparisons were determined by unpaired *t*-test and standard Pearson's correlation.

**Results:** Our study included 40 control participants and 742 AAT-deficient participants, of which 498 received augmentation therapy. In the AAT-deficient participants, the plasma AAT was  $20.2 \pm 11.6 \mu\text{M}$  and  $4.5 \pm 1.3 \mu\text{M}$  ( $P < 0.0001$ ) with and without augmentation therapy, respectively, and the CRP was  $0.32 \pm 0.53 \text{ mg/dL}$  and  $0.69 \pm 1.97 \text{ mg/dL}$  ( $P = 0.0169$ ), respectively. There was a negative correlation between the percentage predicted of forced expiratory volume in 1 second and CRP in the group not receiving augmentation therapy ( $r = -0.2528$ ,  $P < 0.05$ ), and there was no correlation in participants receiving augmentation therapy.

**Conclusion:** Compared to healthy individuals, AAT-deficient individuals with COPD have higher levels of circulating CRP, suggesting increased systemic inflammation. However, AAT-deficient individuals receiving augmentation therapy had lower plasma CRP levels compared to those who are not.

**Keywords:** C-reactive protein; alpha-1 antitrypsin deficiency; augmentation therapy; chronic obstructive pulmonary disease.

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# Inhaled Corticosteroids and Risk of Cardiovascular Disease in Chronic Obstructive Pulmonary Disease: A Systematic Review and Meta-Regression

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## **Abstract**

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

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

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

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

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

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doi: 10.15326/jcopdf.2023.0410.

## Decreased Cardiac Autonomic Function is Associated with Higher Exacerbation Risk and Symptom Burden in Chronic Obstructive Pulmonary Disease

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## **Abstract**

Current measures of chronic obstructive pulmonary disease (COPD) severity, including lung function, do not fully explain symptom burden, and there is a need to identify predictors of exacerbation risk and morbidity. Autonomic dysfunction may be implicated in both cardiovascular and respiratory morbidity in COPD and convey risk for exacerbations. Heart rate variability (HRV) is a marker of cardiac autonomic function that is predictive of cardiovascular health and has promise as a non-invasive COPD biomarker. The CLEAN AIR Heart study provided an opportunity to investigate the association between HRV and COPD morbidity among former smokers with moderate-severe COPD. Eighty-five participants, contributing 305 HRV measurements, underwent repeated clinical assessments over 4 study periods that included a 24-Holter monitoring assessment of HRV. HRV measures of interest were standard deviation of normal-to-normal intervals, (SDNN) (overall HRV) and root-mean-square of successive differences (RMSSD) (parasympathetic function). Exacerbation risk was assessed using negative binomial models, and mixed-effects models analyzed associations between HRV and symptoms. Decreases in SDNN (incidence rate ratio [IRR] 1.40; 95% confidence interval [CI] 1.13 to 1.74) and RMSSD (IRR 1.60; 95% CI 1.07 to 2.37) were associated with severe exacerbation risk. Decreases in SDNN were associated with higher St George's Respiratory Questionnaire scores, COPD Assessment Test scores, and chronic bronchitis symptoms. Findings demonstrate that HRV is associated with COPD symptom burden and exacerbation risk. HRV may represent an important biomarker with the potential to identify high-risk COPD populations.

**Keywords:** COPD morbidity; comorbidity; exacerbations.

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# Clinical Use of an Exposure, Symptom, and Spirometry Algorithm to Stratify Smokers into COPD Risk Phenotypes: A Case Finding Study Combined with Smoking Cessation Counseling

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## **Abstract**

**Background:** Chronic obstructive pulmonary disease (COPD) case-finding aims to detect airflow obstruction in symptomatic smokers and ex-smokers. We used a clinical algorithm including smoking, symptoms, and spirometry to classify smokers into COPD risk phenotypes. In addition, we evaluated the acceptability and effectiveness of including smoking cessation advice in the case-finding intervention.

**Methods:** Smoking, symptoms, and spirometry abnormalities (airflow obstruction: forced expiratory volume in 1 second [FEV<sub>1</sub>] to forced vital capacity [FVC] <0.7 or preserved-ratio

spirometry ( $FEV_1 < 80\%$  of predicted value and  $FEV_1/FVC$  ratio  $\geq 0.7$ )] were assessed in a group of 864 smokers aged  $\geq 30$  years. The combination of these parameters allowed the identification of 4 phenotypes: Phenotype A (no symptoms, normal spirometry; reference), Phenotype B (symptoms; normal spirometry; possible COPD), Phenotype C (no symptoms; abnormal spirometry; possible COPD), and Phenotype D (symptoms; abnormal spirometry; probable COPD). We assessed phenotype differences in clinical variables and modeled the trend from phenotype A to phenotype D. Smoking cessation advice based on spirometry was provided. Follow-up was done by telephone 3 months later.

**Results:** Using smokers without symptoms or abnormal spirometry (phenotype A;  $n=212$  [24.5%]) as a reference, smokers were classified into possible COPD (phenotype B;  $n=332$  [38.4%]; and C:  $n=81$  [9.4%]) and probable COPD (phenotype D:  $n=239$  [27.2%]). The trend from baseline phenotype A to probable COPD phenotype D was significant for the number of cigarettes/day and the number of years of smoking ( $p=0.0001$ ). At follow-up, 58 (7.7%) of the respondents ( $n=749$ ) reported that they had quit smoking.

**Conclusions:** Our clinical algorithm allowed us to classify smokers into COPD phenotypes whose manifestations were associated with smoking intensity and to significantly increase the number of smokers screened for COPD. Smoking cessation advice was well accepted, resulting in a low but clinically significant quit rate.

**Keywords:** COPD phenotypes; COPDGene®; PRISm; screening spirometry; smoking cessation.

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# Impact of Marijuana Smoking on COPD Progression in a Cohort of Middle-Aged and Older Persons

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## **Abstract**

**Background:** Limited data are available regarding marijuana smoking's impact on the development or progression of chronic obstructive pulmonary disease (COPD) in middle-aged or older adults with a variable history of tobacco cigarette smoking.

**Methods:** We divided ever-tobacco smoking participants in the SubPopulations and Intermediate Outcomes In COPD Study (SPIROMICS) into 3 groups based on self-reported marijuana use: current, former, or never marijuana smokers (CMSs, FMSs or NMSs, respectively). Longitudinal data were analyzed in participants with  $\geq 2$  visits over a period of  $\geq 52$  weeks.

**Measurements:** We compared CMSs, FMSs, and NMSs, and those with varying amounts of lifetime marijuana use. Mixed effects linear regression models were used to analyze changes in spirometry, symptoms, health status, and radiographic metrics; zero-inflated negative binomial models were used for exacerbation rates. All models were adjusted for age, sex, race, baseline tobacco smoking amount, and forced expiratory volume in 1 second (FEV<sub>1</sub>) %predicted.

**Results:** Most participants were followed for  $\geq 4$  years. Annual rates of change in FEV<sub>1</sub>, incident COPD, respiratory symptoms, health status, radiographic extent of emphysema or

air trapping, and total or severe exacerbations were not different between CMSs or FMSs versus NMSs or between those with any lifetime amount of marijuana use versus NMSs.

**Conclusions:** Among SPIROMICS participants with or without COPD, neither former nor current marijuana smoking of any lifetime amount was associated with evidence of COPD progression or its development. Because of our study's limitations, these findings underscore the need for further studies to better understand longer-term effects of marijuana smoking in COPD.

**Keywords:** COPD; Exacerbations; HRCT; Marijuana; Spirometry.

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## [Impact of Bronchiectasis on COPD Severity and Alpha-1 Antitrypsin Deficiency as a Risk Factor in Individuals with a Heavy Smoking History](#)



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## Abstract

**Rationale:** Bronchiectasis is common among those with heavy smoking histories, but risk factors for bronchiectasis, including alpha-1 antitrypsin deficiency, and its implications for COPD severity are uncharacterized in such individuals.

**Objectives:** To characterize the impact of bronchiectasis on COPD and explore alpha-1 antitrypsin as a risk factor for bronchiectasis.

**Methods:** SubPopulations and InteRmediate Outcome Measures In COPD Study (SPIROMICS) participants (N=914; ages 40-80 years; ≥20-pack-year smoking) had high-resolution computed tomography (CT) scans interpreted visually for bronchiectasis, based on airway dilation without fibrosis or cicatrization. We performed regression-based models of bronchiectasis with clinical outcomes and quantitative CT measures. We deeply sequenced the gene encoding -alpha-1 antitrypsin, *SERPINA1*, in 835 participants to test for rare variants, focusing on the PiZ genotype (Glu<sup>366</sup>Lys, rs28929474).

**Measurements and main results:** We identified bronchiectasis in 365 (40%) participants, more frequently in women (45% versus 36%,  $p=0.0045$ ), older participants (mean age=66[standard deviation (SD)=8.3] versus 64[SD=9.1] years,  $p=0.0083$ ), and those with lower lung function (forced expiratory volume in 1 second [FEV<sub>1</sub>] percentage predicted=66%[SD=27] versus 77%[SD=25],  $p<0.0001$ ; FEV<sub>1</sub> to forced vital capacity [FVC] ratio=0.54[0.17] versus 0.63[SD=0.16],  $p<0.0001$ ). Participants with bronchiectasis had greater emphysema (%voxels ≤-950 Hounsfield units, 11%[SD=12] versus 6.3%[SD=9],  $p<0.0001$ ) and parametric response mapping functional small airways disease (26[SD=15] versus 19[SD=15],  $p<0.0001$ ). Bronchiectasis was more frequent in the combined PiZZ and PiMZ genotype groups compared to those without PiZ, PiS, or other rare pathogenic variants (N=21 of 40 [52%] versus N=283 of 707[40%], odds ratio [OR]=1.97; 95% confidence interval [CI]=1.002, 3.90,  $p=0.049$ ), an association attributed to White individuals (OR=1.98; 95%CI = 0.9956, 3.9;  $p=0.051$ ).

**Conclusions:** Bronchiectasis was common in those with heavy smoking histories and was associated with detrimental clinical and radiographic outcomes. Our findings support alpha-1 antitrypsin guideline recommendations to screen for alpha-1 antitrypsin deficiency in an appropriate bronchiectasis subgroup with a significant smoking history.

**Keywords:** COPD; alpha-1 antitrypsin; bronchiectasis; lung function.

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## Changes in Lung Volumes with Spirometric Disease Progression in COPD

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## Abstract

**Background:** Abnormal lung volumes representing air trapping identify the subset of smokers with preserved spirometry who develop spirometric chronic obstructive pulmonary disease (COPD) and adverse outcomes. However, how lung volumes evolve in early COPD as airflow obstruction develops remains unclear.

**Methods:** To establish how lung volumes change with the development of spirometric COPD, we examined lung volumes from the pulmonary function data (seated posture) available in the U.S. Department of Veterans Affairs electronic health records (n=71,356) and lung volumes measured by computed tomography (supine posture) available from the COPD Genetic Epidemiology (COPDGene®) study (n=7969) and the SubPopulations and InterMediate Outcome Measures In COPD Study (SPIROMICS) (n=2552) cohorts, and studied their cross-sectional distributions and longitudinal changes across the airflow obstruction spectrum. Patients with preserved ratio-impaired spirometry (PRISm) were excluded from this analysis.

**Results:** Lung volumes from all 3 cohorts showed similar patterns of distributions and longitudinal changes with worsening airflow obstruction. The distributions for total lung capacity (TLC), vital capacity (VC), and inspiratory capacity (IC) and their patterns of change were nonlinear and included different phases. When stratified by airflow obstruction using Global initiative for chronic Obstructive Lung Disease (GOLD) stages, patients with GOLD 1 (mild) COPD had larger lung volumes (TLC, VC, IC) compared to patients with GOLD 0 (smokers with preserved spirometry) or GOLD 2 (moderate) disease. In longitudinal follow-up of baseline GOLD 0 patients who progressed to spirometric COPD, those with an initially higher TLC and VC developed mild obstruction (GOLD 1) while those with an initially lower TLC and VC developed moderate obstruction (GOLD 2).

**Conclusions:** In COPD, TLC, and VC have biphasic distributions, change in nonlinear fashions as obstruction worsens, and could differentiate those GOLD 0 patients at risk for more rapid spirometric disease progression.

**Keywords:** COPD; air trapping; computed tomography; early disease; lung volumes.

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# Impact of Coronavirus Disease 2019 on Hospital Admissions, Health Status, and Behavioral Changes of Patients with COPD

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- PMID: 37140947
- DOI: [10.15326/jcopdf.2022.0383](https://doi.org/10.15326/jcopdf.2022.0383)

**Free article**

**Abstract**

**Introduction:** Patients with chronic obstructive pulmonary disease (COPD) have an increased risk of acquiring severe coronavirus disease 2019 (COVID-19), which is why self-

isolation was recommended. However, long periods of social isolation, accompanied by limited access to health care systems, might influence the outcome of patients with severe COPD negatively.

**Methods:** Data from COPD and pneumonia patients at Charité-Universitätsmedizin Berlin and the volume of endoscopic lung volume reduction (ELVR) surgeries from the German Lung Emphysema Registry (*Lungenemphysem Register e.V.*) were analyzed from pre-pandemic (2012 to 2019) to the pandemic period (2020 and 2021). In addition, 52 patients with COPD Global initiative for chronic Obstructive Lung Disease (GOLD) stage 4 status included in the lung emphysema registry received questionnaires during lockdowns from June 2020 to April 2021.

**Results:** Admissions and ventilation therapies administered to COPD patients significantly decreased during the COVID-19 pandemic. Likewise, there was a reduction in ELVR treatments and follow-ups registered in German emphysema centers. Mortality was slightly higher among patients hospitalized with COPD during the pandemic. Increasing proportions of COPD patients with GOLD stage 3 and GOLD stage 4 status reported behavioral changes and subjective feelings of increasing COPD symptoms the longer the lockdown lasted. However, COPD symptom questionnaires revealed stable COPD symptoms over the pandemic time period.

**Summary:** This study reveals reduced COPD admissions and elective treatment procedures of COPD patients during the pandemic, but a slight increase in mortality among patients hospitalized with COPD, irrespective of COVID-19. Correspondingly, patients with severe COPD reported subjective deterioration of their health status, probably caused by their very strict compliance with lockdown measures.

**Keywords:** COPD; COVID-19; endoscopic lung volume reduction; lockdown measures.

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Chronic Obstr Pulm Dis

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. 2023 Jul 26;10(3):259-269.

doi: 10.15326/jcopdf.2022.0389.

# The Experiences of Individuals with a History of Acute Exacerbations of COPD and Their Thoughts on Death: Empirical Qualitative Research

[Yasemin Ceyhan](#)<sup>1</sup>

Affiliations expand

- PMID: 37140940
- DOI: [10.15326/jcopdf.2022.0389](https://doi.org/10.15326/jcopdf.2022.0389)

**Free article**

## **Abstract**

**Background:** The most important problem of chronic obstructive pulmonary disease (COPD) patients is acute exacerbation. Researching this experience and examining its relationship with death is extremely important in patient care.

**Methods:** This study was conducted to reveal the experiences of individuals with a history of acute exacerbations of chronic obstructive pulmonary disease (AECOPDs) and their thoughts on death by qualitative empirical research. The study was conducted in a pulmonology clinic between July and September 2022. In-depth face-to-face interviews were conducted with patients in their rooms using a semi-structured form created specifically for the study and used as a data collection tool. With patient consent, interviews were recorded and documented. During the data analysis phase, the Colaizzi method was used. The study was presented in accordance with the Consolidated Criteria for Reporting Qualitative Research (COREQ) checklist for qualitative research.

**Results:** The study was completed with 15 patients. A total of 13 of the patients were male and the mean age was 65 years. Patient statements were coded after the interviews and collected under 11 sub-themes. These sub-themes were categorized under the following

main themes: recognizing AECOPDs, AECOPD instant experiences, post-AECOPD, and thoughts on death.

**Conclusion:** Patients were able to recognize the symptoms of an AECOPD, that the severity of the symptoms increased during the exacerbation, that they felt regret or anxiety about re-exacerbation, and that all of these factors contributed to their fear of death.

**Keywords:** acute exacerbations; chronic obstructive pulmonary disease; death; nurse.

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Heart



. 2023 Jul 27;109(16):1216-1222.

doi: 10.1136/heartjnl-2023-322431.

## Systolic blood pressure, chronic obstructive pulmonary disease and cardiovascular risk

[Shishir Rao](#)<sup>1,2</sup>, [Milad Nazarzadeh](#)<sup>1,2</sup>, [Yikuan Li](#)<sup>1,2</sup>, [Dexter Canoy](#)<sup>3</sup>, [Mohammad Mamouei](#)<sup>1,2</sup>, [Gholamreza Salimi-Khorshidi](#)<sup>1,2</sup>, [Kazem Rahimi](#)<sup>4,2,5</sup>

Affiliations expand

- PMID: 37080767
- DOI: [10.1136/heartjnl-2023-322431](https://doi.org/10.1136/heartjnl-2023-322431)

**Free article**  
**Abstract**

**Objective:** In individuals with complex underlying health problems, the association between systolic blood pressure (SBP) and cardiovascular disease is less well recognised. The association between SBP and risk of cardiovascular events in patients with chronic obstructive pulmonary disease (COPD) was investigated.

**Methods and analysis:** In this cohort study, 39 602 individuals with a diagnosis of COPD aged 55–90 years between 1990 and 2009 were identified from validated electronic health records (EHR) in the UK. The association between SBP and risk of cardiovascular end points (composite of ischaemic heart disease, heart failure, stroke and cardiovascular death) was analysed using a deep learning approach.

**Results:** In the selected cohort (46.5% women, median age 69 years), 10 987 cardiovascular events were observed over a median follow-up period of 3.9 years. The association between SBP and risk of cardiovascular end points was found to be monotonic; the lowest SBP exposure group of <120 mm Hg presented nadir of risk. With respect to reference SBP (between 120 and 129 mm Hg), adjusted risk ratios for the primary outcome were 0.99 (95% CI 0.93 to 1.05) for SBP of <120 mm Hg, 1.02 (0.97 to 1.07) for SBP between 130 and 139 mm Hg, 1.07 (1.01 to 1.12) for SBP between 140 and 149 mm Hg, 1.11 (1.05 to 1.17) for SBP between 150 and 159 mm Hg and 1.16 (1.10 to 1.22) for SBP  $\geq$ 160 mm Hg.

**Conclusion:** Using deep learning for modelling EHR, we identified a monotonic association between SBP and risk of cardiovascular events in patients with COPD.

**Keywords:** epidemiology; hypertension.

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## Conflict of interest statement

Competing interests: KR, corresponding author of this research, is a former member of the Editorial Board for BMJ Heart. All of the remaining authors have no relevant financial or non-financial interests to disclose.

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

<sup>1</sup>

BMJ

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. 2023 Jul 28;382:p1708.

doi: 10.1136/bmj.p1708.

## How to reduce medications for people with multiple long term conditions

[Helen Saul](#)<sup>1</sup>, [Samantha Cassidy](#)<sup>1</sup>, [Brendan Deeney](#)<sup>1</sup>, [Candace Imison](#)<sup>1</sup>, [Joanne Reeve](#)<sup>2</sup>

Affiliations expand

- PMID: 37507125
- DOI: [10.1136/bmj.p1708](https://doi.org/10.1136/bmj.p1708)

### **Abstract**

The studyReeve J, Maden M, Hill R, et al. Deprescribing medicines in older people living with multimorbidity and polypharmacy: the TAILOR evidence synthesis. *Health Technol Assess* 2022;26:1-148.To read the full NIHR Alert, go to: <https://evidence.nihr.ac.uk/alert/how-to-safely-deprescribe-medications-for-people-with-multiple-long-term-conditions/>.

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### **Conflict of interest statement**

Competing interests: The BMJ has judged that there are no disqualifying financial ties to commercial companies. The authors declare the following other interests: none. Further details of The BMJ policy on financial interests are here: <https://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/declaration-competing-interests>

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Geroscience



. 2023 Jul 27.

doi: 10.1007/s11357-023-00880-9. Online ahead of print.

# Systemic inflammation and biological aging in the Health and Retirement Study

[Helen C S Meier](#)<sup>1</sup>, [Colter Mitchell](#)<sup>2</sup>, [Thomas Karadimas](#)<sup>2</sup>, [Jessica D Faul](#)<sup>2</sup>

Affiliations expand

- PMID: 37501048
- DOI: [10.1007/s11357-023-00880-9](https://doi.org/10.1007/s11357-023-00880-9)

## **Abstract**

Chronic, low-level systemic inflammation associated with aging, or inflammaging, is a risk factor for several chronic diseases and mortality. Using data from the Health and Retirement Study, we generated a continuous latent variable for systemic inflammation from seven measured indicators of inflammation and examined associations with another biomarker of biological aging, DNA methylation age acceleration measured by epigenetic clocks, and 4-year mortality (N = 3,113). We found that greater systemic inflammation was positively associated with DNA methylation age acceleration for 10 of the 13 epigenetic clocks, after adjustment for sociodemographics and chronic disease risk factors. The latent variable for systemic inflammation was associated with 4-year mortality independent of DNA methylation age acceleration and was a better predictor of 4-year mortality than any

of the epigenetic clocks examined, as well as mortality risk factors, including obesity and multimorbidity. Inflammaging and DNA methylation age acceleration may represent different biological processes contributing to mortality risk. Leveraging multiple measured inflammation markers to capture inflammaging is important for biology of aging research.

**Keywords:** DNA methylation; Epigenetic clocks; Health and Retirement Study; Inflammation.

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Nat Commun

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. 2023 Jul 27;14(1):4518.

doi: 10.1038/s41467-023-40245-6.

## [Increasing number of long-lived ancestors marks a decade of healthspan extension and healthier metabolomics profiles](#)

[Niels van den Berg](#)<sup>1,2</sup>, [Mar Rodríguez-Gironde](#)<sup>3</sup>, [Ingrid K van Dijk](#)<sup>4</sup>, [P Eline Slagboom](#)<sup>#5,6</sup>, [Marian Beekman](#)<sup>#5</sup>

Affiliations expand

- PMID: 37500622
- PMCID: [PMC10374564](#)
- DOI: [10.1038/s41467-023-40245-6](#)

## Abstract

Globally, the lifespan of populations increases but the healthspan is lagging behind. Previous research showed that survival into extreme ages (longevity) clusters in families as illustrated by the increasing lifespan of study participants with each additional long-lived family member. Here we investigate whether the healthspan in such families follows a similar quantitative pattern using three-generational data from two databases, LLS (Netherlands), and SEDD (Sweden). We study healthspan in 2143 families containing index persons with 26 follow-up years and two ancestral generations, comprising 17,539 persons. Our results provide strong evidence that an increasing number of long-lived ancestors associates with up to a decade of healthspan extension. Further evidence indicates that members of long-lived families have a delayed onset of medication use, multimorbidity and, in mid-life, healthier metabolomic profiles than their partners. We conclude that both lifespan and healthspan are quantitatively linked to ancestral longevity, making family data invaluable to identify protective mechanisms of multimorbidity.

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## Conflict of interest statement

The authors declare no competing interests.

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Br J Gen Pract

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

doi: 10.3399/bjgp23X734661. Print 2023 Aug.

## Defining and measuring complex multimorbidity: a critical analysis

[Sanghamitra Pati](#)<sup>1</sup>, [Clare MacRae](#)<sup>2</sup>, [David Henderson](#)<sup>3</sup>, [David Weller](#)<sup>2</sup>, [Bruce Guthrie](#)<sup>2</sup>, [Stewart Mercer](#)<sup>4</sup>

Affiliations expand

- PMID: 37500453
- DOI: [10.3399/bjgp23X734661](https://doi.org/10.3399/bjgp23X734661)

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Hormones (Athens)

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. 2023 Jul 26.

doi: 10.1007/s42000-023-00471-5. Online ahead of print.

# Association between medication adherence and health-related quality of life of patients with hypertension and dyslipidemia

[Athanasios Chantzaras](#)<sup>1</sup>, [John Yfantopoulos](#)<sup>2</sup>

Affiliations expand

- PMID: 37493942
- DOI: [10.1007/s42000-023-00471-5](https://doi.org/10.1007/s42000-023-00471-5)

## Abstract

**Purpose:** To evaluate the association between medication adherence and health-related quality of life (HRQoL) of patients with hypertension and dyslipidemia in Greece.

**Methods:** In a multicenter, cross-sectional, non-interventional study, a total of 721 hypertensive and 463 dyslipidemic adult outpatient patients were recruited during the COVID-19 pandemic using consecutive sampling. The EQ-5D-5L instrument was used to measure HRQoL, and medication adherence was assessed with the Adherence Starts with Knowledge 20 questionnaire. Multiple linear stepwise regressions using robust standard errors were employed.

**Results:** Approximately 28% of hypertensive and 16% of dyslipidemic patients had not been fully adherent during the previous week, while the estimates were 49 and 34%, respectively when the previous month was considered. The HRQoL domain with the highest prevalence of problems was anxiety/depression, followed by mobility and usual activities for both conditions; HRQoL was lower in dyslipidemic patients. Higher medication non-adherence was independently associated with lower EQ-VAS in hypertension and a lower EQ-5D index in dyslipidemia. Other significant risk factors of impaired HRQoL and general health were lack of exercise, longer duration of disease, and multimorbidity, while a curvilinear effect of BMI and age was observed. Also, female gender, employment, and marriage worked as protective factors for hypertensive patients and education for dyslipidemic participants.

**Conclusion:** Medication adherence is suboptimal in patients with hypertension and, in particular, with dyslipidemia in Greece. Moreover, poor medication adherence has a detrimental impact on patients' HRQoL. Therefore, improving treatment outcomes and patients' HRQoL in a sustainable way requires a better understanding of the factors influencing medication adherence.

**Keywords:** Compliance; Dyslipidemia; Greece; Hypertension; Medication adherence; Quality of life.

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Int J Equity Health

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. 2023 Jul 24;22(1):137.

doi: 10.1186/s12939-023-01950-2.

## [20-year trends in multimorbidity by race/ethnicity among hospitalized patient populations in the United States](#)

[Mursal A Mohamud](#)<sup>1</sup>, [David J T Campbell](#)<sup>2,3,4</sup>, [James Wick](#)<sup>2</sup>, [Alexander A Leung](#)<sup>2,3</sup>, [Gabriel E Fabreau](#)<sup>2,3</sup>, [Marcello Tonelli](#)<sup>2,3</sup>, [Paul E Ronksley](#)<sup>5</sup>

Affiliations expand

- PMID: 37488549

- PMCID: [PMC10367428](#)
- DOI: [10.1186/s12939-023-01950-2](#)

### Free PMC article

## Abstract

**Background:** The challenges presented by multimorbidity continue to rise in the United States. Little is known about how the relative contribution of individual chronic conditions to multimorbidity has changed over time, and how this varies by race/ethnicity. The objective of this study was to describe trends in multimorbidity by race/ethnicity, as well as to determine the differential contribution of individual chronic conditions to multimorbidity in hospitalized populations over a 20-year period within the United States.

**Methods:** This is a serial cross-sectional study using the Nationwide Inpatient Sample (NIS) from 1993 to 2012. We identified all hospitalized patients aged  $\geq 18$  years old with available data on race/ethnicity. Multimorbidity was defined as the presence of 3 or more conditions based on the Elixhauser comorbidity index. The relative change in the proportion of hospitalized patients with multimorbidity, overall and by race/ethnicity (Black, White, Hispanic, Asian/Pacific Islander, Native American) were tabulated and presented graphically. Population attributable fractions were estimated from modified Poisson regression models adjusted for sex, age, and insurance type. These fractions were used to describe the relative contribution of individual chronic conditions to multimorbidity over time and across racial/ethnic groups.

**Results:** There were 123,613,970 hospitalizations captured within the NIS between 1993 and 2012. The prevalence of multimorbidity increased in all race/ethnic groups over the 20-year period, most notably among White, Black, and Native American populations (+ 29.4%, + 29.7%, and + 32.0%, respectively). In both 1993 and 2012, Black hospitalized patients had a higher prevalence of multimorbidity (25.1% and 54.8%, respectively) compared to all other race/ethnic groups. Native American populations exhibited the largest overall increase in multimorbidity (+ 32.0%). Furthermore, the contribution of metabolic diseases to multimorbidity increased, particularly among Hispanic patients who had the highest population attributable fraction values for diabetes without complications (15.0%), diabetes with complications (5.1%), and obesity (5.8%).

**Conclusions:** From 1993 to 2012, the secular increases in the prevalence of multimorbidity as well as changes in the differential contribution of individual chronic conditions has varied substantially by race/ethnicity. These findings further elucidate the racial/ethnic gaps prevalent in multimorbidity within the United States.

**Prior presentations:** Preliminary finding of this study were presented at the Society of General Internal Medicine (SGIM) Annual Conference, Washington, DC, April 21, 2017.



**Keywords:** Ethnicity; Hospitalization; Multimorbidity; Race; United States.

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## Conflict of interest statement

The authors have no conflicts of interest to declare.

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- [3 figures](#)

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J Gerontol A Biol Sci Med Sci

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. 2023 Jul 24;glad178.

doi: 10.1093/gerona/glad178. Online ahead of print.

# **Bidirectional Association Between Multimorbidity and Frailty and the Role of Depression in Older Europeans**

[Zhaolong Feng](#)<sup>1</sup>, [Ze Ma](#)<sup>1</sup>, [Wei Hu](#)<sup>1</sup>, [Qida He](#)<sup>1</sup>, [Tongxing Li](#)<sup>1</sup>, [Jiadong Chu](#)<sup>1</sup>, [Xuanli Chen](#)<sup>1</sup>, [Qiang Han](#)<sup>1</sup>, [Na Sun](#)<sup>1</sup>, [Yueping Shen](#)<sup>1</sup>

Affiliations expand

- PMID: 37487182
- DOI: [10.1093/gerona/glad178](https://doi.org/10.1093/gerona/glad178)

## Abstract

**Background:** Although previous studies have reported an association between multimorbidity and frailty, its direction and mechanism remain unclear. This study aimed to investigate the direction of this association, as well as the role of depression among older Europeans.

**Methods:** We used a cross-lagged panel design to evaluate the temporal relationship between multimorbidity and frailty and the role of depression. Multimorbidity status was assessed by the self-reporting of 14 chronic diseases. Frailty was assessed based on the frailty phenotype. The EURO-D 12-item scale was used to assess depression.

**Results:** There was a bidirectional relationship between frailty and multimorbidity. More severe multimorbidity predicted greater frailty ( $\beta = 0.159$ ;  $P < 0.001$ ) and vice versa ( $\beta = 0.107$ ;  $P < 0.001$ ). All paths from multimorbidity to frailty were stronger than the paths from frailty to multimorbidity (b1-a1:  $\beta = 0.051$ ;  $P < 0.001$ ). Likewise, early multimorbidity change was a significant predictive factor for late frailty change ( $\beta = 0.064$ ;  $P < 0.001$ ) and vice versa ( $\beta = 0.048$ ;  $P < 0.001$ ). Depression in wave 5 (T5) mediated the association between frailty in wave 4 (T4) and multimorbidity in wave 6 (T6) (indirect effect:  $\beta = 0.004$ ; bootstrap 95% CI: 0.003, 0.006).

**Conclusions:** A positive, bidirectional association was observed between multimorbidity and frailty. Depression may be a potential cause of an increased risk of multimorbidity later in life in frail older adults. Early monitoring of frailty and depression may slow the progression of multimorbidity, thereby interrupting the vicious cycle.

**Keywords:** Bidirectional association; Depression; Frailty; Mediation; Multimorbidity.

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PLoS One



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doi: 10.1371/journal.pone.0287263. eCollection 2023.

# Lifestyle factors related to prevalent chronic disease multimorbidity: A population-based cross-sectional study

[Jacobien Niebuur](#)<sup>1</sup>, [Judith M Vonk](#)<sup>1</sup>, [Yihui Du](#)<sup>1</sup>, [Geertruida H de Bock](#)<sup>1</sup>, [Gerton Lunter](#)<sup>1</sup>, [Paul F M Krabbe](#)<sup>1</sup>, [Behrooz Z Alizadeh](#)<sup>1</sup>, [Harold Snieder](#)<sup>1</sup>, [Nynke Smidt](#)<sup>1</sup>, [Marieke Boezen](#)<sup>1</sup>, [Eva Corpeleijn](#)<sup>1</sup>

Affiliations expand

- PMID: 37486939
- PMCID: [PMC10365307](#)
- DOI: [10.1371/journal.pone.0287263](#)

**Free PMC article**

## **Abstract**

**Background:** Multimorbidity is associated with poor quality of life, polypharmacy, health care costs and mortality, with those affected potentially benefitting from a healthy lifestyle. We assessed a comprehensive set of lifestyle factors in relation to multimorbidity with major chronic diseases.

**Methods:** This cross-sectional study utilised baseline data for adults from the prospective Lifelines Cohort in the north of the Netherlands (N = 79,345). We defined multimorbidity as the co-existence of two or more chronic diseases (i.e. cardiovascular disease, cancer, respiratory disease, type 2 diabetes) and evaluated factors in six lifestyle domains (nutrition, physical (in)activity, substance abuse, sleep, stress, relationships) among groups by the number of chronic diseases ( $\geq 2$ , 1, 0). Multinomial logistic regression models were

created, adjusted for appropriate confounders, and odds ratios (OR) with 95% confidence intervals (95%CI) were reported.

**Results:** 3,712 participants had multimorbidity (4.7%, age  $53.5 \pm 12.5$  years), and this group tended to have less healthy lifestyles. Compared to those without chronic diseases, those with multimorbidity reported physical inactivity more often (OR, 1.15; 95%CI, 1.06-1.25; not significant for one condition), chronic stress (OR, 2.14; 95%CI, 1.92-2.38) and inadequate sleep (OR, 1.70; 95%CI, 1.41-2.06); as expected, they more often watched television (OR, 1.70; 95%CI, 1.42-2.04) and currently smoked (OR, 1.91; 95%CI, 1.73-2.11), but they also had lower alcohol intakes (OR, 0.66; 95%CI, 0.59-0.74).

**Conclusions:** Chronic stress and poor sleep, in addition to physical inactivity and smoking, are lifestyle factors of great concern in patients with multimorbidity.

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## Conflict of interest statement

The authors have declared that no competing interests exist.

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

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J Investig Allergol Clin Immunol

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. 2023 Jul 27;33(4):281-288.

doi: 10.18176/jiaci.0816. Epub 2002 May 3.

# Exacerbations Among Patients With Asthma Are Largely Dependent on the Presence of Multimorbidity

[J Domínguez-Ortega](#)<sup>1 2 3</sup>, [J A Luna-Porta](#)<sup>1 2 3</sup>, [J M Olaguibel](#)<sup>3 4</sup>, [P Barranco](#)<sup>1 2 3</sup>, [E Arismendi](#)<sup>3 5 6 7</sup>, [B Barroso](#)<sup>3 8</sup>, [D Betancor](#)<sup>3 8</sup>, [I Bobolea](#)<sup>3 5 6 7</sup>, [M L Caballero](#)<sup>1 2 3</sup>, [B Cárdena](#)<sup>3 9</sup>, [M J Cruz](#)<sup>3 10 11</sup>, [E Curto](#)<sup>3 12 13 14</sup>, [F J González-Barcala](#)<sup>3 15 16 17</sup>, [I Losantos-García](#)<sup>2 18</sup>, [C Martínez-Rivera](#)<sup>3 14 19 20</sup>, [P Méndez-Brea](#)<sup>21</sup>, [J Molló](#)<sup>3 5 6 22</sup>, [X Muñoz](#)<sup>3 11</sup>, [C Picado](#)<sup>3 5 6 7</sup>, [V Plaza](#)<sup>3 12 13 14</sup>, [V Del Pozo](#)<sup>3 9</sup>, [M J Rial](#)<sup>3 23</sup>, [J Sastre](#)<sup>3 8</sup>, [L Soto](#)<sup>3 12 13 14</sup>, [A Valero](#)<sup>3 5 6 7</sup>, [M Valverde-Monge](#)<sup>3 8</sup>, [S Quirce](#)<sup>1 2 3</sup>

Affiliations expand

- PMID: 35503227
- DOI: [10.18176/jiaci.0816](https://doi.org/10.18176/jiaci.0816)

## Abstract

**Background and objective:** Comorbidities can influence asthma control and promote asthma exacerbations (AEs). However, the impact of multimorbidity in AEs, assessed based on long-term follow-up of patients with asthma of different degrees of severity, has received little attention in real-life conditions. To describe the epidemiological and clinical characteristics and predictors of AEs in patients who had presented at least 1 AE in the previous year in the MEchanism of Genesis and Evolution of Asthma (MEGA) cohort.

**Methods:** The work-up included a detailed clinical examination, pulmonary function testing, fractional exhaled nitric oxide (FeNO), blood counts, induced sputum, skin prick-tests, asthma questionnaires, and assessment of multimorbidity. The number of moderate-severe AEs in the preceding year was registered for each patient.

**Results:** The study population comprised 486 patients with asthma (23.7% mild, 35% moderate, 41.3% severe). Disease remained uncontrolled in 41.9%, and 47.3% presented  $\geq 1$  moderate-severe AE, with a mean (SD) annual exacerbation rate of 0.47 (0.91) vs 2.11 (2.82) in mild and severe asthma, respectively. Comorbidity was detected in 56.4% (66.6% among those with severe asthma). Bronchiectasis, chronic rhinosinusitis with nasal polyps, atopy, psychiatric illnesses, hyperlipidemia, and hypertension were significantly associated with AEs. No associations were found for FeNO, blood eosinophils, or total serum IgE. Sputum eosinophilia and a high-T2 inflammatory pattern were significantly associated with

AEs. Multivariable regression analysis showed a significant association with asthma severity, uncontrolled disease, and low prebronchodilator FEV1/FVC.

**Conclusion:** Our study revealed a high frequency of AE in the MEGA cohort. This was strongly associated with multimorbidity, asthma severity, poor asthma control, airflow obstruction, higher sputum eosinophils, and a very high-T2 inflammatory pattern.

**Keywords:** Asthma; Asthma control; Exacerbations; MEGA cohort; Multimorbidity.

- [Cited by 1 article](#)

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

<sup>1</sup>  
BMC Pulm Med

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. 2023 Jul 28;23(1):278.

doi: 10.1186/s12890-023-02570-w.

## **Machine learning for prediction of asthma exacerbations among asthmatic patients: a systematic review and meta-analysis**

[Shiqiu Xiong](#)<sup>1,2</sup>, [Wei Chen](#)<sup>3</sup>, [Xinyu Jia](#)<sup>3</sup>, [Yang Jia](#)<sup>4</sup>, [Chuanhe Liu](#)<sup>5,6</sup>

[Affiliations](#) [expand](#)

- PMID: 37507662

- DOI: [10.1186/s12890-023-02570-w](https://doi.org/10.1186/s12890-023-02570-w)

## Abstract

**Background:** Asthma exacerbations reduce the patient's quality of life and are also responsible for significant disease burdens and economic costs. Machine learning (ML)-based prediction models have been increasingly developed to predict asthma exacerbations in recent years. This systematic review and meta-analysis aimed to identify the prediction performance of ML-based prediction models for asthma exacerbations and address the uncertainty of whether modern ML methods could become an alternative option to predict asthma exacerbations.

**Methods:** PubMed, Cochrane Library, EMBASE, and Web of Science were searched for studies published up to December 15, 2022. Studies that applied ML methods to develop prediction models for asthma exacerbations among asthmatic patients older than five years and were published in English were eligible. The prediction model risk of bias assessment tool (PROBAST) was utilized to estimate the risk of bias and the applicability of included studies. Stata software (version 15.0) was used for the random effects meta-analysis of performance measures. Subgroup analyses stratified by ML methods, sample size, age groups, and outcome definitions were conducted.

**Results:** Eleven studies, including 23 prediction models, were identified. Most of the studies were published in recent three years. Logistic regression, boosting, and random forest were the most used ML methods. The most common important predictors were systemic steroid use, short-acting beta2-agonists, emergency department visit, age, and exacerbation history. The overall pooled area under the curve of the receiver operating characteristics (AUROC) of 11 studies (23 prediction models) was 0.80 (95% CI 0.77-0.83). Subgroup analysis based on different ML models showed that boosting method achieved the best performance, with an overall pooled AUROC of 0.84 (95% CI 0.81-0.87).

**Conclusion:** This study identified that ML was the potential tool to achieve great performance in predicting asthma exacerbations. However, the methodology within these models was heterogeneous. Future studies should focus on improving the generalization ability and practicability, thus driving the application of these models in clinical practice.

**Keywords:** Asthma; Exacerbation; Machine learning; Meta-analysis; Prediction model; Systematic review.

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Ann Allergy Asthma Immunol

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. 2023 Jul 26;S1081-1206(23)00522-7.

doi: 10.1016/j.anai.2023.07.017. Online ahead of print.

# Real-world Severe Asthma Biologic Administration and Adherence Differs by Biologic: CHRONICLE Study Results

[Dennis K Ledford](#)<sup>1</sup>, [Weily Soong](#)<sup>2</sup>, [Warner Carr](#)<sup>3</sup>, [Jennifer Trevor](#)<sup>4</sup>, [Laren Tan](#)<sup>5</sup>, [Donna Carstens](#)<sup>6</sup>, [Christopher S Ambrose](#)<sup>7</sup>

Affiliations expand

- PMID: 37506846
- DOI: [10.1016/j.anai.2023.07.017](https://doi.org/10.1016/j.anai.2023.07.017)

## Abstract

**Background:** Patient adherence to biologic therapies is crucial for clinical benefits. Previous assessments of US patients' adherence to severe asthma (SA) biologic therapies have relied on healthcare insurance claims data that have limitations.

**Objective:** To describe real-world, specialist-reported biologic administration and adherence among US adults with SA.

**Methods:** CHRONICLE (ClinicalTrials.gov: [NCT03373045](https://clinicaltrials.gov/ct2/show/study/NCT03373045)) is an ongoing real-world, noninterventional study of patients with SA treated by US subspecialists. Sites report date and location for all biologic administrations. We evaluated biologic (benralizumab,



dupilumab, mepolizumab, omalizumab, reslizumab) adherence as proportion of days covered (PDC) during the first 52 weeks and mean number of days until patients received the expected number of doses for 13, 26, and 52 weeks of treatment.

**Results:** A total of 2117 patients received biologic administrations between February 2018 and February 2022. Most patients (84%) received biologic administrations at a subspecialist site. Over time, administrations at specialist sites decreased, whereas home administrations increased. Median PDC was 87%; mean number of days to receive a 52-week (364-day) equivalent number of doses was 423 for all biologics (average delay of 58 days). Dupilumab had the lowest PDC and highest mean delays in dosing across all intervals; better adherence was observed among commercially insured patients.

**Conclusion:** Patients with SA are mostly adherent to biologic therapies. Biologics with shorter dosing intervals and at-home administration had worse adherence, likely due to greater opportunities for delays. Specialist-reported administration data provide a unique perspective on biologic adherence, which may be overestimated for at-home administrations by insurance claims data.

**Keywords:** Severe asthma; adherence; biologic therapies.

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3  
J Otolaryngol Head Neck Surg

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. 2023 Jul 28;52(1):50.

doi: 10.1186/s40463-023-00657-2.

# Remission: does it already exist in chronic rhinosinusitis with nasal polypsis?

[Yvonne Chan](#)<sup>1</sup>, [Andrew V Thamboo](#)<sup>2</sup>, [Joseph K Han](#)<sup>3</sup>, [Martin Desrosiers](#)<sup>4</sup>

Affiliations expand

- PMID: 37507757
- DOI: [10.1186/s40463-023-00657-2](https://doi.org/10.1186/s40463-023-00657-2)

## **Abstract**

**Background:** Remission, defined as absence of symptoms and objective markers of disease, is emerging as the penultimate goal in the management of several chronic diseases. The concept of remission, well-established in Rheumatology as well as Gastroenterology, is currently emerging in Respiratory Medicine for asthma. It is interesting to consider whether the disease remission concept might successfully be applied to Otolaryngology-Head and Neck Surgery in the management of chronic rhinosinusitis with nasal polypsis (CRSwNP).

**Objective:** The purpose of this letter is to explore the evidence supporting the concept of remission under continued medical therapy in chronic rhinosinusitis with nasal polypsis.

**Methods:** The authors reviewed the literature and summarized studies in chronic rhinosinusitis with nasal polypsis evaluating for evidence of clinical, biochemical, and endoscopic remission.

**Results:** Findings of the studies revealed that endoscopic sinus surgery with continued medical therapy achieved remission in approximately 50% of all patients. CRSwNP patients after primary endoscopic sinus surgery were able to achieve remission in 72% of instances, however this drops to 42% for patients having revision sinus surgery. For CRSwNP patients with co-morbidities such as asthma and aspirin exacerbated respiratory disease, remission rate drops to 23% and 23.5%, respectively compared to non-asthmatic CRSwNP patients who present a remission rate under continued medical therapy of 60%.

**Conclusion:** Remission of symptoms and evidence of disease under medical therapy is indeed a concept achievable in patients with CRSwNP, as demonstrated by studies in the literature. Various co-morbidities, notably asthma, apparently influence rate of remission. Better defining this outcome through consensus-based definitions will allow for the development of strategies in CRSwNP care that can help affected patients attain complete relief from clinical, biochemical, and endoscopic markers of CRS with judicious use of

medication and surgery. Future efforts will attempt to improve on these outcomes by achieving symptomatic and endoscopic control of disease following cessation of therapy, potentially paving the way towards clinical remission or a 'cure' in CRS.

**Keywords:** Asthma; Chronic rhinosinusitis; Endoscopic sinus surgery; Epithelium; Inflammatory bowel diseases; Nasal polyposis; Remission; Type 2 inflammation.

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J Allergy Clin Immunol Pract

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. 2023 Jul 26;S2213-2198(23)00797-3.

doi: 10.1016/j.jaip.2023.07.024. Online ahead of print.

## [Mepolizumab in patients with severe asthma and comorbidities: 1-year REALITI-A analysis](#)

[Mark C Liu](#)<sup>1</sup>, [Diego Bagnasco](#)<sup>2</sup>, [Andrea Matucci](#)<sup>3</sup>, [Charles Pilette](#)<sup>4</sup>, [Robert G Price](#)<sup>5</sup>, [Aoife C Maxwell](#)<sup>6</sup>, [Rafael Alfonso-Cristancho](#)<sup>7</sup>, [Rupert W Jakes](#)<sup>8</sup>, [Jason K Lee](#)<sup>9</sup>, [Peter Howarth](#)<sup>10</sup>

Affiliations [expand](#)

- PMID: 37507070
- DOI: [10.1016/j.jaip.2023.07.024](https://doi.org/10.1016/j.jaip.2023.07.024)

## Abstract

**Background:** Severe asthma is complex; comorbidities may influence disease outcomes.

**Objective:** To assess mepolizumab effectiveness in patients with severe asthma and comorbidities.

**Methods:** REALITI-A was a 2-year international, prospective study enrolling adults with asthma newly prescribed mepolizumab (100 mg subcutaneously) at physician's discretion. This post hoc analysis assessed 1-year outcomes stratified by comorbidities at enrollment: chronic rhinosinusitis with nasal polyps (CRSwNP), gastro-esophageal reflux disease (GERD), depression/anxiety and chronic obstructive pulmonary disease (COPD). Outcomes included the rate of clinically significant asthma exacerbations (CSEs; requiring systemic corticosteroids and/or hospital/emergency room admission) between the 12 months pre- and post-mepolizumab treatment and changes from baseline in daily maintenance oral corticosteroid (mOCS) dose (Month 12), Asthma Control Questionnaire (ACQ)-5 score (Month 12) and forced expiratory volume in 1 second (FEV<sub>1</sub>; Months 9-12).

**Results:** At enrollment (N=822), 321/822 (39%), 309/801 (39%), 203/785 (26%) and 81/808 (10%) patients had comorbid CRSwNP, GERD, depression/anxiety, and COPD, respectively. Post- versus pre-treatment across all comorbidity subgroups: the rate of CSEs decreased by  $\geq 63\%$ ; among 298 (39%) patients on mOCS at baseline, median dose decreased by  $\geq 50\%$ ; ACQ-5 score decreased by  $\geq 0.63$  points; FEV<sub>1</sub> increased by  $\geq 74$  mL. Patients with versus without CRSwNP had the greatest improvements (e.g. rate of CSEs decreased by 75%). Patients without GERD, depression/anxiety or COPD had greater improvements than those with the respective comorbidities, except for FEV<sub>1</sub> in patients with COPD.

**Conclusion:** Mepolizumab improved disease outcomes in patients with severe asthma irrespective of comorbidities, with additional benefit for patients with CRSwNP.

**Keywords:** Asthma; anxiety; chronic obstructive pulmonary disease; chronic rhinosinusitis with nasal polyps; comorbidities; depression; gastro-esophageal reflux disease; mepolizumab; severe asthma.

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Mucosal Immunol



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doi: 10.1016/j.mucimm.2023.07.002. Online ahead of print.

## IL-33-induced neutrophilic inflammation and NETosis underlie rhinovirus-triggered exacerbations of asthma

[Bodie Curren](#)<sup>1</sup>, [Tufael Ahmed](#)<sup>2</sup>, [Daniel R Howard](#)<sup>1</sup>, [Md Ashik Ullah](#)<sup>3</sup>, [Ismail Sebina](#)<sup>4</sup>, [Ridwan B Rashid](#)<sup>1</sup>, [Md Al Amin Sikder](#)<sup>1</sup>, [Patricia Namubiru](#)<sup>1</sup>, [Alec Bissell](#)<sup>3</sup>, [Sylvia Ngo](#)<sup>3</sup>, [David J Jackson](#)<sup>5</sup>, [Marie Toussaint](#)<sup>6</sup>, [Michael R Edwards](#)<sup>6</sup>, [Sebastian L Johnston](#)<sup>6</sup>, [Henry J McSorley](#)<sup>7</sup>, [Simon Phipps](#)<sup>8</sup>

Affiliations expand

- PMID: 37506849
- DOI: [10.1016/j.mucimm.2023.07.002](https://doi.org/10.1016/j.mucimm.2023.07.002)

### **Abstract**

Rhinovirus-induced neutrophil extracellular traps (NETs) contribute to acute asthma exacerbations, however the molecular factors that trigger NETosis in this context remain ill-defined. Here, we sought to implicate a role for IL-33, an epithelial cell-derived alarmin rapidly released in response to infection. In mice with chronic experimental asthma (CEA), but not naïve controls, rhinovirus inoculation induced an early (1 day post infection; dpi) inflammatory response dominated by neutrophils, neutrophil-associated cytokines (IL-1 $\alpha$ , IL-1 $\beta$ , CXCL1) and NETosis, followed by a later, type-2 inflammatory phase (3-7 dpi), characterized by eosinophils, elevated IL-4 levels, and goblet cell hyperplasia. Notably, both phases were ablated by HpARI (Heligmosomoides polygyrus Alarmin Release Inhibitor), which blocks IL-33 release and signalling. Instillation of exogenous IL-33 recapitulated the rhinovirus-induced early phase, including the increased presence of NETs in the airway mucosa, in a PAD4-dependent manner. Ex vivo IL-33-stimulated neutrophils

from mice with CEA, but not naïve mice, underwent NETosis, and produced greater amounts of IL-1 $\alpha$ / $\beta$  IL-4, and IL-5. In nasal samples from rhinovirus-infected people with asthma, but not healthy controls, IL-33 levels correlated with neutrophil elastase and dsDNA. Our findings suggest that IL-33 blockade ameliorates the severity of an asthma exacerbation by attenuating neutrophil recruitment and the downstream generation of NETs.

**Keywords:** Asthma; HpARI; IL-33; NETosis; PAD4; ST2; dsDNA; eosinophil; neutrophil; rhinovirus.

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J Asthma



. 2023 Jul 28;1-19.

doi: 10.1080/02770903.2023.2241905. Online ahead of print.

## [Cost-effectiveness and resource use analysis of patients with asthma before and after treatment with mepolizumab in a real-life setting](#)

[Javier Domínguez-Ortega](#)<sup>1</sup>, [Daniel Laorden](#)<sup>2</sup>, [Francisca Vílchez-Sánchez](#)<sup>1</sup>, [David Bañas-Conejero](#)<sup>3</sup>, [Santiago Quirce](#)<sup>1</sup>

Affiliations expand

- PMID: 37503953

- DOI: [10.1080/02770903.2023.2241905](https://doi.org/10.1080/02770903.2023.2241905)

## Abstract

**Objective:** To define the cost-effectiveness and health resource use of mepolizumab in a cohort of patients with severe eosinophilic asthma in real-life conditions in Spain. **Methods:** This was an observational, retrospective, single-center study. A total of 30 patients included were diagnosed with severe eosinophilic asthma and treated with mepolizumab 100 mg subcutaneous (SC) 4-weekly for 12 months. **Outcomes evaluated:** incremental cost-effectiveness ratio (ICER), number of exacerbations, disease control with the Asthma Control Test (ACT), Asthma Quality of Life Questionnaire (AQLQ), and direct and indirect cost per patient. **Results:** 12 months after mepolizumab initiation, a significant decrease in exacerbations was shown, from a mean (standard deviation [SD]) of 3.1 (2.6) to 0.7 (1.5), an increase from 4.9 (0.4) to 6.1 (0.5) in AQLQ, and from 14.9 (5.7) to 21.5 (3.9) in ACT scores. The number of cortico-dependent patients significantly decreased from 53.3% to 13.3% during this period. There was a significant decrease of 94% in the cost of hospitalization, from a mean (SD) of €4063.9 (5423.9) pre-treatment to €238.6 (1306.9) post-treatment ( $P = 0.0003$ ). Total costs decreased significantly from a median (IQR) of €2,423.1 (1,512.8; 9,320.9) in the pre-treatment period to €1,177.5 (965.0; 1,737.8) in the post-treatment period if mepolizumab was excluded. ICER per exacerbation avoided was €3606.9, per 3-point ACT score increase €3934.8, and per 0.5-point AQLQ score increase €3606.9. **Conclusions:** Mepolizumab improves control of asthma and quality of life in patients with severe diseases in a cost-effectiveness range. The number of exacerbations decreased, and there was a clear reduction in primary care visits and hospitalizations. Further economic analyses of biological therapies for asthma are required.

**Keywords:** Treatment; economics; management/control.

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**Review**

Nat Rev Dis Primers

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. 2023 Jul 27;9(1):39.

doi: 10.1038/s41572-023-00450-5.

# HIV-associated lung disease

[Ioannis Konstantinidis](#)<sup>1</sup>, [Kristina Crothers](#)<sup>2</sup>, [Ken M Kunisaki](#)<sup>3</sup>, [M Bradley Drummond](#)<sup>4</sup>, [Thomas Benfield](#)<sup>5</sup>, [Heather J Zar](#)<sup>6,7</sup>, [Laurence Huang](#)<sup>8,9</sup>, [Alison Morris](#)<sup>10</sup>

Affiliations expand

- PMID: 37500684
- DOI: [10.1038/s41572-023-00450-5](https://doi.org/10.1038/s41572-023-00450-5)

## Abstract

Lung disease encompasses acute, infectious processes and chronic, non-infectious processes such as chronic obstructive pulmonary disease, asthma and lung cancer. People living with HIV are at increased risk of both acute and chronic lung diseases. Although the use of effective antiretroviral therapy has diminished the burden of infectious lung disease, people living with HIV experience growing morbidity and mortality from chronic lung diseases. A key risk factor for HIV-associated lung disease is cigarette smoking, which is more prevalent in people living with HIV than in uninfected people. Other risk factors include older age, history of bacterial pneumonia, *Pneumocystis pneumonia*, pulmonary tuberculosis and immunosuppression. Mechanistic investigations support roles for aberrant innate and adaptive immunity, local and systemic inflammation, oxidative stress, altered lung and gut microbiota, and environmental exposures such as biomass fuel burning in the development of HIV-associated lung disease. Assessment, prevention and treatment strategies are largely extrapolated from data from HIV-uninfected people. Smoking cessation is essential. Data on the long-term consequences of HIV-associated lung disease are limited. Efforts to continue quantifying the effects of HIV infection on the lung, especially in low-income and middle-income countries, are essential to advance our knowledge and optimize respiratory care in people living with HIV.

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## Published Erratum

BMJ



. 2023 Jul 27;382:p1743.

doi: 10.1136/bmj.p1743.

# Self-management interventions to reduce healthcare use and improve quality of life among patients with asthma: systematic review and network meta-analysis

*No authors listed*

- PMID: 37500118
- DOI: [10.1136/bmj.p1743](https://doi.org/10.1136/bmj.p1743)

**No abstract available**

## Erratum for

- [Self-management interventions to reduce healthcare use and improve quality of life among patients with asthma: systematic review and network meta-analysis.](#)  
Hodkinson A, Bower P, Grigoroglou C, Zghebi SS, Pinnock H, Kontopantelis E, Panagioti M. *BMJ*. 2020 Aug 18;370:m2521. doi: 10.1136/bmj.m2521. PMID: 32816816 **Free PMC article.**

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Environ Res

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. 2023 Jul 25;116754.

doi: 10.1016/j.envres.2023.116754. Online ahead of print.

# **Airborne grass pollen and thunderstorms influence emergency department asthma presentations in a subtropical climate**

[Marko Simunovic](#)<sup>1</sup>, [Justin Boyle](#)<sup>2</sup>, [Bircan Erbas](#)<sup>3</sup>, [Philip Baker](#)<sup>4</sup>, [Janet M Davies](#)<sup>5</sup>

Affiliations expand

- PMID: 37500047
- DOI: [10.1016/j.envres.2023.116754](https://doi.org/10.1016/j.envres.2023.116754)

## **Abstract**

**Background:** Grass pollen is considered a major outdoor aeroallergen source worldwide. It is proposed as a mechanism for thunderstorm asthma that lightning during thunderstorms promotes electrical rupture of pollen grains that leads to allergic airway inflammation. However, most evidence of associations between grass pollen and asthma comes from temperate regions. The objective of this study was to investigate short-term associations

between airborne grass pollen exposure and asthma emergency department presentations in a subtropical population.

**Methods:** Episode level public hospital presentations for asthma (2016-2020) were extracted for greater Brisbane from Queensland Health's Emergency Data Collection. Concentrations of airborne pollen were determined prospectively using a continuous flow volumetric impaction sampler. Daily time series analysis using a generalised additive mixed model were applied to determine associations between airborne grass pollen concentrations, and lightning count data, with asthma presentations.

**Results:** Airborne grass pollen showed an association with asthma presentations in Brisbane; a significant association was detected from same day exposure to three days lag. Grass pollen exposure increased daily asthma presentations up to 48.5% (95% CI: 12%, 85.9%) in female children. Lightning did not modify the effect of grass pollen on asthma presentations, however a positive association was detected between cloud-to-cloud lightning strikes and asthma presentations ( $P = 0.048$ ).

**Conclusion:** Airborne grass pollen exposure may exacerbate symptoms of asthma requiring urgent medical care of children and adults in a subtropical climate. This knowledge indicates an opportunity for targeted management of respiratory allergic disease to reduce patient and health system burden. For the first time, an influence of lightning on asthma was detected in this context. The outcomes support a need for continued pollen monitoring and surveillance of thunderstorm asthma risk in subtropical regions.

**Keywords:** Allergic rhinitis; Asthma; Emergency department; Grass pollen; Lightning; Subtropical.

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## Conflict of interest statement

**Declaration of competing interest** The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: JMD reports grants from National Health and Medical Research Council (Australia), grants from Australian Research Council, grants from Emergency Medicine Foundation, grants from Victorian Government Department of Health and Human Services, grants from Australian Bureau of Meteorology, grants from National Foundation of Medical Research Innovation, outside the submitted work; QUT has a patent US PTO 14/311944 issued, a patent AU2008/316301 issued, and a provisional patent application (800373PRV). QUT has received research co-sponsorship from Abionic Switzerland in the last five years. BE reports grants from National Health and Medical Research Council (Australia) for research outside the submitted work. The other authors declare no actual or potential competing financial interests.

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J Pediatr Nurs



. 2023 Jul 25;72:113-120.

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

## [A pilot study to improve provider adherence to NAEPP guidelines](#)

[Joanne M Fierro](#)<sup>1</sup>, [Mary Ann Lewis](#)<sup>2</sup>, [Mary-Lynn Brecht](#)<sup>2</sup>, [Gary Rachelefsky](#)<sup>2</sup>, [William Feaster](#)<sup>3</sup>, [Louis Ehwerhemuepha](#)<sup>3</sup>, [Wendie Robbins](#)<sup>2</sup>

Affiliations expand

- PMID: 37499439
- DOI: [10.1016/j.pedn.2023.07.016](https://doi.org/10.1016/j.pedn.2023.07.016)

### **Abstract**

The prevalence and morbidity of Asthma in the United States has increased since the 1991 National Asthma Education and Prevention Program (NAEPP) and updated Expert Panel Report -3 (EPR-3) guidelines in 2007 were published. To improve provider adherence to the NAEPP EPR-3 guidelines Children's Hospital of Orange County (CHOC) in California integrated the HealthIntent<sup>SM</sup> Pediatric Asthma Registry (PAR) into the electronic medical record (EMR) in 2015.

**Methods:** A serial cross-sectional design was used to compare provider management of CHOC MediCal asthma patients before 2014 (N = 6606) and after 2018 (N = 6945) integration of the Registry with NAEPP guidelines into the EMR. Four provider adherence

measures (Asthma Control Test [ACT], Asthma Action Plan [AAP], inhaled corticosteroids [ICS] and spacers) were evaluated using General Linear Mixed Models and Chi square.

**Findings:** In 2018, patients were more likely to receive an ACT, (OR = 14.95, 95% CI 12.67, 17.65,  $p < .001$ ), AAP (OR = 12.70, 95% CI 11.10, 14.54,  $p < .001$ ), ICS (OR = 1.85, 95% CI 8.52, 14.54,  $p < .001$ ) and spacer (OR = 1.45, 95% CI 1.31, 1.6,  $p < .001$ ) compared to those in 2014.

**Discussion:** The pilot study showed integration of the Pediatric Asthma Registry into the EMR, as a computer decision support tool that was an effective intervention to increase provider adherence to NAEPP guidelines. Ongoing monitoring and education are needed to promote and sustain provider behavioral change. Additional research to include multi-sites and decreased time between evaluation years is recommended.

**Application to practice:** Can be used for excellent health policy decision making as a direct impact on patient care and outcomes, by improving provider adherence to the NAEPP guidelines.

**Keywords:** Adherence; Asthma; Children; Electronic medical record; Guidelines; Pediatric; Providers; Registry.

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## Conflict of interest statement

Declaration of Competing Interest None.

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**Review**

J Investig Allergol Clin Immunol

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. 2023 Jul 26;0.

doi: 10.18176/jiaci.0923. Online ahead of print.

# From MASK-air® and SILAM to CATALYSE (Climate Action to Advance HeaLthY Societies in Europe)

[B Sousa-Pinto](#)<sup>1 2 3</sup>, [Y Palamarchuk](#)<sup>4 3</sup>, [L Leemann](#)<sup>5</sup>, [S Jankin](#)<sup>6</sup>, [X Basagaña](#)<sup>7 8 9 10</sup>, [J Ballester](#)<sup>7</sup>, [A Bedbrook](#)<sup>11</sup>, [W Czarlewski](#)<sup>11</sup>, [R Almeida](#)<sup>1 2</sup>, [T Haahtela](#)<sup>12</sup>, [H Haveri](#)<sup>13</sup>, [M Prass](#)<sup>14 15</sup>, [T Henriques](#)<sup>1 2</sup>, [R J Vieira](#)<sup>1 2</sup>, [L Klimek](#)<sup>16 17</sup>, [M Ollert](#)<sup>18 19 20</sup>, [M H Shamji](#)<sup>21 22</sup>, [M Jutel](#)<sup>23 24</sup>, [S Del Giacco](#)<sup>25</sup>, [M J Torres](#)<sup>26</sup>, [I Zuberbier](#)<sup>26 27</sup>, [J A Fonseca](#)<sup>1 2 28</sup>, [M Sofiev](#)<sup>4 28</sup>, [J M Anto](#)<sup>7 9 10 28</sup>, [J Bousquet](#)<sup>11 27 29 30 28</sup>

Affiliations expand

- PMID: 37498647
- DOI: [10.18176/jiaci.0923](https://doi.org/10.18176/jiaci.0923)

## Abstract

Plant species vary under different climate conditions and the distribution of pollen in the air and their trends can be used to assess the impact of climate change on public health. In 2015, MASK-air® (Mobile Airways Sentinel network for rhinitis and asthma) was launched as a project of the European Innovation Partnership on Active and Healthy Ageing (EIP-on-AHA, DG Santé and DG CONNECT). This project aimed to develop a warning system to inform patients about the pollen season onset. SILAM (System for Integrated modelling of Atmospheric composition), a global-to-meso-scale dispersion model was developed by the Finnish Meteorological Institute (FMI). It provides quantitative information on atmospheric pollution of anthropogenic and natural origins, particularly on allergenic pollens. POLLAR (Impact of Air Pollution on Asthma and Rhinitis, EIT Health) has combined MASK-air clinical data with SILAM forecasts. A new Horizon Europe grant, CATALYSE (Climate Action to Advance HeaLthY Societies in Europe; grant agreement number 101057131), which started in September 2022, aims at better understanding climate change and finding ways to counteract it. One objectives of this project is to develop early warning systems and predictive models to improve the effectiveness of adaptation strategies to climate change. One of warning system is focused on allergic rhinitis (CATALYSE Task 3.2). with a collaboration between the FMI (Finland), Porto University (Portugal), MASK-air SAS (France), ISGlobal (Spain), Hertie School (Germany) and the University of Zurich (Switzerland). It is to be implemented with the support of EAACI. This paper reports the planning of CATALYSE Task 3.2.

**Keywords:** Catalyse; Climate change; MASK-air; Pollen; SILAM.

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Thorax



. 2023 Jul 26;thorax-2022-219708.

doi: 10.1136/thorax-2022-219708. Online ahead of print.

## Changes in exhaled volatile organic compounds following indirect bronchial challenge in suspected asthma

[Adam Peel](#)<sup>#1</sup>, [Ran Wang](#)<sup>#2,3</sup>, [Waqar Ahmed](#)<sup>2</sup>, [Iain White](#)<sup>2,4</sup>, [Maxim Wilkinson](#)<sup>2</sup>, [Yoon K Loke](#)<sup>5,6</sup>, [Andrew M Wilson](#)<sup>5,6</sup>, [Stephen J Fowler](#)<sup>7,3</sup>

Affiliations expand

- PMID: 37495368
- DOI: [10.1136/thorax-2022-219708](https://doi.org/10.1136/thorax-2022-219708)

### Abstract

**Background:** Inhaled mannitol provokes bronchoconstriction *via* mediators released during osmotic degranulation of inflammatory cells, and, hence represents a useful

diagnostic test for asthma and model for acute attacks. We hypothesised that the mannitol challenge would trigger changes in exhaled volatile organic compounds (VOCs), generating both candidate biomarkers and novel insights into their origin.

**Methods:** Participants with a clinical diagnosis of asthma, or undergoing investigation for suspected asthma, were recruited. Inhaled mannitol challenges were performed, followed by a sham challenge after 2 weeks in participants with bronchial hyper-responsiveness (BHR). VOCs were collected before and after challenges and analysed using gas chromatography-mass spectrometry.

**Results:** Forty-six patients (mean (SD) age 52 (16) years) completed a mannitol challenge, of which 16 (35%) were positive, and 15 of these completed a sham challenge. Quantities of 16 of 51 identified VOCs changed following mannitol challenge ( $p < 0.05$ ), of which 11 contributed to a multivariate sparse partial least square discriminative analysis model, with a classification error rate of 13.8%. Five of these 16 VOCs also changed ( $p < 0.05$ ) in quantity following the sham challenge, along with four further VOCs. In patients with BHR to mannitol distinct postchallenge VOC signatures were observed compared with post-sham challenge.

**Conclusion:** Inhalation of mannitol was associated with changes in breath VOCs, and in people with BHR resulted in a distinct exhaled breath profile when compared with a sham challenge. These differentially expressed VOCs are likely associated with acute airway inflammation and/or bronchoconstriction and merit further investigation as potential biomarkers in asthma.

**Keywords:** asthma.

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## Conflict of interest statement

Competing interests: None declared.

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## Editorial

J Bras Pneumol

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. 2023 Jul 24;49(3):e20230220.

doi: 10.36416/1806-3756/e20230220.

# Anti-alarmin asthma therapies: where do we go from here?

[Article in English, Portuguese]

[Ibrahim Sulaiman](#)<sup>1</sup>, [Gail M Gauvreau](#)<sup>2</sup>

Affiliations expand

- PMID: 37493796
- DOI: [10.36416/1806-3756/e20230220](https://doi.org/10.36416/1806-3756/e20230220)

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. 2023 Jul 23;S1081-1206(23)00520-3.

doi: 10.1016/j.anai.2023.07.012. Online ahead of print.

# Preference for and Impact of Telehealth vs. In-person Asthma Visits Among Black and Latinx Adults

[Israel C Ugalde](#)<sup>1</sup>, [Amanda Ratigan](#)<sup>2</sup>, [Conner Merriman](#)<sup>3</sup>, [Jing Cui](#)<sup>4</sup>, [Brianna Ericson](#)<sup>5</sup>, [Paula Busse](#)<sup>6</sup>, [Jennifer K Carroll](#)<sup>7</sup>, [Thomas Casale](#)<sup>8</sup>, [Juan Carlos Celedón](#)<sup>9</sup>, [Tamera Coyne-Beasley](#)<sup>10</sup>, [Maureen Fagan](#)<sup>11</sup>, [Anne L Fuhlbrigge](#)<sup>12</sup>, [Gabriela Gaona Villarreal](#)<sup>13</sup>, [Paulina Arias Hernandez](#)<sup>14</sup>, [Sunit Jariwala](#)<sup>15</sup>, [Jean Kruse](#)<sup>16</sup>, [Nancy E Maher](#)<sup>17</sup>, [Brian Manning](#)<sup>18</sup>, [Giselle Mosnaim](#)<sup>19</sup>, [Sylvette Nazario](#)<sup>20</sup>, [Wilson D Pace](#)<sup>21</sup>, [Wanda Phipatanakul](#)<sup>22</sup>, [Victor Pinto-Plata](#)<sup>23</sup>, [Isaretta Riley](#)<sup>24</sup>, [Jacqueline Rodriguez-Louis](#)<sup>25</sup>, [Justin Salciccioli](#)<sup>26</sup>, [Kartik Shenoy](#)<sup>27</sup>, [Joel B Shields](#)<sup>28</sup>, [Yasir Tarabichi](#)<sup>29</sup>, [Bonnie Telon Sosa](#)<sup>30</sup>, [Michael E Wechsler](#)<sup>31</sup>, [Juan Wisnivesky](#)<sup>32</sup>, [Barbara Yawn](#)<sup>33</sup>, [Elliot Israel](#)<sup>34</sup>, [Juan Carlos Cardet](#)<sup>35</sup>

Affiliations expand

- PMID: 37490981
- DOI: [10.1016/j.anai.2023.07.012](https://doi.org/10.1016/j.anai.2023.07.012)

## Abstract

**Background:** Black and Latinx adults experience disproportionate asthma-related morbidity and limited specialty care access. The SARS-CoV-2 pandemic expanded telehealth use.

**Objective:** To evaluate visit type (telehealth [TH] vs. in-person [IP]) preferences and the impact of visit type on asthma outcomes among Black and Latinx adults with moderate-severe asthma.

**Methods:** For this PREPARE trial ancillary study, visit type preference was surveyed by email or telephone post-trial. EMR data on visit types and asthma outcomes were available for a subset (3/2020-4/2021). Characteristics associated with visit type preferences, and relationships between visit type and asthma outcomes (control [ACT®] and asthma-related quality of life [ASUI]), were tested using multivariable regression.

**Results:** N=866 participants consented to be surveyed, with 847 respondents. Among participants with asthma care experience with both visit types, 41.0% preferred TH for regular checkups, which associated with employment (OR=1.61; 95%CI 1.09-2.39; p=0.02), lower asthma medication adherence (OR=1.06; 95%CI 1.01-1.11; p=0.03), and having more historical ER/UC asthma visits (OR=1.10 for each additional visit; 95%CI 1.02-1.18; p=0.02), after adjustment. EMR data were available for 98 participants (62 TH, 36 IP). Those with TH visits were more likely Latinx, from the Southwest, employed, using ICS-only controller therapy, with lower BMI, and lower self-reported asthma medication adherence vs. those with IP visits only. Both groups had comparable ACT (18.4 vs. 18.9, p=0.52) and ASUI scores (0.79 vs. 0.84, p=0.16) after adjustment.

**Conclusion:** TH may be similarly efficacious as and often preferred over IP among Black and Latinx adults with moderate-severe asthma, especially for regular checkups.

**Keywords:** asthma control; asthma exacerbations; asthma-related quality of life; electronic health records; health equity; healthcare disparity; underrepresented minorities.

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J Physiol



. 2023 Jul 24.

doi: 10.1113/JP284686. Online ahead of print.

## Tissue-resident innate lymphoid cells in asthma

[Xiaoxu Wang](#)<sup>1</sup>, [Yue Kong](#)<sup>2</sup>, [Bingqing Zheng](#)<sup>3</sup>, [Xiaomin Zhao](#)<sup>4</sup>, [Mingzhe Zhao](#)<sup>3</sup>, [Bin Wang](#)<sup>3</sup>, [Chang Liu](#)<sup>3</sup>, [Peizheng Yan](#)<sup>3</sup>

Affiliations expand

- PMID: 37488944
- DOI: [10.1113/JP284686](https://doi.org/10.1113/JP284686)

## Abstract

Asthma is a chronic airway inflammatory disease whose global incidence increases annually. The role of innate lymphoid cells (ILCs) is a crucial aspect of asthma research with respect to different endotypes of asthma. Based on its pathological and inflammatory features, asthma is divided into type 2 high and type 2 low endotypes. Type-2 high asthma is distinguished by the activation of type 2 immune cells, including T helper 2 (Th2) cells and ILC2s; the production of cytokines interleukin (IL)-4, IL-5 and IL-13; eosinophilic aggregation; and bronchial hyper-responsiveness. Type-2 low asthma represents a variety of endotypes other than type 2 high endotype such as the IL-1 $\beta$ /ILC3/neutrophil endotype and a paucigranulocytic asthma, which may be insensitive to corticosteroid treatment and/or associated with obesity. The complexity of asthma is due to the involvement of multiple cell types, including tissue-resident ILCs and other innate immune cells including bronchial epithelial cells, dendritic cells, macrophages and eosinophils, which provide immediate defence against viruses, pathogens and allergens. On this basis, innate immune cells and adaptive immune cells combine to induce the pathological condition of asthma. In addition, the plasticity of ILCs increases the heterogeneity of asthma. This review focuses on the phenotypes of tissue-resident ILCs and their roles in the different endotypes of asthma, as well as the mechanisms of tissue-resident ILCs and other immune cells. Based on the phenotypes, roles and mechanisms of immune cells, the therapeutic strategies for asthma are reviewed.

**Keywords:** asthma; cytokines; innate immune cells; mechanisms; tissue-resident innate lymphoid cells.

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**Review**

NPJ Prim Care Respir Med



. 2023 Jul 24;33(1):27.

doi: 10.1038/s41533-023-00347-6.

# Rational use of inhaled corticosteroids for the treatment of COPD

[Jennifer K Quint](#)<sup>1</sup>, [Amnon Ariel](#)<sup>2</sup>, [Peter J Barnes](#)<sup>3</sup>

Affiliations expand

- PMID: 37488104
- PMCID: [PMC10366209](#)
- DOI: [10.1038/s41533-023-00347-6](#)

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## **Abstract**

Inhaled corticosteroids (ICS) are the mainstay of treatment for asthma, but their role in chronic obstructive pulmonary disease (COPD) is debated. Recent randomised controlled trials (RCTs) conducted in patients with COPD and frequent or severe exacerbations demonstrated a significant reduction (~25%) in exacerbations with ICS in combination with dual bronchodilator therapy (triple therapy). However, the suggestion of a mortality benefit associated with ICS in these trials has since been rejected by the European Medicines Agency and US Food and Drug Administration. Observational evidence from routine clinical practice demonstrates that dual bronchodilation is associated with better clinical outcomes than triple therapy in a broad population of patients with COPD and infrequent

exacerbations. This reinforces guideline recommendations that ICS-containing maintenance therapy should be reserved for patients with frequent or severe exacerbations and high blood eosinophils (~10% of the COPD population), or those with concomitant asthma. However, data from routine clinical practice indicate ICS overuse, with up to 50-80% of patients prescribed ICS. Prescription of ICS in patients not fulfilling guideline criteria puts patients at unnecessary risk of pneumonia and other long-term adverse events and also has cost implications, without any clear benefit in disease control. In this article, we review the benefits and risks of ICS use in COPD, drawing on evidence from RCTs and observational studies conducted in primary care. We also provide a practical guide to prescribing ICS, based on the latest global treatment guidelines, to help primary care providers identify patients for whom the benefits of ICS outweigh the risks.

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## Conflict of interest statement

J.K.Q. declares personal fees for advisory board participation or speaking fees from GlaxoSmithKline, Boehringer Ingelheim, AstraZeneca and Chiesi, but declares no non-financial competing interests. A.A. declares personal fees from AstraZeneca, and personal fees and non-financial support from Boehringer Ingelheim, outside the submitted work. P.J.B. declares research funding from AstraZeneca and Boehringer Ingelheim; consulting fees from AstraZeneca, Boehringer Ingelheim and Teva; and payment or honoraria for lectures, presentations, speaker bureaus, manuscript writing or educational events from AstraZeneca, Boehringer Ingelheim, Novartis and Teva. P.J.B. declares no non-financial competing interests.

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. 2023 Jul 24.

doi: 10.1111/all.15824. Online ahead of print.

# Identification of extracellular vesicle microRNA signatures specifically linked to inflammatory and metabolic mechanisms in obesity-associated low type-2 asthma

[Fahd Alhamdan](#)<sup>1,2</sup>, [Timm Greulich](#)<sup>3</sup>, [Christian Daviaud](#)<sup>4</sup>, [Leigh M Marsh](#)<sup>5</sup>, [Frauke Pedersen](#)<sup>6</sup>, [Clemens Thölken](#)<sup>7</sup>, [Petra Ina Pfefferle](#)<sup>8</sup>, [Thomas Bahmer](#)<sup>6,9</sup>, [Daniel P Potaczek](#)<sup>1,10,11</sup>, [Jörg Tost](#)<sup>4</sup>, [Holger Garn](#)<sup>1</sup>

Affiliations expand

- PMID: 37486026
- DOI: [10.1111/all.15824](https://doi.org/10.1111/all.15824)

## Abstract

**Rationale and objective:** Plasma extracellular vesicles (EVs) represent a vital source of molecular information about health and disease states. Due to their heterogenous cellular sources, EVs and their cargo may predict specific pathomechanisms behind disease phenotypes. Here we aimed to utilize EV microRNA (miRNA) signatures to gain new insights into underlying molecular mechanisms of obesity-associated low type-2 asthma.

**Methods:** Obese low type-2 asthma (OA) and non-obese low type-2 asthma (NOA) patients were selected from an asthma cohort conjointly with healthy controls. Plasma EVs were isolated and characterised by nanoparticle tracking analysis. EV-associated small RNAs were extracted, sequenced and bioinformatically analysed.

**Results:** Based on EV miRNA expression profiles, a clear distinction between the three study groups could be established using a principal component analysis. Integrative pathway analysis of potential target genes of the differentially expressed miRNAs revealed

inflammatory cytokines (e.g., interleukin-6, transforming growth factor-beta, interferons) and metabolic factors (e.g., insulin, leptin) signalling pathways to be specifically associated with OA. The miR-17-92 and miR-106a-363 clusters were significantly enriched only in OA. These miRNA clusters exhibited discrete bivariate correlations with several key laboratory (e.g., C-reactive protein) and lung function parameters. Plasma EV miRNA signatures mirrored blood-derived CD4<sup>+</sup> T-cell transcriptome data, but achieved an even higher sensitivity in identifying specifically affected biological pathways.

**Conclusion:** The identified plasma EV miRNA signatures and particularly the miR-17-92 and -106a-363 clusters were capable to disentangle specific mechanisms of the obesity-associated low type-2 asthma phenotype, which may serve as basis for stratified treatment development.

**Keywords:** asthma endotypes; asthma phenotypes; extracellular vesicles; microRNA clusters; obesity-associated asthma.

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Environ Sci Pollut Res Int

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. 2023 Jul 24.

doi: 10.1007/s11356-023-28740-1. Online ahead of print.



# Biomarkers of organophosphate insecticides exposure and asthma in general US adults: findings from NHANES 1999-2018 data

[Jing-Hong Liang](#)<sup>1</sup>, [Mei-Ling Liu](#)<sup>1</sup>, [Ying-Qi Pu](#)<sup>1</sup>, [Shan Huang](#)<sup>1</sup>, [Nan Jiang](#)<sup>1</sup>, [Shao-Yi Huang](#)<sup>1</sup>, [Xue-Ya Pu](#)<sup>1</sup>, [Guang-Hui Dong](#)<sup>2</sup>, [Ya-Jun Chen](#)<sup>3</sup>

Affiliations expand

- PMID: 37482592
- DOI: [10.1007/s11356-023-28740-1](https://doi.org/10.1007/s11356-023-28740-1)

## **Abstract**

The limited evidence linking exposure to organophosphate insecticides (OPIs) and asthma in the general population prompted us to investigate this association. Our study focused on US adults and utilized representative samples from the National Health and Nutrition Examination Survey (NHANES). From the 7 NHANES waves (1999-2018), we detected OPIs exposure using the urinary concentrations of six metabolites of dialkyl phosphates (DAPs). To evaluate the relationship between these OPIs and asthma, we employed three statistical methods: survey-multivariable logistic regression (SMLR), generalized weighted quantile sum (WQS) regression, and Bayesian kernel machine regression (BKMR). Stratified analyses were done based on the relevant variable subgroups, and sensitivity analyses were carried out to evaluate the robustness of findings. A total of 6009 adults aged from 20 to 85 years old, representing the 313.5 million adults in the non-institutionalized US population, were included in our analyses. Among them, 842 participants were determined as asthma patients with an age-adjusted prevalence of 14.2%. Our results showed that dimethyl phosphate (DMP) (adjusted odd ratio (AOR) = 1.471, 95% CI: 1.086, 1.993), diethyl phosphate (DEP) (AOR = 1.453, 95% CI: 1.118, 1.888), dimethyl thiophosphate (DMTP) (AOR = 1.454, 95% CI: 1.071, 1.973), and dimethyl dithiophosphate (DMDTP) (AOR = 1.478, 95% CI: 1.119, 1.953) had a positive correlation with asthma in adults. This association was stronger in females, non-Hispanic White populations and those with a small amount of physical activity. Our study findings indicated that exposure to OPIs may elevate the risk of asthma in US general adults. Specifically, females, individuals from non-Hispanic White backgrounds, and those with lower levels of physical activity are more susceptible to developing asthma when exposed to OPIs.

**Keywords:** Asthma; Environmental exposure; General adults; NHANES; Organophosphate insecticides.

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## 19 Review

Expert Rev Clin Immunol

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. 2023 Jul 24;1-14.

doi: 10.1080/1744666X.2023.2239504. Online ahead of print.

# Update on virus-induced asthma exacerbations

[Francesca Urbani](#)<sup>1</sup>, [Marianna Cometa](#)<sup>1</sup>, [Chiara Martelli](#)<sup>1</sup>, [Federica Santoli](#)<sup>1</sup>, [Roberto Rana](#)<sup>1</sup>, [Antonio Ursitti](#)<sup>1</sup>, [Matteo Bonato](#)<sup>2</sup>, [Simonetta Baraldo](#)<sup>2</sup>, [Marco Contoli](#)<sup>1</sup>, [Alberto Papi](#)<sup>1</sup>

Affiliations expand

- PMID: 37470413
- DOI: [10.1080/1744666X.2023.2239504](https://doi.org/10.1080/1744666X.2023.2239504)

## Abstract

**Introduction:** Viral infections are common triggers for asthma exacerbation. Subjects with asthma are more susceptible to viral infections and develop more severe or long-lasting lower respiratory tract symptoms than healthy individuals owing to impaired immune responses. Of the many viruses associated with asthma exacerbation, rhinovirus (RV) is the most frequently identified virus in both adults and children.

**Areas covered:** We reviewed epidemiological and clinical links and mechanistic studies on virus-associated asthma exacerbations. We included sections on severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), the latest evidence of coronavirus disease 2019 (COVID-19) in asthma patients, and past and future searches for therapeutic and prevention targets.

**Expert opinion:** Early treatment or prevention of viral infections might significantly reduce the rate of asthma exacerbation, which is one of the key points of disease management. Although it is hypothetically possible nowadays to interfere with every step of the infectious cycle of respiratory tract viruses, vaccination development has provided some of the most encouraging results. Future research should proceed toward the development of a wider spectrum of vaccines to achieve a better quality of life for patients with asthma and to reduce the economic burden on the healthcare system.

**Keywords:** Asthma; CoV2; SAR; exacerbation; pathogenesis; respiratory syncytial virus; rhinovirus.

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## 20 Review

Allergy Asthma Proc

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. 2023 Jul 26;44(4):220-228.

doi: 10.2500/aap.2023.44.230030.

# The third pandemic: The respiratory syncytial virus landscape and specific considerations for the allergist/immunologist

[Lawrence D Frenkel](#)<sup>1</sup>, [Sunanda Gaur](#)<sup>2</sup>, [Joseph A Bellanti](#)<sup>3</sup>

Affiliations expand

- PMID: 37236777
- DOI: [10.2500/aap.2023.44.230030](https://doi.org/10.2500/aap.2023.44.230030)

## Abstract

**Background:** Since its initial identification in 1956, respiratory syncytial virus (RSV) has been the second most common cause of mortality in infants <6 months of age and a major cause of morbidity and mortality associated with lower respiratory tract infection (LRTI) in older adults (ages >60 years) worldwide. Of particular interest to the allergist/immunologist is a growing body of evidence that suggests an association between LRTI caused by RSV in infants with later-life development of asthma, wheezing, or impaired lung function in adults. Efforts to develop a RSV vaccine have been thwarted for >70 years by the occurrence of enhanced respiratory disease (ERD), an adverse RSV vaccine reaction, in the 1960s, in which more-severe illness occurred on natural infection after vaccination of infants who were RSV naive and with a formalin-inactivated RSV vaccine. Recent advances in knowledge of the structural biology of the RSV surface fusion glycoprotein, however, have revolutionized RSV vaccine development for preventive interventions and have offered, at last, the hope of an effective and safe vaccine for the prevention of RSV disease. **Objective:** The purpose of this report was to examine the current evidence that supports the epidemiology, disease manifestations, molecular biology, treatments, and new vaccine development of RSV vaccines. **Results:** The host-immune response to RSV infection is carried out by two distinct but overlapping universes of mucosal and systemic immune systems in which a balanced set of B- and T-cell responses are involved in protective immunity that includes the mucosal immune system in which immunoglobulin A (IgA) prevails and the systemic immune system in which IgG neutralizing antibody predominates. The key to developing an effective vaccine is now thought to be linked to the availability of a stabilized prefusion F protein in the immunizing

vaccine, which can perform a dual function of a balanced mucosal and/or systemic immune response as well as an effective antibody specifically directed to critical epitopes on the requisite prefusion F protein. **Conclusion:** The unfortunate manifestation of RSV ERD that occurred in the 1960s has led to a better understanding of the structural biology of the RSV surface fusion glycoprotein and has provided a basis for the development of more effective and safer RSV vaccines and monoclonal antibody preparations for immunoprophylaxis of the dread effects of RSV disease. There are now a large number of clinical trials in progress that are evaluating these products, which include recombinant vector, subunit, particle-based, live-attenuated, chimeric, and nucleic acid vaccines; and monoclonal antibodies. This article gives an overview of the many aspects of RSV disease and development of virus (RSV) vaccines of particular interest to the allergist/immunologist.

## Comment in

- [A trajectory of the FDA approval of the first vaccine targeting RSV: A greek tragedy with a happy ending.](#)

Bellanti JA, Settipane RA. *Allergy Asthma Proc.* 2023 Jul 1;44(4):217-219. doi: 10.2500/aap.2023.44.230037.PMID: 37480204 **Free PMC article.** No abstract available.

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**21**  
**Review**

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. 2023 Jul 27;33(4):250-262.

doi: 10.18176/jiaci.0887. Epub 2023 Jan 4.

# Impact of Asthma Inhalers on Global Climate: A Systematic Review of Their Carbon Footprint and Clinical Outcomes in Spain

[J Montoro](#)<sup>1,2</sup>, [D Antolín-Amérigo](#)<sup>3,4</sup>, [A Izquierdo-Domínguez](#)<sup>5</sup>, [J J Zapata](#)<sup>6</sup>, [G González](#)<sup>7</sup>, [A Valero](#)<sup>8,9,10</sup>

Affiliations expand

- PMID: 36648318
- DOI: [10.18176/jiaci.0887](https://doi.org/10.18176/jiaci.0887)

## **Abstract**

**Background:** Pressurized metered-dose inhalers (pMDIs) exert an environmental impact resulting from CO<sub>2</sub> emissions. Therapeutic alternatives with less environmental impact are widely used. Nevertheless, the choice of device and appropriate therapy should meet the clinical needs and the characteristics of the patient.

**Objective:** The primary objective was to estimate the impact of pMDIs prescribed for any indication on annual CO<sub>2</sub> emissions in Spain. The secondary objective was to evaluate the potential impact of switching pMDIs to dry-powder inhalers (DPIs) in patients with asthma.

**Methods:** A systematic review of the evidence published during 2010-2021 was carried out. Average annual CO<sub>2</sub> emissions of DPIs and pMDIs were calculated in 2 scenarios: the current situation and a hypothetical situation involving a switch from all pMDIs to DPIs. The impact of the switch on clinical outcomes was also evaluated.

**Results:** The total value of CO<sub>2</sub>-eq/year due to DPIs and pMDIs accounted for 0.0056% and 0.0909%, respectively, of total emissions in Spain. In the event of switching pMDIs to DPIs, except those used for rescue medication, the percentages were 0.0076% and 0.0579%. The evaluation of efficacy, handling, satisfaction, safety, and use of health care resources was not conclusive.

**Conclusions:** Current CO<sub>2</sub> emissions by pMDIs account for a small percentage of the total CO<sub>2</sub> footprint in Spain. Nevertheless, there is a need for research into new and more

sustainable devices. Suitability and patient clinical criteria such as age and inspiratory flow should be prioritized when prescribing an inhaler.

**Keywords:** Antiasthmatic agents; Asthma. Inhaler devices; Carbon footprint; Climate change; Environment; Global warming; Metered-dose inhalers.

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J Investig Allergol Clin Immunol

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. 2023 Jul 27;33(4):314-316.

doi: 10.18176/jiaci.0862. Epub 2022 Oct 4.

## Exhaled Breath Temperature Is Not Helpful for Identifying Cellular Bronchitis in Severe Asthma

[B Moya](#)<sup>12</sup>, [C Huang](#)<sup>13</sup>, [M Kjarsgaard](#)<sup>13</sup>, [C Martín-Arriscado](#)<sup>4</sup>, [P Nair](#)<sup>13</sup>

Affiliations expand

- PMID: 36193746
- DOI: [10.18176/jiaci.0862](https://doi.org/10.18176/jiaci.0862)

**No abstract available**

**Keywords:** Eosinophilic bronchitis; Exhaled breath temperature; Severe asthma.

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**23**

J Investig Allergol Clin Immunol

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. 2023 Jul 27;33(4):281-288.

doi: 10.18176/jiaci.0816. Epub 2002 May 3.

## Exacerbations Among Patients With Asthma Are Largely Dependent on the Presence of Multimorbidity

[J Domínguez-Ortega](#)<sup>1 2 3</sup>, [J A Luna-Porta](#)<sup>1 2 3</sup>, [J M Olaguibel](#)<sup>3 4</sup>, [P Barranco](#)<sup>1 2 3</sup>, [E Arismendi](#)<sup>3 5 6 7</sup>, [B Barroso](#)<sup>3 8</sup>, [D Betancor](#)<sup>3 8</sup>, [I Bobolea](#)<sup>3 5 6 7</sup>, [M L Caballero](#)<sup>1 2 3</sup>, [B Cádaba](#)<sup>3 9</sup>, [M J Cruz](#)<sup>3 10 11</sup>, [E Curto](#)<sup>3 12 13 14</sup>, [F J González-Barcala](#)<sup>3 15 16 17</sup>, [I Losantos-García](#)<sup>2 18</sup>, [C Martínez-Rivera](#)<sup>3 14 19 20</sup>, [P Mendez-Brea](#)<sup>21</sup>, [J Mulloj](#)<sup>3 5 6 22</sup>, [X Muñoz](#)<sup>3 11</sup>, [C Picado](#)<sup>3 5 6 7</sup>, [V Plaza](#)<sup>3 12 13 14</sup>, [V Del Pozo](#)<sup>3 9</sup>, [M J Rial](#)<sup>3 23</sup>, [J Sastre](#)<sup>3 8</sup>, [L Soto](#)<sup>3 12 13 14</sup>, [A Valero](#)<sup>3 5 6 7</sup>, [M Valverde-Monge](#)<sup>3 8</sup>, [S Quirce](#)<sup>1 2 3</sup>

Affiliations expand

- PMID: 35503227
- DOI: [10.18176/jiaci.0816](https://doi.org/10.18176/jiaci.0816)

**Abstract**



**Background and objective:** Comorbidities can influence asthma control and promote asthma exacerbations (AEs). However, the impact of multimorbidity in AEs, assessed based on long-term follow-up of patients with asthma of different degrees of severity, has received little attention in real-life conditions. To describe the epidemiological and clinical characteristics and predictors of AEs in patients who had presented at least 1 AE in the previous year in the MEchanism of Genesis and Evolution of Asthma (MEGA) cohort.

**Methods:** The work-up included a detailed clinical examination, pulmonary function testing, fractional exhaled nitric oxide (FeNO), blood counts, induced sputum, skin prick-tests, asthma questionnaires, and assessment of multimorbidity. The number of moderate-severe AEs in the preceding year was registered for each patient.

**Results:** The study population comprised 486 patients with asthma (23.7% mild, 35% moderate, 41.3% severe). Disease remained uncontrolled in 41.9%, and 47.3% presented  $\geq 1$  moderate-severe AE, with a mean (SD) annual exacerbation rate of 0.47 (0.91) vs 2.11 (2.82) in mild and severe asthma, respectively. Comorbidity was detected in 56.4% (66.6% among those with severe asthma). Bronchiectasis, chronic rhinosinusitis with nasal polyps, atopy, psychiatric illnesses, hyperlipidemia, and hypertension were significantly associated with AEs. No associations were found for FeNO, blood eosinophils, or total serum IgE. Sputum eosinophilia and a high-T2 inflammatory pattern were significantly associated with AEs. Multivariable regression analysis showed a significant association with asthma severity, uncontrolled disease, and low prebronchodilator FEV1/FVC.

**Conclusion:** Our study revealed a high frequency of AE in the MEGA cohort. This was strongly associated with multimorbidity, asthma severity, poor asthma control, airflow obstruction, higher sputum eosinophils, and a very high-T2 inflammatory pattern.

**Keywords:** Asthma; Asthma control; Exacerbations; MEGA cohort; Multimorbidity.

supplementary info

MeSH terms, Substancesexpand

full text links

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

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. 2023 Jul 25;116754.

doi: 10.1016/j.envres.2023.116754. Online ahead of print.

# **Airborne grass pollen and thunderstorms influence emergency department asthma presentations in a subtropical climate**

[Marko Simunovic](#)<sup>1</sup>, [Justin Boyle](#)<sup>2</sup>, [Bircan Erbas](#)<sup>3</sup>, [Philip Baker](#)<sup>4</sup>, [Janet M Davies](#)<sup>5</sup>

Affiliations expand

- PMID: 37500047
- DOI: [10.1016/j.envres.2023.116754](https://doi.org/10.1016/j.envres.2023.116754)

## **Abstract**

**Background:** Grass pollen is considered a major outdoor aeroallergen source worldwide. It is proposed as a mechanism for thunderstorm asthma that lightning during thunderstorms promotes electrical rupture of pollen grains that leads to allergic airway inflammation. However, most evidence of associations between grass pollen and asthma comes from temperate regions. The objective of this study was to investigate short-term associations between airborne grass pollen exposure and asthma emergency department presentations in a subtropical population.

**Methods:** Episode level public hospital presentations for asthma (2016-2020) were extracted for greater Brisbane from Queensland Health's Emergency Data Collection. Concentrations of airborne pollen were determined prospectively using a continuous flow volumetric impaction sampler. Daily time series analysis using a generalised additive mixed model were applied to determine associations between airborne grass pollen concentrations, and lightning count data, with asthma presentations.

**Results:** Airborne grass pollen showed an association with asthma presentations in Brisbane; a significant association was detected from same day exposure to three days lag. Grass pollen exposure increased daily asthma presentations up to 48.5% (95% CI: 12%, 85.9%) in female children. Lightning did not modify the effect of grass pollen on asthma presentations, however a positive association was detected between cloud-to-cloud lightning strikes and asthma presentations ( $P = 0.048$ ).

**Conclusion:** Airborne grass pollen exposure may exacerbate symptoms of asthma requiring urgent medical care of children and adults in a subtropical climate. This

knowledge indicates an opportunity for targeted management of respiratory allergic disease to reduce patient and health system burden. For the first time, an influence of lightning on asthma was detected in this context. The outcomes support a need for continued pollen monitoring and surveillance of thunderstorm asthma risk in subtropical regions.

**Keywords:** Allergic rhinitis; Asthma; Emergency department; Grass pollen; Lightning; Subtropical.

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## Conflict of interest statement

**Declaration of competing interest** The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: JMD reports grants from National Health and Medical Research Council (Australia), grants from Australian Research Council, grants from Emergency Medicine Foundation, grants from Victorian Government Department of Health and Human Services, grants from Australian Bureau of Meteorology, grants from National Foundation of Medical Research Innovation, outside the submitted work; QUT has a patent US PTO 14/311944 issued, a patent AU2008/316301 issued, and a provisional patent application (800373PRV). QUT has received research co-sponsorship from Abionic Switzerland in the last five years. BE reports grants from National Health and Medical Research Council (Australia) for research outside the submitted work. The other authors declare no actual or potential competing financial interests.

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## 2 Review

J Investig Allergol Clin Immunol

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. 2023 Jul 26;0.

doi: 10.18176/jiaci.0923. Online ahead of print.

# From MASK-air® and SILAM to CATALYSE (Climate Action to Advance HeaLthY Societies in Europe)

[B Sousa-Pinto](#)<sup>1 2 3</sup>, [Y Palamarchuk](#)<sup>4 3</sup>, [L Leemann](#)<sup>5</sup>, [S Jankin](#)<sup>6</sup>, [X Basagaña](#)<sup>7 8 9 10</sup>, [J Ballester](#)<sup>7</sup>, [A Bedbrook](#)<sup>11</sup>, [W Czarlewski](#)<sup>11</sup>, [R Almeida](#)<sup>1 2</sup>, [T Haahtela](#)<sup>12</sup>, [H Haveri](#)<sup>13</sup>, [M Prass](#)<sup>14 15</sup>, [T Henriques](#)<sup>1 2</sup>, [R J Vieira](#)<sup>1 2</sup>, [L Klimek](#)<sup>16 17</sup>, [M Ollert](#)<sup>18 19 20</sup>, [M H Shamji](#)<sup>21 22</sup>, [M Jutel](#)<sup>23 24</sup>, [S Del Giacco](#)<sup>25</sup>, [M J Torres](#)<sup>26</sup>, [I Zuberbier](#)<sup>26 27</sup>, [J A Fonseca](#)<sup>1 2 28</sup>, [M Sofiev](#)<sup>4 28</sup>, [J M Anto](#)<sup>7 9 10 28</sup>, [J Bousquet](#)<sup>11 27 29 30 28</sup>

Affiliations expand

- PMID: 37498647
- DOI: [10.18176/jiaci.0923](https://doi.org/10.18176/jiaci.0923)

## Abstract

Plant species vary under different climate conditions and the distribution of pollen in the air and their trends can be used to assess the impact of climate change on public health. In 2015, MASK-air® (Mobile Airways Sentinel network for rhinitis and asthma) was launched as a project of the European Innovation Partnership on Active and Healthy Ageing (EIP-on-AHA, DG Santé and DG CONNECT). This project aimed to develop a warning system to inform patients about the pollen season onset. SILAM (System for Integrated modelling of Atmospheric composition), a global-to-meso-scale dispersion model was developed by the Finnish Meteorological Institute (FMI). It provides quantitative information on atmospheric pollution of anthropogenic and natural origins, particularly on allergenic pollens. POLLAR (Impact of Air Pollution on Asthma and Rhinitis, EIT Health) has combined MASK-air clinical data with SILAM forecasts. A new Horizon Europe grant, CATALYSE (Climate Action to Advance HeaLthY Societies in Europe; grant agreement number 101057131), which started in September 2022, aims at better understanding climate change and finding ways to counteract it. One objectives of this project is to develop early warning systems and predictive models to improve the effectiveness of adaptation strategies to climate change. One of warning system is focused on allergic rhinitis (CATALYSE Task 3.2). with a collaboration between the FMI (Finland), Porto University (Portugal), MASK-air SAS (France), ISGlobal (Spain), Hertie School (Germany) and the University of Zurich (Switzerland). It is to be implemented with the support of EAACI. This paper reports the planning of CATALYSE Task 3.2.

**Keywords:** Catalyse; Climate change; MASK-air; Pollen; SILAM.

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**3**

Laryngoscope



. 2023 Jul 27.

doi: 10.1002/lary.30907. Online ahead of print.

# **Pediatric Inferior Turbinate Hypertrophy: Diagnosis and Management. A YO-IFOS Consensus Statement**

[Antonino Maniaci](#)<sup>1,2</sup>, [Christian Calvo-Henriquez](#)<sup>1,3</sup>, [Giovanni Cammaroto](#)<sup>1,4</sup>, [Carlos Garcia-Magan](#)<sup>5</sup>, [Vanessa Garcia-Paz](#)<sup>6</sup>, [Giannicola Iannella](#)<sup>1,7</sup>, [Ignacio Jiménez-Huerta](#)<sup>1,8</sup>, [Ignazio La Mantia](#)<sup>2</sup>, [Jérôme R Lechien](#)<sup>1,9</sup>, [Samuel C Leong](#)<sup>1,10</sup>, [David Lobo-Duro](#)<sup>1,11</sup>, [Juan Maza-Solano](#)<sup>1,12</sup>, [Ron Mitchell](#)<sup>1,3</sup>, [Andrea Otero-Alonso](#)<sup>6</sup>, [You Peng](#)<sup>1,14</sup>, [Thomas Radulesco](#)<sup>1,15</sup>, [François Simon](#)<sup>1,16</sup>, [Natasha Teissier](#)<sup>1,17</sup>, [Salvatore Cocuzza](#)<sup>2</sup>, [Alberto M Saibene](#)<sup>1,18</sup>

Affiliations expand

- PMID: 37497872
- DOI: [10.1002/lary.30907](https://doi.org/10.1002/lary.30907)

**Abstract**

**Objective:** Pediatric inferior turbinate hypertrophy (PedTH) is a frequent and often overlooked cause or associated cause of nasal breathing difficulties. This clinical consensus statement (CCS) aims to provide a diagnosis and management framework covering the lack of specific guidelines for this condition and addressing the existing controversies.

**Methods:** A clinical consensus statement (CCS) was developed by a panel of 20 contributors from 7 different European and North American countries using the modified Delphi method. The aim of the CCS was to offer a multidisciplinary reference framework for the management of PedTH on the basis of shared clinical experience and analysis of the strongest evidence currently available.

**Results:** A systematic literature review following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria was performed. From the initial 96 items identified, 7 articles were selected based on higher-evidence items such as randomized-controlled trials, guidelines, and systematic reviews. A 34-statement survey was developed, and after three rounds of voting, 2 items reached strong consensus, 17 reached consensus or near consensus, and 15 had no consensus.

**Conclusions:** Until further prospective data are available, our CCS should provide a useful reference for PedTH management. PedTH should be considered a nasal obstructive disease not necessarily related to an adult condition but frequently associated with other nasal or craniofacial disorders. Diagnosis requires clinical examination and endoscopy, whereas rhinomanometry, nasal cytology, and questionnaires have little clinical role. Treatment choice should consider the specific indications and features of the available options, with a preference for less invasive procedures.

**Level of evidence:** 5 Laryngoscope, 2023.

**Keywords:** endoscopy; guideline; nasal breathing difficulties; pediatric otolaryngology; rhinitis.

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Sci Rep



. 2023 Jul 26;13(1):12101.

doi: 10.1038/s41598-023-39149-8.

## Eosinophil-mast cell pattern of intraepithelial infiltration as a marker of severity in CRSwNP

[Matteo Gelardi](#)<sup>1</sup>, [Rossana Giancaspro](#)<sup>2</sup>, [Loren Duda](#)<sup>3</sup>, [Vitaliano Nicola Quaranta](#)<sup>4</sup>, [Cristina Pizzulli](#)<sup>3</sup>, [Eugenio Maiorano](#)<sup>5</sup>, [Filomena Milena Di Canio](#)<sup>1</sup>, [Annamaria Ruzza](#)<sup>1</sup>, [Lucia Iannuzzi](#)<sup>6</sup>, [Nicola Antonio Adolfo Quaranta](#)<sup>6</sup>, [Francesca Parisi](#)<sup>7</sup>, [Michele Cassano](#)<sup>1</sup>, [Andrea Marzullo](#)<sup>5</sup>

Affiliations expand

- PMID: 37495667
- PMCID: [PMC10372103](#)
- DOI: [10.1038/s41598-023-39149-8](#)

### **Abstract**

Chronic rhinosinusitis with nasal polyps (CRSwNP) is defined as a Type 2 eosinophilic disease, while CRSsNP is considered a Type 1 neutrophilic disease. Since neutrophils are also activated in eosinophilic CRSwNP, the eosinophil-neutrophil dualism has been reevaluated. Among the inflammatory cells infiltrating sinus-nasal tissues, the role of mast cells (MCs) is not already recognized, although Clinical-Cytological Grading, which defines the severity of CRSwNP, attributes to mixed eosinophil-MC forms of CRSwNP a greater risk of recurrence. We aimed to examine nasal polyps from both a cytological and histopathological point of view, to evaluate the presence and localization of MCs. Cytological and histological examination of 39 samples of nasal polyps were performed. Immunohistochemistry was used to evaluate the presence of Tryptase + CD117 + MCs, which were counted both in the epithelial layer and in the lamina propria. A statistically significant correlation was found between intraepithelial MCs and CRSwNP severity ( $p < 0.001$ ) and between the total eosinophil count and the total mast cell count ( $p < 0.001$ ). Cytological examination and immunohistochemistry were comparable in detecting the

presence of intraepithelial MCs ( $p = 0.002$ ). The histological cut-off of 6 intraepithelial MCs was identified to detect severe CRSwNP ( $p < 0.001$ ). MCs have been shown to be located in the lamina propria of almost all eosinophilic nasal polyps without significantly affecting their severity. Intraepithelial MCs are associated with greater severity of CRSwNP. Histopathological criteria of the eosinophil-MC form of CRSwNP in addition to the eosinophilic one, should be defined to guarantee patients effective and tailored treatments.

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## Conflict of interest statement

The authors declare no competing interests.

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- [7 figures](#)

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## 5 Review

Clin Rev Allergy Immunol

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. 2023 Jul 25.

doi: 10.1007/s12016-023-08964-2. Online ahead of print.



# Environmental Risk Factors, Protective Factors, and Biomarkers for Allergic Rhinitis: A Systematic Umbrella Review of the Evidence

[Xianpeng Xu](#)<sup>1,2</sup>, [Xinghong Liu](#)<sup>1,2</sup>, [Jiongke Li](#)<sup>1,2</sup>, [Xinxing Deng](#)<sup>1,2</sup>, [Tianrong Dai](#)<sup>1,2</sup>, [Qingjie Ji](#)<sup>3</sup>, [Dajing Xiong](#)<sup>1,2</sup>, [Hui Xie](#)<sup>4,5</sup>

Affiliations expand

- PMID: 37490237
- DOI: [10.1007/s12016-023-08964-2](https://doi.org/10.1007/s12016-023-08964-2)

## **Abstract**

Many potential environmental risk factors, protective factors, and biomarkers of AR have been published, but so far, the strength and consistency of their evidence are unclear. We conducted a comprehensive review of environmental risk, protective factors, and biomarkers for AR to establish the evidence hierarchy. We systematically searched Embase, PubMed, Cochrane Library, and Web of Science electronic database from inception to December 31, 2022. We calculated summary effect estimate (odds ratio (OR), relative risk (RR), hazard ratio (HR), and standardized mean difference (SMD)), 95% confidence interval, random effects p value,  $I^2$  statistic, 95% prediction interval, small study effects, and excess significance biases, and stratification of the level of evidence. Methodological quality was assessed by AMSTAR 2 (A Measurement Tool to Assess Systematic Reviews 2). We retrieved 4478 articles, of which 43 met the inclusion criteria. The 43 eligible articles identified 31 potential environmental risk factors (10,806,206 total population, two study not reported), 11 potential environmental protective factors (823,883 total population), and 34 potential biomarkers (158,716 total population) for meta-analyses. The credibility of evidence was convincing (class I) for tic disorders (OR = 2.89, 95% CI 2.11-3.95); and highly suggestive (class II) for early-life antibiotic use (OR = 3.73, 95% CI 3.06-4.55), exposure to indoor dampness (OR = 1.49, 95% CI 1.27-1.75), acetaminophen exposure (OR = 1.54, 95% CI 1.41-1.69), childhood acid suppressant use (OR = 1.40, 95% CI 1.23-1.59), exposure to indoor mold (OR = 1.66, 95% CI 1.26-2.18), coronavirus disease 2019 (OR = 0.11, 95% CI 0.06-0.22), and prolonged breastfeeding (OR = 0.72, 95% CI 0.65-0.79). This study is registered in PROSPERO (CRD42022384320).

**Keywords:** Allergic rhinitis; Biomarkers; Environmental risk and protective factors; Umbrella review.

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## 6 Review

Expert Rev Respir Med

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. 2023 Jul 28;1-15.

doi: 10.1080/17476348.2023.2241364. Online ahead of print.

# [Pharmacotherapy and immunotherapy of allergic rhinitis induced by house dust mite, grass, and birch pollen allergens: a meta-analysis of randomized clinical trials](#)

[Monika Marko](#)<sup>1</sup>, [Rafał Pawliczak](#)<sup>1</sup>

[Affiliations](#) [expand](#)

- PMID: 37489655
- DOI: [10.1080/17476348.2023.2241364](https://doi.org/10.1080/17476348.2023.2241364)

## Abstract

**Background:** The aim of this study was to assess the efficacy and safety of oral antihistamines (AHs), intranasal antihistamines (INAH) intranasal glucocorticosteroids (INCS), subcutaneous immunotherapy (SCIT), and sublingual immunotherapy (SLIT) in the management of allergic rhinitis (AR). The authors focused on the division into selected AR's triggers: house dust mites (HDMs), grass pollen, and birch pollen.

**Methods:** For each drug and allergen class, a meta-analysis of the efficacy and adverse events (AEs) was performed. The obtained results were presented as a therapeutic index (TIX-Score).

**Results:** Twenty-seven randomized clinical trials (RCTs) were included. The best total efficacy was observed for: HDMs for INCS and grass pollen for combination of INCS with INAH in a single device and for INAH. Considering the data that was obtained for birch pollen, SLIT showed statistically significant total efficacy. Summation scores for efficacy and AEs showed highest TIX-Score for combination of INCS and INAH in a single device in grass pollen.

**Conclusions:** Treatment methods selected for this review may serve as an effective and safe treatment in reducing perennial and seasonal AR's symptoms. However, due to high heterogeneity probably associated with potential confounders existence in control in some cases, results should be interpreted with caution.

**Keywords:** Allergic rhinitis; efficacy; immunotherapy; pharmacotherapy; safety.

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**7**

Pediatrics

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. 2023 Jul 25;e2022060531.

doi: 10.1542/peds.2022-060531. Online ahead of print.

# Patterns in the Development of Pediatric Allergy

[Stanislaw J Gabryszewski](#)<sup>1</sup>, [Jesse Dudley](#)<sup>2</sup>, [Di Shu](#)<sup>2,3</sup>, [Jennifer A Faerber](#)<sup>2</sup>, [Robert W Grundmeier](#)<sup>2</sup>, [Alexander G Fiks](#)<sup>2</sup>, [David A Hill](#)<sup>1,4</sup>

Affiliations expand

- PMID: 37489286
- DOI: [10.1542/peds.2022-060531](https://doi.org/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  $\geq 5$  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  $\geq 2$  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.

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## Conflict of interest statement

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

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## 8 Review

Clin Exp Allergy

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. 2023 Jul 24.

doi: 10.1111/cea.14372. Online ahead of print.

## Beyond ARIA: Will e-diaries replace retrospective questionnaires in measuring the severity of allergic rhinitis in clinical research and daily practice?

[Paolo M Matricardi](#)<sup>1</sup>, [Bernardo Sousa-Pinto](#)<sup>2,3</sup>, [Stephanie Dramburg](#)<sup>1</sup>, [Jean Bousquet](#)<sup>4,5,6</sup>

Affiliations expand

- PMID: 37488953

- DOI: [10.1111/cea.14372](https://doi.org/10.1111/cea.14372)

## Abstract

Retrospective questionnaires are used since decades to assess the severity and/or control of allergic diseases. Applications on smartphones have recently facilitated the use of prospective clinical diaries, based on questionnaires filled every day by the patient. Once limited to clinical trials, these e-diaries, based on validated disease control scores and visual analogue scales, permit a quantitative day-by-day measure free of recall bias. Given the advantages of this procedure, its use could be extended to the daily clinical practice. E-diaries may facilitate (1) a more precise identification of the culprit allergen in the diagnostic work-up of poly-sensitized patients, (2) the stratification of patients for treatment, (3) the follow-up of the patients under treatment for optimized shared decision-making, and (4) a careful assessment of preventive therapies. While a few apps are being used in scientific studies, consensus on their use in daily practice should be reached and guidelines for specialists should be elaborated by scientific associations.

**Keywords:** allergic rhinitis; apps; ehealth; mobile health; monitoring; patient-reported outcomes.

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- [50 references](#)

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**9**

Stem Cell Res Ther

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. 2023 Jul 24;14(1):180.

doi: 10.1186/s13287-023-03408-2.

# Dendritic cells mediated by small extracellular vesicles derived from MSCs attenuated the ILC2 activity via PGE2 in patients with allergic rhinitis

[Xiao-Qing Liu](#) <sup>#1,2</sup>, [Ya-Qi Peng](#) <sup>#3</sup>, [Long-Xin Huang](#) <sup>1,2</sup>, [Chan-Gu Li](#) <sup>1,2</sup>, [Peng-Peng Kuang](#) <sup>1,2</sup>, [De-Hua Chen](#) <sup>1,2</sup>, [Zi-Cong Wu](#) <sup>1</sup>, [Bi-Xin He](#) <sup>1,2</sup>, [Zhi-Rou Zhou](#) <sup>1,2</sup>, [Qing-Ling Fu](#) <sup>4,5</sup>

Affiliations expand

- PMID: 37488601
- PMCID: [PMC10367306](#)
- DOI: [10.1186/s13287-023-03408-2](#)

**Free PMC article**

## **Abstract**

**Background:** Mesenchymal stromal cells-derived small extracellular vesicles (MSC-sEVs) have recently attracted considerable attention because of their therapeutic potential in various immune diseases. We previously reported that MSC-sEVs could exert immunomodulatory roles in allergic airway inflammation by regulating group 2 innate lymphoid cell (ILC2) and dendritic cell (DC) functions. Therefore, this study aimed to investigate the indirect effects of MSC-sEVs on ILC2s from patients with allergic rhinitis (AR) via DCs.

**Methods:** Here, we isolated sEVs from induced pluripotent stem cells-MSCs using anion-exchange chromatography and mature DCs (mDCs) were treated with MSC-sEVs. sEV-mDCs were co-cultured with peripheral blood mononuclear cells from patients with AR or purified ILC2s. The levels of IL-13 and GATA3 in ILC2s were examined by flow cytometry. Bulk RNA sequence for mDCs and sEV-mDCs was employed to further probe the potential mechanisms, which were then validated in the co-culture systems.

**Results:** sEV-mDCs showed impaired capacity in priming the levels of IL-13 and GATA3 in ILC2s when compared with mDCs. Furthermore, there was higher PGE2 and IL-10 production from sEV-mDCs, and the blockade of them especially the former one reversed the inhibitory effects of sEV-mDCs.

**Conclusions:** We demonstrated that MSC-sEVs were able to dampen the activating effects of mDCs on ILC2s in patients with AR. Mechanismly, the PGE2-EP2/4 axis played an essential role in the immunomodulatory effects of sEV-mDCs on ILC2s. Herein, we provided new insights into the mechanism underlying the therapeutic effects of MSC-sEVs in allergic airway inflammation.

**Keywords:** Allergic rhinitis; Dendritic cells; Group 2 innate lymphoid cells; Mesenchymal stromal cells; Prostaglandin E2; Small extracellular vesicles.

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## Conflict of interest statement

The authors declare no conflicts of interest in this work.

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

[supplementary info](#)

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. 2023 Jul 27;2201519.

doi: 10.1183/13993003.01519-2022. Online ahead of print.

**European Respiratory Society/American Thoracic Society Technical Standard on**



# Standardisation of the Measurement of Lung Volumes - 2023 Update

[Nirav R Bhakta](#)<sup>1</sup>, [Aisling McGowan](#)<sup>2</sup>, [Kathryn A Ramsey](#)<sup>3</sup>, [Brigitte Borg](#)<sup>4,5</sup>, [Jana Kivastik](#)<sup>6</sup>, [Shandra Lee Knight](#)<sup>7</sup>, [Karl Sylvester](#)<sup>8,9</sup>, [Felip Burgos](#)<sup>10</sup>, [Erik R Swenson](#)<sup>11</sup>, [Kevin McCarthy](#)<sup>12</sup>, [Brendan G Cooper](#)<sup>13</sup>, [Francisco García-Río](#)<sup>14</sup>, [Gwen Skloot](#)<sup>15</sup>, [Meredith McCormack](#)<sup>16</sup>, [Carl Mottram](#)<sup>17</sup>, [Charles G Irvin](#)<sup>18</sup>, [Irene Steenbruggen](#)<sup>19</sup>, [Allan L Coates](#)<sup>20</sup>, [David A Kaminsky](#)<sup>21</sup>

Affiliations expand

- PMID: 37500112
- DOI: [10.1183/13993003.01519-2022](https://doi.org/10.1183/13993003.01519-2022)

## **Abstract**

This document updates the 2005 European Respiratory Society (ERS) and American Thoracic Society (ATS) technical standard for the measurement of lung volumes [1]. The 2005 document integrated the recommendations of an ATS/ERS task force with those from an earlier National Heart, Lung and Blood Institute (NHLBI) workshop that led to the publication of background papers between 1995 and 1999 and a consensus workshop report with more in-depth descriptions and discussion. Advancements in hardware and software, new research, and emerging approaches have necessitated an update to the 2005 technical standard to guide laboratory directors, physiologists, operators, pulmonologists, and manufacturers.

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**2**

Respir Physiol Neurobiol

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. 2023 Jul 24;316:104123.

doi: 10.1016/j.resp.2023.104123. Online ahead of print.

# **Effects of TRPV4 channel blocker on airway inflammation and airway defense reflexes in experimentally induced model of allergic asthma**

[Jozef Mažerik](#)<sup>1</sup>, [Eduard Gondáš](#)<sup>2</sup>, [Lukáš Smieško](#)<sup>3</sup>, [Soňa Fraňová](#)<sup>3</sup>, [Martina Šutovská](#)<sup>3</sup>

Affiliations expand

- PMID: 37495166
- DOI: [10.1016/j.resp.2023.104123](https://doi.org/10.1016/j.resp.2023.104123)

## **Abstract**

The transient receptor potential (TRP) channels regulate physiological and pathological processes. Changes in their activity and sensitivity may be involved in the pathophysiology of asthma. The present study investigates the effect of an inhaled TRPV4 channel blocker HC-067047 in an experimental guinea pig model of ovalbumin-induced allergic asthma. We monitored the effect of 50 nM, 100 nM, and 150 nM HC-067047 concentrations on airway defense reflexes in vivo and tracheal smooth muscle contractility in vitro. The anti-inflammatory action of HC-067047 was investigated by analysis of chronic inflammation markers from lung homogenates. The results suggest that HC-067047 can suppress airway defense reflexes in vivo and acetylcholine-induced contractility in vitro. Immunological analysis revealed that TRPV4 channel blockade leads to a decrease in the levels of inflammatory cytokines. An effect on airway defence reflexes and airway inflammation was observed using tested concentrations (50 mM, 100 mM, 150 mM) of HC-067047. The effects of HC-067047 on both airway defense reflexes and inflammation underline the role of TRPV4 channels in asthma and uncover therapeutic targets for developing innovative drugs in asthma therapy.

**Keywords:** Asthma; Bronchoconstriction; Cough; HC-067047; Inflammation; TRPV4 channel.

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Korean J Gastroenterol

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# Validity and Reliability of the Reflux Symptoms Index Translated into Indonesian: The Role of Upper Endoscopy in Assessing Extra-Esophageal Gastroesophageal Reflux Disease Symptoms

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## **Abstract**

**Background/aims:** The Reflux Symptom Index (RSI) is a questionnaire that evaluates the severity of extra-esophageal symptoms and is one of the most widely used measures to evaluate LPR. This study assessed the validity and reliability of the RSI questionnaire in Bahasa Indonesia and investigated the association between each extra-esophageal

symptom reported in the questionnaire and the severity of erosive esophagitis as determined by endoscopic findings.

**Methods:** 85 adult patients with GERD symptoms had an upper endoscopy examination and were asked to complete the translated RSI. The validity and reliability of the questionnaire were assessed.

**Results:** The construct validity of the RSI translated into Bahasa Indonesia was verified with the  $r$  value of each question being higher than the crucial table value ( $r > 0.213$ ,  $p < 0.05$ ). Our questionnaire had a Cronbach alpha value of 0.81, which indicates an acceptable level of internal consistency. At least one extra-esophageal symptom was seen in 91.7% of patients with Los Angeles (LA) grade B or higher-grade esophagitis. In addition, the presence of extra-esophageal symptoms was associated with significant mucosal erosion ( $p = 0.20$ ). The symptoms of cough after eating or lying down and chronic cough were associated with the severity of esophageal mucosal erosion ( $p < 0.05$ ).

**Conclusions:** The version of RSI translated into Bahasa Indonesia is a valid and reliable tool for assessing extra-esophageal GERD symptoms. The occurrence of extra-esophageal symptoms in patients with typical GERD symptoms is associated with endoscopic findings of LA grade B or erosive esophagitis of higher severity.

**Keywords:** Endoscopy; Extra-Esophageal Symptoms; GERD; Gastroenterology; RSI.

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

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### Review

Pediatr Pulmonol

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. 2023 Jul 26.

doi: 10.1002/ppul.26603. Online ahead of print.

# Pediatric Pulmonology 2022 year in review: Rare and diffuse lung disease

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Affiliations expand

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- DOI: [10.1002/ppul.26603](https://doi.org/10.1002/ppul.26603)

## Abstract

The field of rare and diffuse pediatric lung disease continues to evolve and expand rapidly as clinicians and researchers make advancements in the diagnosis and treatment of children's interstitial and diffuse lung disease, non-cystic fibrosis bronchiectasis, and primary ciliary dyskinesia. Papers published on these topics in Pediatric Pulmonology and other journals in 2022 describe newly recognized disorders, elucidate disease mechanisms and courses, explore potential biomarkers, and assess novel treatments. In this review, we will discuss these important advancements and place them in the context of existing literature.

**Keywords:** bronchiectasis; congenital abnormalities; interstitial lung disease; primary ciliary dyskinesia.

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Chronic Obstr Pulm Dis

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. 2023 Jul 26;10(3):199-210.

doi: 10.15326/jcopdf.2023.0388.

# Impact of Bronchiectasis on COPD Severity and Alpha-1 Antitrypsin Deficiency as a Risk Factor in Individuals with a Heavy Smoking History

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Affiliations expand

- PMID: 37199731
- DOI: [10.15326/jcopdf.2023.0388](https://doi.org/10.15326/jcopdf.2023.0388)

**Free article**

## **Abstract**

**Rationale:** Bronchiectasis is common among those with heavy smoking histories, but risk factors for bronchiectasis, including alpha-1 antitrypsin deficiency, and its implications for COPD severity are uncharacterized in such individuals.

**Objectives:** To characterize the impact of bronchiectasis on COPD and explore alpha-1 antitrypsin as a risk factor for bronchiectasis.

**Methods:** SubPopulations and InteRmediate Outcome Measures In COPD Study (SPIROMICS) participants (N=914; ages 40-80 years; ≥20-pack-year smoking) had high-resolution computed tomography (CT) scans interpreted visually for bronchiectasis, based on airway dilation without fibrosis or cicatrization. We performed regression-based models

of bronchiectasis with clinical outcomes and quantitative CT measures. We deeply sequenced the gene encoding  $\alpha$ -1 antitrypsin, *SERPINA1*, in 835 participants to test for rare variants, focusing on the PiZ genotype (Glu<sup>366</sup>Lys, rs28929474).

**Measurements and main results:** We identified bronchiectasis in 365 (40%) participants, more frequently in women (45% versus 36%,  $p=0.0045$ ), older participants (mean age=66[standard deviation (SD)=8.3] versus 64[SD=9.1] years,  $p=0.0083$ ), and those with lower lung function (forced expiratory volume in 1 second [FEV<sub>1</sub>] percentage predicted=66%[SD=27] versus 77%[SD=25],  $p<0.0001$ ; FEV<sub>1</sub> to forced vital capacity [FVC] ratio=0.54[0.17] versus 0.63[SD=0.16],  $p<0.0001$ ). Participants with bronchiectasis had greater emphysema (%voxels  $\leq$ -950 Hounsfield units, 11%[SD=12] versus 6.3%[SD=9],  $p<0.0001$ ) and parametric response mapping functional small airways disease (26[SD=15] versus 19[SD=15],  $p<0.0001$ ). Bronchiectasis was more frequent in the combined PiZZ and PiMZ genotype groups compared to those without PiZ, PiS, or other rare pathogenic variants (N=21 of 40 [52%] versus N=283 of 707[40%], odds ratio [OR]=1.97; 95% confidence interval [CI]=1.002, 3.90,  $p=0.049$ ), an association attributed to White individuals (OR=1.98; 95%CI = 0.9956, 3.9;  $p=0.051$ ).

**Conclusions:** Bronchiectasis was common in those with heavy smoking histories and was associated with detrimental clinical and radiographic outcomes. Our findings support  $\alpha$ -1antitrypsin guideline recommendations to screen for  $\alpha$ -1 antitrypsin deficiency in an appropriate bronchiectasis subgroup with a significant smoking history.

**Keywords:** COPD;  $\alpha$ -1 antitrypsin; bronchiectasis; lung function.

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J Investig Allergol Clin Immunol

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. 2023 Jul 27;33(4):281-288.

doi: 10.18176/jiaci.0816. Epub 2002 May 3.

# Exacerbations Among Patients With Asthma Are Largely Dependent on the Presence of Multimorbidity

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Affiliations expand

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- DOI: [10.18176/jiaci.0816](https://doi.org/10.18176/jiaci.0816)

## Abstract

**Background and objective:** Comorbidities can influence asthma control and promote asthma exacerbations (AEs). However, the impact of multimorbidity in AEs, assessed based on long-term follow-up of patients with asthma of different degrees of severity, has received little attention in real-life conditions. To describe the epidemiological and clinical characteristics and predictors of AEs in patients who had presented at least 1 AE in the previous year in the MEchanism of Genesis and Evolution of Asthma (MEGA) cohort.

**Methods:** The work-up included a detailed clinical examination, pulmonary function testing, fractional exhaled nitric oxide (FeNO), blood counts, induced sputum, skin prick-tests, asthma questionnaires, and assessment of multimorbidity. The number of moderate-severe AEs in the preceding year was registered for each patient.

**Results:** The study population comprised 486 patients with asthma (23.7% mild, 35% moderate, 41.3% severe). Disease remained uncontrolled in 41.9%, and 47.3% presented  $\geq 1$  moderate-severe AE, with a mean (SD) annual exacerbation rate of 0.47 (0.91) vs 2.11 (2.82) in mild and severe asthma, respectively. Comorbidity was detected in 56.4% (66.6% among those with severe asthma). Bronchiectasis, chronic rhinosinusitis with nasal polyps, atopy, psychiatric illnesses, hyperlipidemia, and hypertension were significantly associated with AEs. No associations were found for FeNO, blood eosinophils, or total serum IgE.



Sputum eosinophilia and a high-T2 inflammatory pattern were significantly associated with AEs. Multivariable regression analysis showed a significant association with asthma severity, uncontrolled disease, and low prebronchodilator FEV1/FVC.

**Conclusion:** Our study revealed a high frequency of AE in the MEGA cohort. This was strongly associated with multimorbidity, asthma severity, poor asthma control, airflow obstruction, higher sputum eosinophils, and a very high-T2 inflammatory pattern.

**Keywords:** Asthma; Asthma control; Exacerbations; MEGA cohort; Multimorbidity.

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