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

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## A Double-Blind, Randomised, Placebo-controlled Trial of Long-Term Doxycycline Therapy on Exacerbation Rate in Patients with Stable COPD

James P Allinson [1 2], Ben H Vlies [3], Simon E Brill [4], Martin Law [5], Girvan Burnside [6], Lydia J Finney [7], Luana Alves-Moreira [1], Gavin C Donaldson [1], Peter M A Calverley [8], Paul P Walker [9], Jadwiga A Wedzicha [1]
Affiliations expand

# Abstract

**Rationale:** COPD exacerbations are a major cause of morbidity and mortality and preventing them is a key treatment target. Long-term macrolide treatment is effective at reducing exacerbations but there is a paucity of evidence for other antibiotic classes. To assess whether 12-month use of doxycycline reduces exacerbation rate in people with COPD.

**Methods:** People with moderate to very severe COPD and an exacerbation history were recruited from 3 UK centres and randomised to 12-months doxycycline 100mg once daily or placebo. The primary study outcome was exacerbation rate per person year.

**Results:** 222 people were randomised. Baseline mean FEV1 was 1.35 (SD 0.35) L; 52.5 (SD 15.9) % predicted. Median number of treated exacerbations in the year before the study was 2 (1-4). 71% of patients reported ≥2 exacerbations. 81% were already prescribed inhaled corticosteroids at baseline. COPD exacerbation rate did not differ between the groups - doxycycline/placebo rate ratio 0.86 (0.67, 1.10); p=0.23. No difference was seen if only treated exacerbations or hospitalisations were considered. In pre-planned sub-group analysis, doxycycline appeared to better reduce the exacerbation rate among people with severe COPD (RR:0.36 (0.15, 0.85); p=0.019), and in those with an eosinophil count <300 cells/μL (RR:0.50 (0.29, 0.84); p=0.01). Health status measured by SGRQ was 5.2 points worse in the doxycycline group at 12-months (p<0.007).

**Conclusions:** Doxycycline did not significantly reduce exacerbation rate, over 12-months, in participants with COPD, who exacerbated regularly, but may have benefitted those with more severe COPD or blood eosinophil counts <300 cells/μL. Clinical trial registration available at www.

**Clinicaltrials:** gov, ID: [NCT02305940](NCT02305940).

**Keywords:** Antibiotic; Eosinophil; Infection; Long-term.

# Randomized Controlled Trials on Chronic Obstructive Pulmonary Disease in Africa: A Systematic Review

Eric Sven Kroeber [1], Thomas Frese [1], Eva Johanna Kantelhardt [2], Benjarong Nanuppakrankijkun [1], Etienne Ngeh Ngeh [3][4][5], Anne Schrimpf [6], Mulugeta Tamire [7], Susanne Unverzagt [1]
Affiliations expand

- PMID: 37450850

- DOI: 10.15326/jcopdf.2023.0387

## Abstract

**Background:** The rising burden of chronic obstructive pulmonary disease (COPD) in African countries is attributed to the growing and ageing of the populations, lifestyle, and environmental changes. This systematic review aims to map the available evidence on interventions on COPD in Africa.

**Methods:** We performed a systematic search in six (including local African) databases and registries with updates until January 2022. We included randomized controlled trials (RCTs) the included patients diagnosed with COPD that were conducted in Africa, studying outcomes on acute respiratory episodes and rates, physical and functional abilities, and adverse events. We followed the PRISMA guidelines. The study quality was assessed using the Cochrane Risk of Bias tool. We primarily summarized the results in a narrative way.

**Results:** Out of 1594 identified publications we included 18 studies with altogether 1504 participants, conducted in Egypt, South Africa, and Tunisia. Eight studies investigated interventions for patients in stable phases treated in outpatient settings and ten included patients with acute COPD exacerbation treated in emergency or intensive care settings. The interventions mainly include ventilatory support, pharmacological and rehabilitative
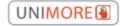
interventions. Reported treatment effects were heterogeneous ranging from no beneficial effects to clinically relevant benefits.

**Conclusions:** The included studies were conducted in countries with high infrastructural development and half of them were set in intensive care units. Despite the paucity of RCTs on COPD management, research activities have been increasing over the last years.

**Keywords:** chronic lung diseases; non-communicable diseases; pulmonology; randomized controlled trials; systematic review.

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# Out-of-Hospital Cardiac Arrest in individuals with Human Immunodeficiency Virus infection – A nationwide population-based cohort study

[Rodrigue Garcia](#) [1][2][3], [Peder Emil Warming](#) [1], [Carl Johann Hansen](#) [1], [Deepthi Rajan](#) [1], [Christian Torp-Pedersen](#) [4][5], [Thomas Benfield](#) [6][7], [Fredrik Folke](#) [8][9][10], [Jacob Tfelt-Hansen](#) [1][11]
Affiliations expand

- PMID: 37448334

# Abstract

**Background:** Little data exist on the risk and outcomes of out-of-hospital cardiac arrest (OHCA) in people with HIV (PWH). We aimed to describe OHCA in PWH as compared to the general population in terms of incidence, characteristics, and survival.

**Methods:** This nationwide study assessed all individuals aged 18-85 years between 2001 and 2019 in Denmark. Cumulative incidence of OHCA was computed using cause-specific Cox models accounting for competing risk of death.

**Results:** Among 6 565 309 individuals, 6 925 (median age 36 [IQR 28-44], 74% males) were infected at some point with HIV. Incidence of OHCA was 149 (95% CI 123-180)/100 000 person-years in PWH versus 64 (95% CI 64-65)/100 000 person-years in non-HIV patients (P<0.001). Age at the time of cardiac arrest was 52 (IQR 44-61) years in PWH (vs. 69 [IQR 59-77] years in individuals without HIV; P<0.001). In a multivariable model adjusted for age, sex, hypertension, diabetes, heart failure, ischemic heart disease, atrial fibrillation, chronic obstructive pulmonary disease, cancer and renal failure, PWH had a two-fold higher risk of OHCA (HR 2.84, 95% CI 2.36-3.43; P<0.001). Thirty-day mortality (89% vs 88%; P=0.80) was comparable to individuals without HIV.

**Conclusions:** HIV is an independent risk factor of OHCA and OHCA victims with HIV are much younger than those without HIV. Almost 90% of PWH died one month after OHCA. Further research should strive to find out how to reduce OHCA occurrence in this population.

**Keywords:** Epidemiology; Human immunodeficiency virus; Out-of-Hospital Cardiac Arrest.

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Review

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# Effects of long-term oxygen therapy on the mental state of patients with chronic obstructive pulmonary disease: A systematic review

Xiaohan Zhang [1] [2], Fei Fei [1] [3]
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## Abstract

**Objectives:** This systematic review aimed to examine the effects of long-term oxygen therapy on the mental state of patients with chronic obstructive pulmonary disease.

**Methods:** Web of Science, Medline, CINAHL, EMBASE, ProQuest, and Cochrane Library were selected to search for relevant studies. We followed the Cochrane Handbook for Systematic Reviews of Interventions, adopted the Cochrane risk-of-bias tool and Risk Of Bias In Non-randomized Studies of Interventions tool, and synthesized the outcomes narratively with Grading of Recommendations, Assessment, Development and Evaluations evidence profile.

**Results:** Six studies were included. Moderate quality of evidence supported no effects of long-term oxygen therapy on the mental state in patients with severe resting hypoxemia and moderate resting hypoxemia (or exertional desaturation) at follow-up of 6 to 12 months; however, adverse effects on mental state among patients with moderate resting or exertional desaturation were reported at the follow-up of 36 to 48 months.

**Discussion:** Nurses should focus on the mental state of patients treated with long-term oxygen therapy, especially those who use it for a prolonged time. Due to ethical constraints in this study, a quasi-experimental study with faithful consideration of internal validity can be commenced in the future.

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# Significant role of circRNA BBS9 in chronic obstructive pulmonary disease via miRNA-103a-3p/BCL2L13

Pujian Guo [# 1], Jing Lu [1], Yu Lei [# 2]
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## Abstract

**Background:** Various studies have shown that circular RNA (circRNA) plays a pivotal role in chronic obstructive pulmonary disease (COPD). We aimed to determine the role of circRNA BBS9 in COPD progression.

**Methods:** Real-time quantitative reverse transcription PCR (qRT-PCR) was performed to determine the levels and the linkages of circRNA BBS9, miRNA-103a-3p, and BCL2L13 in cigarette smoke extract (CSE)-treated human pulmonary microvascular endothelial cells (HPMECs). The target binding sites of circRNA BBS9 and miRNA-103a-3p were predicted using the starBase database, and the TargetScan algorithm was used to forecast the potential binding sites of BCL2L13 and miRNA-103a-3p, which were verified using a dual-luciferase reporter assay. An flow cytometry (FCM) assay was performed to determine the rate of apoptosis of HPMECs. Caspase3 activity was determined using a Caspase3 assay kit. The apoptosis-related protein bands were determined by western blotting.

**Results:** The level of circRNA BBS9 increased in 1% CSE-induced cells, and silencing of circRNA BBS9 decreased the ratio of apoptotic cells among the 1% CSE-induced HPMECs. The results of dual-luciferase reporter assays showed that miRNA-103a-3p associates with circRNA BBS9. miRNA-103a-3p was downregulated in COPD, and upregulation of miRNA-103a-3p inhibited apoptosis in CSE-stimulated cells. Moreover, BCL2L13 was found to act downstream of miRNA-103a-3p. Silencing of miRNA-103a-3p reversed the inhibitory effect of circRNA BBS9-siRNA. The effects of the miRNA-103a-3p mimic were reversed by the BCL2L13-plasmid.

**Conclusion:** circRNA BBS9 is involved in COPD development as it inhibits the functioning of miRNA-103a-3p. Our results suggest that circRNA BBS9 may act as a novel target for treating COPD.

**Keywords:** BCL2L13; Chronic obstructive pulmonary disease; circRNA BBS9; miRNA-103a-3p.

- 42 references

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# [Oxidised IL-33 drives COPD epithelial pathogenesis *via* ST2-independent RAGE/EGFR signalling complex](#)

[Sam Strickson](#) [1][2], [Kirsty F Houslay](#) [1][2], [Victor A Negri](#) [1], [Yoichiro Ohne](#) [3], [Tomas Ottosson](#) [4], [Roger B Dodd](#) [5], [Catherine Chaillan Huntington](#) [5], [Tina Baker](#) [6], [Jingjing Li](#) [1], [Katherine E Stephenson](#) [1], [Andy J O'Connor](#) [1], [J Sophie Sagawe](#) [1], [Helen Killick](#) [6], [Tom Moore](#) [1], [D Gareth Rees](#) [5], [Sofia Koch](#) [7], [Caroline Sanden](#) [8][9], [Yixin Wang](#) [10], [Elise Gubbins](#) [1], [Mahboobe Ghaedi](#) [11], [Roland Kolbeck](#) [3][12], [Saumyaa Saumyaa](#) [13], [Jonas S Erjefält](#) [8][14], [Gary P Sims](#) [15], [Alison A Humbles](#) [1][16], [Ian C Scott](#) [6], [Xavier Romero Ros](#) [1][17], [E Suzanne Cohen](#) [18][17]
Affiliations expand

## Abstract

**Background:** Epithelial damage, repair and remodelling are critical features of chronic airway diseases including chronic obstructive pulmonary disease (COPD). Interleukin (IL)-33 released from damaged airway epithelia causes inflammation *via* its receptor, serum stimulation-2 (ST2). Oxidation of IL-33 (IL-33ox) to a non-ST2-binding form is thought to limit its activity. We investigated whether IL-33ox has functional activities that are independent of ST2 in the airway epithelium.

**Methods:** *In vitro* epithelial damage assays and three-dimensional, air-liquid interface (ALI) cell culture models of healthy and COPD epithelia were used to elucidate the functional role of IL-33ox. Transcriptomic changes occurring in healthy ALI cultures treated with IL-33ox and COPD ALI cultures treated with an IL-33-neutralising antibody were assessed with bulk and single-cell RNA-sequencing analysis.

**Results:** We demonstrate that IL-33ox forms a complex with receptor for advanced glycation end products (RAGE) and epidermal growth factor receptor (EGFR) expressed on airway epithelium. Activation of this alternative, ST2-independent pathway impaired epithelial wound closure and induced airway epithelial remodelling *in vitro*. IL-33ox increased the proportion of mucus-producing cells and reduced epithelial defence functions, mimicking pathogenic traits of COPD. Neutralisation of the IL-33ox pathway reversed these deleterious traits in COPD epithelia. Gene signatures defining the

pathogenic effects of IL-33$^{ox}$ were enriched in airway epithelia from patients with severe COPD.

**Conclusions:** Our study reveals for the first time that IL-33, RAGE and EGFR act together in an ST2-independent pathway in the airway epithelium and govern abnormal epithelial remodelling and muco-obstructive features in COPD.

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# Which spontaneous breathing trial to predict effort to breathe after extubation according to five critical illnesses: the cross-over GLOBAL WEAN study protocol

Mathieu Capdevila [1][2], Audrey De Jong [1][2], Yassir Aarab [1], Aurelie Vonarb [1], Julie Carr [1], Nicolas Molinari [3], Xavier Capdevila [4][5], Laurent Brochard [6][7], Samir Jaber [8][2]
Affiliations expand

- PMID: 37438068

- DOI: 10.1136/bmjopen-2022-070931

# Abstract

**Introduction:** Readiness to be freed from ventilatory support can be evaluated by spontaneous breathing trial (SBT) assessing the patient's ability to sustain respiratory effort after extubation. Current SBT practices are heterogenous and there are few physiological studies on the topic. The objective of this study is to assess which SBT best reproduces inspiratory effort to breathe after extubation depending on the patient's illness.

**Methods and analysis:** This will be a multicentre randomised cross-over physiological study, in a large population, in the era of modern intensive care units using last generation modern ventilators. Each included patient will perform three 15-minute SBTs in a random order: pressure support ventilation (PSV) level of 7 cmH$_2$O with positive end expiratory pressure (PEEP) level of 0 cmH$_2$O, PSV 0 cmH$_2$O with PEEP 0 cmH$_2$O and T-piece trial. A rest period of baseline state ventilation will be observed between the SBTs (10 min) and before extubation (30 min). Primary outcome will be the inspiratory muscle effort, reflected by pressure time product per minute (PTPmin). This will be calculated from oesophageal pressure measurements at baseline state, before and after each SBT and 20 min after extubation. Secondary outcomes will be PTPmin at 24 hours and 48 hours after extubation, changes in physiological variables and respiratory parameters at each step, postextubation respiratory management and the rate of successful extubation. One hundred patients with at least 24 hours of invasive mechanical ventilation will be analysed, divided into five categories of critical illness: abdominal surgery, brain injury, chest trauma, chronic obstructive pulmonary disease and miscellaneous (pneumonia, sepsis, heart disease).

**Ethics and dissemination:** The study project was approved by the appropriate ethics committee (2019-A01063-54, Comité de Protection des Personnes TOURS - Région Centre - Ouest 1, France). Informed consent is required, for all patients or surrogate in case of inability to give consent.

**Trial registration number:** [NCT04222569](NCT04222569).

**Keywords:** adult intensive & critical care; rehabilitation medicine; respiratory physiology.

# Conflict of interest statement

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Review

# Performance-based outcome measures to assess functionality in hospitalised patients with COPD exacerbations: a systematic review of the measurement properties

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

Affiliations expand

- PMID: 37437913

- PMCID: PMC10336549

# Abstract

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

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

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

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

# Conflict of interest statement

Conflict of interest: N.T. Leonardi reports support for the present manuscript from FAPESP (São Paulo Research Foundation) in the form of English review and article processing charges, as well as support in attending meetings and travels to present products/results of the project. J.R. Hurst reports consulting fees from AstraZeneca, GSK; lecture honoraria

- 68 references

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Am J Respir Crit Care Med

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. 2023 Jul 12.
 doi: 10.1164/rccm.202307-1175ED. Online ahead of print.

# Icenticaftor, Novel Therapy for COPD: This Glass Is Half Full

Stephen I Rennard [1]
Affiliations expand

- PMID: 37437299

- DOI: 10.1164/rccm.202307-1175ED

*No abstract available*

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# Feasibility of a Home-Based Cognitive-Physical Exercise Program in Patients With Chronic Obstructive Pulmonary Disease: Protocol for a Feasibility and Pilot Randomized Controlled Trial

Dmitry Rozenberg [1][2], Josh Shore [3], Encarna Camacho Perez [3], Sahar Nourouzpour [3], Megha Ibrahim Masthan [3], Daniel Santa Mina [4][5], Jennifer L Campos [6][7], Ella Huszti [8], Robin Green [6], Mohammad Hashim Khan [3], Ambrose Lau [2][3], David Gold [9], Matthew B Stanbrook [2][3], W Darlene Reid [6][10][11]

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## Abstract

**Background:** Chronic obstructive pulmonary disease (COPD) is a progressive condition associated with physical and cognitive impairments contributing to difficulty in performing activities of daily living (ADLs) that require dual tasking (eg, walking and talking). Despite evidence showing that cognitive decline occurs among patients with COPD and may contribute to functional limitations and decreased health-related quality of life (HRQL), pulmonary rehabilitation continues to focus mainly on physical training (ie, aerobic and strength exercises). An integrated cognitive and physical training program compared to physical training alone may be more effective in increasing dual-tasking ability among people living with COPD, leading to greater improvements in performance of ADLs and HRQL.

**Objective:** The aims of this study are to evaluate the feasibility of an 8-week randomized controlled trial of home-based, cognitive-physical training versus physical training for patients with moderate to severe COPD and derive preliminary estimates of cognitive-physical training intervention efficacy on measures of physical and cognitive function, dual task performance, ADLs, and HRQL.

**Methods:** A total of 24 participants with moderate to severe COPD will be recruited and randomized into cognitive-physical training or physical training. All participants will be prescribed an individualized home physical exercise program comprising 5 days of moderate-intensity aerobic exercise (30-50 minutes/session) and 2 days of whole-body strength training per week. The cognitive-physical training group will also perform cognitive training for approximately 60 minutes, 5 days per week via the BrainHQ platform (Posit Science Corporation). Participants will meet once weekly with an exercise professional (via videoconference) who will provide support by reviewing the progression of their training and addressing any queries. Feasibility will be assessed through the recruitment rate, program adherence, satisfaction, attrition, and safety. The intervention efficacy regarding dual task performance, physical function, ADLs, and HRQL will be evaluated at baseline and at 4 and 8 weeks. Descriptive statistics will be used to summarize intervention feasibility. Paired 2-tailed t tests and 2-tailed t tests will be used to compare the changes in the outcome measures over the 8-week study period within and between the 2 randomized groups, respectively.

**Results:** Enrollment started in January 2022. It is estimated that the enrollment period will be 24 months long, with data collection to be completed by December 2023.

**Conclusions:** A supervised home-based cognitive-physical training program may be an accessible intervention to improve dual-tasking ability in people living with COPD. Evaluating the feasibility and effect estimates is a critical first step to inform future clinical trials evaluating this approach and its effects on physical and cognitive function, ADL performance, and HRQL.

**Trial registration:** ClinicalTrials.gov NCT05140226; https://clinicaltrials.gov/ct2/show/NCT05140226.

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# Prevalence and risk factors of frailty in patients with chronic obstructive pulmonary disease: systematic review and meta-analysis

Li-Cong Yan [#1], Hong-Yan Lu [#2], Xiao-Yan Wang [3], Gang Xiao [4], Yan Chang [5], Ping Yuan [1], Bei Wang [1]
Affiliations expand

- PMID: 37436687

# Abstract

**Objective:** To systematically review the prevalence and risk factors for frailty in patients with chronic obstructive pulmonary disease (COPD).

**Methods:** A systematic review and meta-analysis were conducted, and a search of the PubMed, Embase and Web of Science databases was carried out to collect Chinese and English studies on frailty and COPD published up to September 5, 2022.

**Results:** A total of 38 articles were included for the quantitative analysis after the collected literature was either included or omitted based on pertinent criteria. The results indicated that the estimated overall pooled prevalence of frailty was 36% (95% confidence interval [CI] = 31-41%), and the estimated pre-frailty was 43% (95% CI = 37-49%). A higher age (odds ratio [OR] = 1.04; 95% CI = 1.01-1.06) and higher COPD assessment test (CAT) score (OR = 1.19; 95% CI = 1.12-1.27) were associated with a significantly increased likelihood of frailty in patients with COPD. However, a higher educational attainment (OR = 0.55; 95% CI = 0.43-0.69) and higher income (OR = 0.63; 95% CI = 0.45-0.88) were associated with a significantly reduced risk of frailty in patients with COPD. A total of 17 other risk factors for frailty were identified via qualitative synthesis.

**Conclusion:** The incidence of frailty in patients with COPD is high, and there are many influencing factors.

**Keywords:** Chronic obstructive pulmonary disease; Frailty; Meta-analysis; Risk factors.

- 69 references

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# Towards regional progress: APSR 2022 Big Five Lung Diseases Workshop

Paul N Reynolds[1], Sameera Ansari[2][3], Rosalyn Hernandez-Sebastian[4], Watchara Boonsawat[5], Shih-Yu Chen[6], Landy Lan[7][8], Dawei Yang[8], G M Monsur Habib[9], Jennifer Ann Mendoza-Wi[10], Hung-Ling Huang[11][12][13], Le Thi Tuyet Lan[14], Nguyen Nhu Vinh[14], Maria Lowella F De Leon[15], Anne B Chang[16][17]
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*No abstract available*

**Keywords:** COPD; COVID-19; asthma; lung cancer; respiratory infections; tuberculosis.

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# A New Treatment for COPD: Ensifentrine Moves Closer

Dave Singh [1]
Affiliations expand

- PMID: 37433204

- DOI: [10.1164/rccm.202307-1164ED](#)

*No abstract available*

**Keywords:** COPD; Ensifentrine; phosphodiesterase inhibitor.

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# Clinical Practices Surrounding the Prescription of Home Oxygen in Patients with COPD and Desaturation

Sandra E Zaeh [1], Meredith Case [2], David H Au [3][4], Michele DaSilva [5], Karen Deitemeyer [5], Julie DeLisa [6], Laura C Feemster [3], Lynn B Gerald [6][7], Jerry A Krishnan [6][7], Jennifer Sculley [7], Annette Woodruff [5], Michelle N Eakin [2]
Affiliations expand

# Abstract

**Purpose:** While home oxygen therapy increases survival in patients with chronic obstructive pulmonary disease (COPD) who have severe resting hypoxemia, recent evidence suggests that there is no survival benefit of home oxygen for patients with COPD who have isolated exertional desaturation. We aimed to understand clinician practice patterns surrounding the prescription of home oxygen for patients with COPD.

**Methods:** We conducted semi-structured qualitative interviews via videoconference with 18 physicians and nurse practitioners who provide care for patients with COPD. Clinicians were recruited through the American Lung Association Airways Clinical Research Centers. Interview guides were created with the assistance of patient investigators and included questions regarding clinician practices surrounding prescription of oxygen for patients with COPD and use of clinical guidelines. Interviews were recorded, transcribed, and coded for themes.

**Results:** Of the 18 clinician interviewees (15 physicians, 3 nurse practitioners), one-third were women, with most participants (n=11) being < 50 years. Results of the semi-structured interviews suggested research evidence, clinical experience, and patient preferences contributed to clinician decision-making. Most clinicians described a shared decision-making process for prescribing home oxygen for patients including discussion of risks and benefits and developing an understanding of patient values and preferences. Clinicians did not use a structured tool to conduct these conversations.

**Conclusions:** Clinicians consider a number of patient and clinical factors when prescribing home oxygen based, often using a shared decision-making process. Tools to support shared decision-making about the use of home oxygen are needed.

**Keywords:** Qualitative research; obstructive lung disease; patient preferences; shared decision making.

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# Causes of Death in Smokers: Implications for COPD Management Across Disease Severity

Jadwiga A Wedzicha [1]
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- PMID: 37429287

- DOI: 10.1164/rccm.202306-1065ED

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# Age of Initiating Smoking: An Independent Predictor of COPD in Later Life

Donald P Tashkin [1]
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**Keywords:** Age smoking began; COPD.

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# Measuring skill-based health literacy in chronic airway disease patients: the development and psychometric

# evaluation of the Vancouver airways health literacy tool (VAHLT)

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

- PMID: 37428406

## Abstract

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

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

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

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

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

- <u>31 references</u>

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# Chronic airflow obstruction attributable to poverty in the multinational Burden of Obstructive Lung Disease (BOLD) study

Jaymini H Patel [1], Andre F S Amaral [2], Cosetta Minelli [2], Fadlalla G Elfadaly [3], Kevin Mortimer [4], Asma El Sony [5], Karima El Rhazi [6], Terence A R Seemungal [7], Padukudru Anand Mahesh [8], Daniel O Obaseki [9], Meriam Denguezli [10], Rana Ahmed [11], Hamid Cherkaski [12], Parvaiz Koul [13], Abdul Rashid [14], Richard Li Cher Loh [15], Herve Lawin [16], Mohammed Al Ghobain [17], Asaad Ahmed Nafees [18], Althea Aquart-Stewart [19], Imed Harrabi [20], Sonia Buist [21], Peter G J Burney [2]; Burden of Obstructive Lung Disease (BOLD) Collaborative Research Group
Collaborators, Affiliations expand

- PMID: 37423762

## Abstract

Poverty is strongly associated with all-cause and chronic obstructive pulmonary disease (COPD) mortality. Less is known about the contribution of poverty to spirometrically defined chronic airflow obstruction (CAO)-a key characteristic of COPD. Using cross-sectional data from an asset-based questionnaire to define poverty in 21 sites of the Burden of Obstructive Lung Disease study, we estimated the risk of CAO attributable to poverty. Up to 6% of the population over 40 years had CAO attributable to poverty. Understanding the relationship between poverty and CAO might suggest ways to improve lung health, especially in low-income and middle-income countries.

## Conflict of interest statement

Competing interests: None declared.

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# [Donors in lung transplantation: does age matter?](#)

[Charlotte Ponte](#)[123], [Omar Alkhatiri](#)[13], [Anne Olland](#)[123], [Pierre-Emmanuel Falcoz](#)[123]
Affiliations expand

**Free article**

# Abstract

A best-evidence topic was written according to a structured protocol. The question addressed was the following: in patient undergoing lung transplantation (LTx), are lungs from donors of age > 60 years old (yo) associated with equivalent outcomes-including primary graft dysfunction (PGD), respiratory function and survival-than lungs from donors ≤60yo? Altogether, more than 200 papers were found using the reported search, of which 12 represented the best evidence to answer the clinical question. The authors, journals, dates, country of publication, patients group studied, study type, relevant outcomes, and results of these papers were tabulated. Amongst the 12 papers reviewed, survival results were different depending on whether donor age was analyzed raw or adjusted for recipients' age and initial diagnosis. Indeed, recipients with interstitial lung disease (ILD), pulmonary hypertension or cystic fibrosis (CF) had significantly inferior overall survival when receiving grafts from older donors. When older grafts are allocated to younger donors, a significant decrease in survival has been noticed in the case of single LTx. In addition, three papers showed worse results regarding peak forced expiratory volume in 1 second (FEV1) in patients receiving older organs, and four showed comparable PGD incidence rates. We conclude that when carefully assessed and allocated to the recipient who could benefit most from the transplant (e.g., a patient with a diagnosis of chronic obstructive pulmonary disease (COPD), who would not require a prolonged cardiopulmonary bypass (CPB)), lung grafts from donors of more than 60yo offer comparable results to younger donors.

**Keywords:** donors > 60 years old; lung transplantation; outcomes; respiratory function; survival.

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# Implementation of a screening and management pathway for chronic obstructive pulmonary disease in patients with atrial fibrillation

Rachel M J van der Velden [1], Maartje Hereijgers [1], Nazia Arman [1], Naomi van Middeldorp [1], Frits M E Franssen [2][3][4], Monika Gawalko [1][5], Dominique V M Verhaert [1][6], Zarina Habibi [1][6], Kevin Vernooy [1][6], Lukasz Koltowski [5], Jeroen M Hendriks [7][8], Hein Heidbuchel [9][10][11], Lien Desteghe [9][10][11][12], Sami O Simons [3][4], Dominik Linz [1][6][7][13]

Affiliations expand

## Abstract

**Background and aims:** Chronic obstructive pulmonary disease (COPD) negatively impacts the efficacy of heart rhythm control treatments in patients with atrial fibrillation (AF). Although COPD is recognized as a risk factor for AF, practical guidance about how and when to screen for COPD is not available. Herein, we describe the implementation of an integrated screening and management pathway for COPD into the existing pre-ablation work-up in an AF outpatient clinic infrastructure.

**Methods:** Consecutive unselected patients accepted for AF catheter ablation in the Maastricht University Medical Center + were prospectively screened for airflow limitation using handheld (micro)spirometry at the pre-ablation outpatient clinic supervised by an AF nurse. Patients with results suggestive of airflow limitation were offered referral to the pulmonologist.

**Results:** Handheld (micro)spirometry was performed in 232 AF patients, which provided interpretable results in 206 (88.8%) patients. Airflow limitation was observed in 47 patients (20.3%). Out of these 47 patients, 29 (62%) opted for referral to the pulmonologist. The primary reason for non-referral was low perceived symptom burden. Using this screening strategy 17 (out of 232; 7.3%) ultimately received a diagnosis of chronic respiratory disease, either COPD or asthma.

**Conclusion:** A COPD care pathway can successfully be embedded in an existing AF outpatient clinic infrastructure, using (micro)spirometry and remote analysis of results. Although 1 out of 5 patients had results suggestive of an underlying chronic respiratory disease, only 62% of these patients opted for referral. Preselection of patients as well as patient education might increase the diagnostic yield and requires further research.

**Keywords:** atrial fibrillation; care pathway; chronic obstructive pulmonary disease; microspirometry; screening.

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# ADME properties of CHF6366, a novel bi-functional M3 muscarinic receptor antagonist and ß₂ adrenoceptor agonist (MABA) radiolabelled at both functional moieties

Alberto Ghiglieri [1], Monica Messina [1], Valentina Cenacchi [2], Claudia Piutti [1], Flavio Cinato [1], Giandomenico Brogin [2], Paola Puccini [2]
Affiliations expand

# Abstract

CHF6366, a dual action $\beta_2$-receptor agonist and M3-muscarinic receptor antagonist developed for chronic obstructive pulmonary disease (COPD) was [$^{14}$C]-radiolabelled on the two different functional moieties of the molecule (either aminobutanolic or carbamate) to characterise its ADME profile following intravenous (IV), intratracheal (IT) and oral (PO) administration.A very low oral bioavailability and a good balance between absorption and lung retention after IT administration were observed, together with a rapid distribution throughout the body and a complete metabolic transformation of the parent drug without relevant gender difference.CHF6366 was observed fully hydrolysed to alcohol (CHF6387) and carboxylic acid (CHF6361) in plasma and urine after IV and IT administration, and mainly unchanged in faeces only after oral administration. An important number of metabolites containing aminobutanolic moiety was excreted via urine, whereas carbamate-containing derivatives were excreted mainly by bile.The major metabolic routes of the alcoholic moiety (CHF6387) included isomerisation (Ma7), conjugation with glucuronic acid and dehydrogenation, while the carboxylic acid moiety (CHF6361) was mainly metabolised through oxidation, glucuronide conjugation and, in both pathways, combinations of those metabolic reactions.No major differences arose also from *in vitro* metabolism profiles investigated using liver microsomes and hepatocytes of different species.

**Keywords:** 14C-labelled; ADME; COPD; MABA; in vitro metabolism; in vivo metabolism.

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Editorial

Am J Respir Crit Care Med

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# Finding the Right Biological: Eosinophil Subset Differences in Asthma and Chronic Obstructive Pulmonary Disease

[Christine M Freeman](#) [1] [2] [3], [Jeffrey L Curtis](#) [1] [2] [4], [Annette T Hastie](#) [5]
Affiliations expand

*No abstract available*

## Comment on

- [Eosinophil Subtypes in Adults with Asthma and Adults with Chronic Obstructive Pulmonary Disease.](#)
Cabrera López C, Sánchez Santos A, Lemes Castellano A, Cazorla Rivero S, Breña Atienza J, González Dávila E, Celli B, Casanova Macario C.Am J Respir Crit Care Med. 2023 Jul 15;208(2):155-162. doi: 10.1164/rccm.202301-0149OC.PMID: 37071848

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# Is One Exacerbation Enough to Modify Therapy in Chronic Obstructive Pulmonary Disease?

David M Mannino [1]
Affiliations expand

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## Comment on

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# Association of multiple air pollutants with oxygen saturation during sleep in COPD patients: Effect modification by smoking status and airway inflammatory phenotypes

Wenlou Zhang [1], Junyi Wang [1], Baiqi Chen [2], Xuezhao Ji [2], Chen Zhao [3], Maike Chen [2], Sha Liao [4], Simin Jiang [4], Zihan Pan [4], Wanzhou Wang [2], Luyi Li [2], Yahong Chen [5], Xinbiao Guo [2], Furong Deng [6]
Affiliations expand

## Abstract

Air pollution contributes substantially to the development of chronic obstructive pulmonary disease (COPD). To date, the effect of air pollution on oxygen saturation ($SpO_2$) during sleep and potential susceptibility factors remain unknown. In this longitudinal panel study, real-time $SpO_2$ was monitored in 132 COPD patients, with 270 nights (1615 h) of sleep $SpO_2$ recorded. Exhaled nitric oxide (NO), hydrogen sulfide ($H_2S$) and carbon monoxide (CO) were measured to assess airway inflammatory characteristics. Exposure levels of air pollutants were estimated by infiltration factor method. Generalized estimating equation was used to investigate the effect of air pollutants on sleep $SpO_2$. Ozone, even at low levels (<60 $\mu g/m^3$), was significantly associated with decreased $SpO_2$ and extended time of oxygen desaturation ($SpO_2$ < 90%), especially in the warm season. The associations of other pollutants with $SpO_2$ were weak, but significant adverse effects of $PM_{10}$ and $SO_2$ were observed in the cold season. Notably, stronger effects of ozone were observed in

current smokers. Consistently, smoking-related airway inflammation, characterized by higher levels of exhaled CO and $H_2S$ but lower NO, significantly augmented the effect of ozone on $SpO_2$ during sleep. This study highlights the importance of ozone control in protecting sleep health in COPD patients.

## Conflict of interest statement

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

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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# Eosinophil Subtypes in Adults with Asthma and Adults with Chronic Obstructive Pulmonary Disease

Carlos Cabrera López [1], Alejandra Sánchez Santos [2], Angelina Lemes Castellano [3], Sara Cazorla Rivero [2][4], Joaquín Breña Atienza [5], Enrique González Dávila [6], Bartolomé Celli [7], Ciro Casanova Macario [8]

# Abstract

**Rationale:** There is a differential response to eosinophilic modulation between patients with asthma and those with chronic obstructive pulmonary disease (COPD). There is also evidence of different subtypes of eosinophils in murine models. However, no study has compared eosinophil subtypes in individuals with COPD and in those with asthma. **Objectives:** Study the differences in eosinophils subtypes based in the surface protein expression in COPD patients and asthmatic patients. **Methods:** We studied 10 stable subjects in each of four groups: subjects with COPD, subjects with asthma, smokers without COPD, and healthy volunteers. Subjects with COPD and those with asthma were matched by age, sex, and $FEV_1$% predicted. The following variables were determined: anthropometrics, smoking, exacerbation history, medication use, lung function, and comorbidities. Using flow cytometry and confocal microscopy from blood samples, we determined differences in eosinophil surface proteins and classified them as *1)* resident eosinophils (Siglec-8$^+$CD62L$^+$IL-3R$^{lo}$) or *2)* inflammatory eosinophils (iEos; Siglec-8$^+$CD62L$^{lo}$IL-3R$^{hi}$). IL-5 receptor was also determined. Findings were validated in 59 patients with COPD and in 17 patients with asthma. **Measurements and Main Results:** Patients with asthma had a higher proportion of iEos (25 ± 15%) compared with those with COPD (0.5 ± 1%), smokers without COPD (0.14 ± 0.24%), and healthy volunteers (0.67 ± 1.72%). In patients with asthma, the proportion of iEos was independent of total eosinophil number. iEos had more IL-5 receptors than resident eosinophils (777.02 ± 124.55 vs. 598.35 ± 318.69; $P$ < 0.01). In patients with COPD, there was no relation between iEos number and inhaled corticosteroid use, disease severity, or exacerbations rate. The findings in patients with COPD and those with asthma were confirmed in validation cohorts. **Conclusions:** There are differences in the subtypes of circulating eosinophils between patients with asthma and those with COPD. This could have clinical implications in the interpretation of eosinophil significance and the approach to therapy in these patients.

**Keywords:** COPD; asthma; eosinophils; subtypes.

# Comment in

- [Finding the Right Biological: Eosinophil Subset Differences in Asthma and Chronic Obstructive Pulmonary Disease.](#)
Freeman CM, Curtis JL, Hastie AT.Am J Respir Crit Care Med. 2023 Jul 15;208(2):121-123. doi: 10.1164/rccm.202305-0811ED.PMID: 37311240 No abstract available.

# Exacerbation Risk and Mortality in Global Initiative for Chronic Obstructive Lung Disease Group A and B Patients with and without Exacerbation History

Lowie E G W Vanfleteren [1][2], Anne Lindberg [3], Caddie Zhou [4], Fredrik Nyberg [5], Caroline Stridsman [3]
Affiliations expand

- PMID: 37040482


- DOI: 10.1164/rccm.202209-1774OC

## Abstract

**Rationale:** Risk stratification of patients according to chronic obstructive pulmonary disease severity is clinically important and forms the basis of therapeutic recommendations. No studies have examined the association for Global Initiative for

Chronic Obstructive Lung Disease (GOLD) group A and group B patients with (A1 and B1, respectively) and without (A0 and B0, respectively) an exacerbation in the past year with future exacerbations, hospitalizations, and mortality in perspective with the new GOLD ABE classification. **Objectives:** The aim was to examine the association between GOLD A0, A1, B0, B1, and E patients and future exacerbations, respiratory and cardiovascular hospitalizations, and mortality. **Methods:** In this nationwide cohort study, we identified patients with a diagnosis of chronic obstructive pulmonary disease, aged ⩾30 years, and registered in the Swedish National Airway Register between January 2017 and August 2020. Patients were stratified in GOLD groups A0, A1, B0, B1, and E and were followed until January 2021 for exacerbations, hospitalizations, and mortality in national registries. **Measurements and Main Results:** The 45,350 eligible patients included 25% A0, 4% A1, 44% B0, 10% B1, and 17% E. Moderate exacerbations, all-cause and respiratory hospitalizations, and all-cause and respiratory mortality increased by GOLD group A0-A1-B0-B1-E, except for moderate exacerbations, which were higher in A1 than in B0. Group B1 had a substantially higher hazard ratio for future exacerbation (2.56; 95% confidence interval [95% CI] 2.40-2.74), all-cause hospitalization (1.28; 1.21-1.35), and respiratory hospitalization (1.44; 1.27-1.62), but not all-cause (1.04; 0.91-1.18) or respiratory (1.13; 0.79-1.64) mortality than group B0. The exacerbation rate for group B1 was 0.6 events per patient-year versus 0.2 for group B0 (rate ratio, 2.55; 95% CI, 2.36-2.76). Results were similar for group A1 versus group A0. **Conclusions:** Stratification of GOLD A and B patients with one or no exacerbation in the past year provides valuable information on future risk, which should influence treatment recommendations for preventive strategies.

# Comment in

- [Is One Exacerbation Enough to Modify Therapy in Chronic Obstructive Pulmonary Disease?](#)
  Mannino DM.Am J Respir Crit Care Med. 2023 Jul 15;208(2):124-125. doi: 10.1164/rccm.202304-0783ED.PMID: 37167624 No abstract available.

SUPPLEMENTARY INFO

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# Temporal variation in the association between temperature and cause-specific mortality in 15 German cities

Masna Rai [1], Susanne Breitner [2], Veronika Huber [3], Siqi Zhang [3], Annette Peters [4], Alexandra Schneider [3]
Affiliations expand

## Abstract

**Background:** There is limited evidence of temporal changes in the association between air temperature and the risk of cause-specific cardiovascular [CVD] and respiratory [RD] mortality.

**Method:** We explored temporal variations in the association between short-term exposures to air temperature and non-accidental and cause-specific CVD and RD mortality in the 15 largest German cities over 24 years (1993-2016) using time-stratified time series analysis. We applied location-specific confounder-adjusted Poisson regression with distributed lag non-linear models with a lag period of 14 days to estimate the temperature-mortality associations. We then pooled the estimates by a multivariate meta-analytical model. We analysed the whole study period and the periods 1993-2004 and 2005-16, separately. We also carried out age- and sex-stratified analysis. Cold and heat effects are reported as relative risk [RR] at the 1st and the 99th temperature percentile, relative to the 25th and the 75th percentile, respectively.

**Result:** We analysed a total of 3,159,292 non-accidental, 1,063,198 CVD and 183,027 RD deaths. Cold-related RR for CVD mortality was seen to rise consistently over time from 1.04 (95% confidence interval [95% CI] 1.02, 1.06) in the period 1993-2004 to 1.10 (95% CI 1.09, 1.11) in the period 2005-16. A similar increase in cold-related RR was also observed for RD

mortality with risk increasing from 0.99 (95% CI 0.96, 1.03) to 1.07 (95% CI 1.03, 1.10). Cold-related ischemic, cerebrovascular, and heart failure mortality risk were seen to be increasing over time. Similarly, COPD, the commonly speculated driver of heat-related RD mortality was found to have a constant heat-related risk over time. Males were increasingly vulnerable to cold with time for all causes of death. Females showed increasing sensitivity to cold for CVD mortality. Our results indicated a significant increased cold and heat vulnerability of the youngest age-groups (<64) to non-accidental and RD mortality, respectively. Similarly, the older age group (>65) were found to have significantly increased susceptibility to cold for CVD mortality.

**Conclusion:** We found evidence of rising population susceptibility to both heat- and cold-related CVD and RD mortality risk from 1993 to 2016. Climate change mitigation and targeted adaptation strategies might help to reduce the number of temperature-related deaths in the future.

**Keywords:** Cardiovascular mortality; Cause-specific mortality; Germany; Respiratory mortality; Temperature; Temporal variation.

# Conflict of interest statement

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

SUPPLEMENTARY INFO

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# Pulmonary Function Trajectories Preceding Death Among Older Adults: A Long-Term Community-Based Cohort Study

Jiao Wang [1][2], Jie Guo [3], Abigail Dove [3], Wenzhe Yang [1][2], Xuerui Li [1][2], Xiuying Qi [1][2], David A Bennett [4], Weili Xu [1][3]

Affiliations expand

## Abstract

**Background:** Poor pulmonary function (PF) has been linked to mortality, but the timing of PF changes before death remains unclear. We aimed to examine the association between PF and mortality and identify different PF trajectories precedes death.

**Methods:** Within the Rush Memory and Aging Project, 1 438 participants without chronic obstructive pulmonary disease were followed for up to 22 years. PF was assessed annually using a composite score (tertiled as low, medium, and high) based on forced vital capacity (FVC), forced expiratory volume in 1s (FEV1), and peak expiratory flow (PEF). Survival status was observed during the follow-up period. Data were analyzed using Cox regression, Laplace regression, and mixed-effect models.

**Results:** During the follow-up, 737 (51.25%) participants died. Compared to high PF, the hazard ratio (95% confidence interval [CI]) of mortality was 1.35 (1.05, 1.72)/1.63 (1.25, 2.12) for medium/low PF. The median survival time (95% CI) was shortened by 0.80 (0.01-1.61)/1.72 (0.43-3.01) years for participants with medium/low PF, compared to high PF. In multiadjusted trajectory analysis, the significant differences between decedents and survivors occurred at 7 years before death for composite PF (mean difference [95% CI]: 0.14 [0.02-0.25]), 6 years for FEV1 (0.21 [0.08-0.33]) and FVC (0.21 [0.08-0.34]), and 8 years for PEF (0.21 [0.06-0.37]), and became greater thereafter.

**Conclusion:** Poor PF is associated with elevated mortality and shortens survival for nearly 2 years. An acceleration in PF decline tends to occur 7 years before death. Poor PF, together with its decline, might be a predictor of mortality among community-dwelling older adults.

**Keywords:** Cohort study; Mortality; Pulmonary function; Trajectory.

# Conflict of interest statement

None declared.

- Cited by 1 article
- 51 references
- 2 figures

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

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

# The effects of community interventions on unplanned healthcare use in patients with multimorbidity: a systematic review

[Tavleen Wasan](#)[1], [Benedict Hayhoe](#)[1], [Meryem Cicek](#)[1], [Elena Lammila-Escalera](#)[1], [Dasha Nicholls](#)[1], [Azeem Majeed](#)[1], [Geva Greenfield](#)[1]

Affiliations expand

# Abstract

**Objectives:** To summarise the impact of community-based interventions for multimorbid patients on unplanned healthcare use. The prevalence of multimorbidity (co-existence of multiple chronic conditions) is rapidly increasing and affects one-third of the global population. Patients with multimorbidity have complex healthcare needs and greater unplanned healthcare usage. Community-based interventions allow for continued care of patients outside hospitals, but few studies have explored the effects of these interventions on unplanned healthcare usage.

**Design:** A systematic review was conducted. MEDLINE, EMBASE, PsychINFO and Cochrane Library online databases were searched. Studies were screened and underwent risk of bias assessment. Data were synthesised using narrative synthesis.

**Setting:** Community-based interventions.

**Participants:** Patients with multimorbidity.

**Main outcome measures:** Unplanned healthcare usage.

**Results:** Thirteen studies, including a total of 6148 participants, were included. All included studies came from high-income settings and had elderly populations. All studies measured emergency department attendances as their primary outcome. Risk of bias was generally low. Most community interventions were multifaceted with emphasis on education, self-monitoring of symptoms and regular follow-ups. Four studies looked at improved care coordination, advance care planning and palliative care. All 13 studies found a decrease in emergency department visits post-intervention with risk reduction ranging from 0 (95% confidencec interval [CI]: -0.37 to 0.37) to 0.735 (95% CI: 0.688-0.785).

**Conclusions:** Community-based interventions have potential to reduce emergency department visits in patients with multimorbidity. Identification of specific successful components of interventions was challenging given the overlaps between interventions. Policymakers should recognise the importance of community interventions and aim to integrate aspects of these into existing healthcare structures. Future research should investigate the impact of such interventions with broader participant characteristics.

FULL TEXT LINKS

# A Novel Mobile App to Identify Patients With Multimorbidity in the Emergency Setting: Development of an App and Feasibility Trial

Claire Barthlow Rosen [1], Sanford Eugene Roberts [1], Solomiya Syvyk [1], Caitlin Finn [1], Jason Tong [1], Christopher Wirtalla [1], Hunter Spinks [1], Rachel Rapaport Kelz [1]
Affiliations expand

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## Abstract

**Background:** Multimorbidity is associated with an increased risk of poor surgical outcomes among older adults; however, identifying multimorbidity in the clinical setting can be a challenge.

**Objective:** We created the Multimorbid Patient Identifier App (MMApp) to easily identify patients with multimorbidity identified by the presence of a Qualifying Comorbidity Set and tested its feasibility for use in future clinical research, validation, and eventually to guide clinical decision-making.

**Methods:** We adapted the Qualifying Comorbidity Sets' claims-based definition of multimorbidity for clinical use through a modified Delphi approach and developed MMApp. A total of 10 residents input 5 hypothetical emergency general surgery patient scenarios, common among older adults, into the MMApp and examined MMApp test characteristics for a total of 50 trials. For MMApp, comorbidities selected for each scenario were recorded, along with the number of comorbidities correctly chosen, incorrectly chosen, and missed for each scenario. The sensitivity and specificity of identifying a patient as multimorbid using MMApp were calculated using composite data from all scenarios. To assess model feasibility, we compared the mean task completion by scenario to that of the American College of Surgeons National Surgical Quality Improvement Program Surgical Risk Calculator (ACS-NSQIP-SRC) using paired t tests. Usability and satisfaction with MMApp were assessed using an 18-item questionnaire administered immediately after completing all 5 scenarios.

**Results:** There was no significant difference in the task completion time between the MMApp and the ACS-NSQIP-SRC for scenarios A (86.3 seconds vs 74.3 seconds, P=.85) or C (58.4 seconds vs 68.9 seconds, P=.064), MMapp took less time for scenarios B (76.1 seconds vs 87.4 seconds, P=.03) and E (20.7 seconds vs 73 seconds, P<.001), and more time for scenario D (78.8 seconds vs 58.5 seconds, P=.02). The MMApp identified multimorbidity with 96.7% (29/30) sensitivity and 95% (19/20) specificity. User feedback was positive regarding MMApp's usability, efficiency, and usefulness.

**Conclusions:** The MMApp identified multimorbidity with high sensitivity and specificity and did not require significantly more time to complete than a commonly used web-based risk-stratification tool for most scenarios. Mean user times were well under 2 minutes. Feedback was overall positive from residents regarding the usability and usefulness of this app, even in the emergency general surgery setting. It would be feasible to use MMApp to identify patients with multimorbidity in the emergency general surgery setting for validation, research, and eventual clinical use. This type of mobile app could serve as a template for other research teams to create a tool to easily screen participants for potential enrollment.

**Keywords:** clinical operationalization; delphi; development; emergency; general surgery; mHealth; mobile app; mobile health; morbidity; multimorbidity; qualifying comorbidity set; surgery; usability.

Review

# A Systematic Review of Outcomes Related to Nurse Practitioner–Delivered Primary Care for Multiple Chronic Conditions

Amy McMenamin [1], Eleanor Turi [1], Amelia Schlak [2], Lusine Poghosyan [1]
Affiliations expand

## Abstract

Multiple chronic conditions (MCCs) are more common and costly than any individual health condition in the United States. The growing workforce of nurse practitioners (NPs) plays an active role in providing primary care to this patient population. This study identifies the effect of NP primary care models, compared with models without NP involvement, on cost, quality, and service utilization by patients with MCCs. We conducted a literature search of six databases and performed critical appraisal. Fifteen studies met inclusion criteria (years: 2003-2021). Overall, most studies showed reduced or similar costs, equivalent or better quality, and similar or lower rates of emergency department use and

hospitalization associated with NP primary care models for patients with MCCs, compared with models without NP involvement. No studies found them associated with worse outcomes. Thus, NP primary care models, compared with models without NP involvement, have similar or positive impacts on MCC patient outcomes.

**Keywords:** multimorbidity; multiple chronic conditions; nurse practitioners; primary care.

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# Correction to: evaluation of the implementation progress through key performance indicators in a new multimorbidity patient-centered care model in Chile

Teresita Varela[1], Paula Zamorano[2][3][4], Paulina Muñoz[1], Carolina Rain[5], Esteban Irazoqui[1], Jaime C Sapag[5][6][7], Alvaro Tellez[1][5]
Affiliations expand

- PMID: 37438730

*No abstract available*

# Erratum for

- [Evaluation of the implementation progress through key performance indicators in a new multimorbidity patient-centered care model in Chile.](#)
  Varela T, Zamorano P, Muñoz P, Rain C, Irazoqui E, Sapag JC, Tellez A.BMC Health Serv Res. 2023 May 4;23(1):439. doi: 10.1186/s12913-023-09412-9.PMID: 37143071 **Free PMC article.**

- 1 reference

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. 2023 Jul 11;23(1):423.
 doi: 10.1186/s12877-023-04109-4.

# Multimorbidity and polypharmacy in hospitalized older patients: a cross-sectional study

[Yong Zhao](#) [1], [Jianchun Wang](#) [2], [Xiaojuan Zhu](#) [3], [Xiyu Zhang](#) [4], [Yahui Zhang](#) [5], [Wen Zhang](#) [5], [Yan Dong](#) [6]

Affiliations expand

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# Abstract

**Background:** The growing trend of ageing population has become a worldwide concern. In comparison with the youth, older people are more likely to suffer from multimorbidity and polypharmacy, both of which are associated with adverse outcomes and increased healthcare costs. This study aimed to investigate the status of multimorbidity and polypharmacy in a large sample of hospitalized older patients aged 60 years and over.

**Methods:** A retrospective cross-sectional study was conducted among 46,799 eligible patients aged 60 years and over, who were hospitalized from January 1, 2021 to December 31, 2021. Multimorbidity was defined as the presence of 2 or more morbidities in one patient during the stay in hospital, and polypharmacy as prescription of 5 or more different oral medications. Spearman rank correlation analysis was used to assess the relationship of factors with the number of morbidities or oral medications. Odds ratio (OR) and 95% confidence interval (95% CI) were estimated from logistic regression models to determine the predictors for polypharmacy and all-cause death.

**Results:** The prevalence of multimorbidity was 91.07% and increased with age. The prevalence of polypharmacy was 56.32%. Older age, polypharmacy, prolonged length of stay (LOS), higher cost on medications were significantly associated with an increased number of morbidities (all $P < 0.01$). The number of morbidities (OR = 1.29, 95% CI: 1.208-1.229) and LOS (OR = 1.171, 95% CI: 1.166-1.177) were potential risk factors for polypharmacy. As for all-cause death, age (OR = 1.107, 95% CI: 1.092-1.122), number of morbidities (OR = 1.495, 95% CI: 1.435-1.558) and LOS (OR = 1.020, 95% CI: 1.013-1.027) were the potential risk factors, but the number of medications (OR = 0.930, 95% CI: 0.907-0.952) and polypharmacy (OR = 0.764, 95% CI: 0.608-0.960) were associated with a reduction of mortality.

**Conclusion:** Morbidities and LOS might be predictors for polypharmacy and all-cause death. The number of oral medications was inversely associated with the risk of all-cause mortality. Appropriate polypharmacy was beneficial for the clinical outcomes of older patients during hospitalization.

**Keywords:** Hospitalization; Multimorbidity; Older patient; Polypharmacy; Prevalence.

## Conflict of interest statement

The authors declare that they have no competing interests.

- 20 references
- 2 figures

SUPPLEMENTARY INFO

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# Technologies for frailty, comorbidity, and multimorbidity in older adults: a systematic review of research designs

Alessia Gallucci #1, Pietro D Trimarchi #2, Cosimo Tuena 3, Silvia Cavedoni 4, Elisa Pedroli 4 5, Francesca Romana Greco 6, Antonio Greco 6, Carlo Abbate 2, Fabrizia Lattanzio 7, Marco Stramba-Badiale 8, Fabrizio Giunco 2

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# Abstract

**Background:** Frailty, neurodegeneration and geriatric syndromes cause a significant impact at the clinical, social, and economic level, mainly in the context of the aging world. Recently, Information and Communication Technologies (ICTs), virtual reality tools, and machine learning models have been increasingly applied to the care of older patients to improve diagnosis, prognosis, and interventions. However, so far, the methodological limitations of studies in this field have prevented to generalize data to real-word. This review systematically overviews the research designs used by studies applying technologies for the assessment and treatment of aging-related syndromes in older people.

**Methods:** Following the PRISMA guidelines, records from PubMed, EMBASE, and Web of Science were systematically screened to select original articles in which interventional or observational designs were used to study technologies' applications in samples of frail, comorbid, or multimorbid patients.

**Results:** Thirty-four articles met the inclusion criteria. Most of the studies used diagnostic accuracy designs to test assessment procedures or retrospective cohort designs to build predictive models. A minority were randomized or non-randomized interventional studies. Quality evaluation revealed a high risk of bias for observational studies, while a low risk of bias for interventional studies.

**Conclusions:** The majority of the reviewed articles use an observational design mainly to study diagnostic procedures and suffer from a high risk of bias. The scarce presence of methodologically robust interventional studies may suggest that the field is in its infancy. Methodological considerations will be presented on how to standardize procedures and research quality in this field.

## Conflict of interest statement

All Author have not conflict of interests to declare.

- 81 references
- 4 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

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

Takuma Kimura [1], Ken Shinmura [2]
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- PMID: 37433747

# Abstract

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

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

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

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

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

- 19 references

SUPPLEMENTARY INFO

Grant supportexpand

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# Person-Centered Models for Cardiovascular Care: A Review of the Evidence: A Scientific Statement From the American Heart Association

Laura P Rossi, Bradi B Granger, Jeffrey T Bruckel, Deborah L Crabbe, Lucinda J Graven, Kimberly S Newlin, Megan M Streur, Maya K Vadiveloo, Benita Jeanne Walton-Moss, Bruce A Warden, Annabelle Santos Volgman, Melissa Lydston; American Heart Association Complex Cardiovascular Patient and Family Care Committee of the Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; and Council on Quality of Care and Outcomes Research

## Abstract

Cardiovascular disease remains the leading cause of death and disability in the United States and globally. Disease burden continues to escalate despite technological advances associated with improved life expectancy and quality of life. As a result, longer life is associated with multiple chronic cardiovascular conditions. Clinical guidelines provide recommendations without considering prevalent scenarios of multimorbidity and health system complexities that affect practical adoption. The diversity of personal preferences, cultures, and lifestyles that make up one's social and environmental context is often overlooked in ongoing care planning for symptom management and health behavior

support, hindering adoption and compromising patient outcomes, particularly in groups at high risk. The purpose of this scientific statement was to describe the characteristics and reported outcomes in existing person-centered care delivery models for selected cardiovascular conditions. We conducted a scoping review using Ovid MEDLINE, Embase.com, Web of Science, CINAHL Complete, Cochrane Central Register of Controlled Trials through Ovid, and ClinicalTrials.gov from 2010 to 2022. A range of study designs with a defined aim to systematically evaluate care delivery models for selected cardiovascular conditions were included. Models were selected on the basis of their stated use of evidence-based guidelines, clinical decision support tools, systematic evaluation processes, and inclusion of the patient's perspective in defining the plan of care. Findings reflected variation in methodological approach, outcome measures, and care processes used across models. Evidence to support optimal care delivery models remains limited by inconsistencies in approach, variation in reimbursement, and inability of health systems to meet the needs of patients with chronic, complex cardiovascular conditions.

**Keywords:** AHA Scientific Statements; cardiovascular diseases; delivery of health care; multimorbidity; multiple chronic conditions; outcome assessment, health care.

SUPPLEMENTARY INFO

Publication typesexpand

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# Ambient air pollution and incidence, progression to multimorbidity and death of hypertension, diabetes, and

# chronic kidney disease: A national prospective cohort

[Gan Wu](#) [1], [Miao Cai](#) [1], [Chongjian Wang](#) [2], [Hongtao Zou](#) [1], [Xiaojie Wang](#) [1], [Junjie Hua](#) [3], [Hualiang Lin](#) [4]
Affiliations expand

## Abstract

**Background:** The link between ambient air pollution and the incidence of hypertension, diabetes, and chronic kidney disease (CKD) has been widely studied. However, the associations of air pollution with the dynamic progression to multimorbidity and mortality of these diseases are unknown.

**Methods:** This study included 162,334 participants from the UK Biobank. Multimorbidity was defined as the coexistence of at least two of hypertension, diabetes, and CKD. Land use regression was used to estimate annual concentrations of particulate matter ($PM_{2.5}$), $PM_{10}$, nitrogen dioxide ($NO_2$), and nitrogen oxides ($NO_x$). Multi-state models were used to assess the association between ambient air pollutants and the dynamic progression of hypertension, diabetes, and CKD.

**Results:** During a median follow-up of 11.7 years, 18,496 participants experienced at least one of hypertension, diabetes, and CKD, 2216 experienced multimorbidity, and 302 died afterwards. We observed differential associations of four air pollutants on different transitions from healthy status to incident disease (hypertension, diabetes, or CKD), to multimorbidity, and to death. The hazard ratios (HRs) of each IQR increment in $PM_{2.5}$, $PM_{10}$, $NO_2$, and $NO_x$ for the transition to incident disease were 1.07 [95 % confidence intervals (CI): 1.04, 1.09], 1.02 (1.00, 1.03), 1.07 (1.04, 1.09), and 1.05 (1.03, 1.07), but the associations with the transition to death were significant for $NO_x$ only [HR: 1.04 (95 % CI: 1.01, 1.08)].

**Conclusions:** Air pollution exposure might be one important determinant for the incidence and dynamic progression of hypertension, diabetes, and CKD, suggesting that more attention should be paid to ambient air pollution control in the prevention of hypertension, diabetes, and CKD, as well as their progression.

**Keywords:** Air pollution; CKD; Diabetes; Hypertension; Multi-state model; Multimorbidity.

## Conflict of interest statement

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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ELSEVIER FULL-TEXT ARTICLE UNIMORE

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

# Encouraging adherence in adolescents with asthma using financial incentives: An RCT

Heather H De Keyser [1][2][3], John T Brinton [2], Samantha Bothwell [2], Megan Camacho [1], Allison Kempe [2][3], Stanley J Szefler [1][2][3]

Affiliations expand

# Abstract

**Background:** Medication adherence in adolescents remains a significant management challenge and innovative strategies are needed to improve medication adherence. Financial incentives have been used to improve outcomes for health behaviors among adults, but have not been well-studied among adolescents. The objective of this study was to test if a modest financial incentive improved medication adherence in adolescents with asthma compared with a control group.

**Methods:** Participants were randomized to either control (electronic medication monitoring [EMM] with App reminders/feedback for 4 months) or intervention (EMM + $1 per day for perfect medication adherence for 3 months [maximum $84] followed by 1 month of EMM only). A repeated measures mixed model, with a first order autoregressive correlation structure between errors, was used to test the null hypothesis for an interaction of treatment group and week.

**Results:** Fifty-two participants were enrolled, and 48 completed primary analysis. Mean adherence rates declined in both groups over time, and there was no significant difference in the change in adherence rates between the groups (F-statistic = 0.72, ndf = 15, ddf = 625, p = 0.76). Adherence rates (during the 12 weeks when incentives were given) declined from 80% to 64% in the control group, and from 90% to 58% in the incentive group. There was no significant change in the slope of decline in the incentives group in the month following payment discontinuation.

**Conclusion:** A modest financial incentive did not lead to significantly different medication adherence rates in adolescents with asthma who were receiving a monitoring and reminder intervention. Further study is needed to determine viable interventions to optimize medication use in this group.

**Keywords:** adherence; adolescent; asthma; motivation.

- 37 references

SUPPLEMENTARY INFO

Grant supportexpand

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# Association of selected inflammatory biomarkers with cough reflex sensitivity in asthmatic children

P Kunč [1], J Fábry, M Grendár, P Ferenc, T Strachan, K Ištvánková, T Hurtová, R Péčová

Affiliations expand

- PMID: 37449748

## Abstract

Bronchial asthma is the most common chronic respiratory disease of childhood. Cough is one of its defining symptoms. This study investigated the associations between selected inflammatory biomarkers and cough reflex sensitivity after capsaicin inhalation in children with mild and moderate well-controlled type 2 endotype asthma compared with non-asthmatic probands. Sensitivity to the cough reflex was measured by recording the cough response after capsaicin inhalation. The sandwich ELISA method was used to measure serum concentrations of the investigated potential inflammatory biomarkers (interleukin 13, interleukin 1beta, eosinophil-derived neurotoxin). The acquired data were statistically evaluated according to descriptive analyses for summarization and comparison between cough reflex sensitivity parameters and individual biomarker values in the observed and control groups modeled by a simple linear regression model. Statistical significance was defined as $p<0.05$. We showed a statistically significant association (p-value 0.03) between cough reflex sensitivity - C2 value (capsaicin concentration required for two cough responses) and interleukin 1beta serum concentrations in the asthma group compared with the control group of non-asthmatic children. Our results support the possibility of interleukin 1beta as a potential additive inflammatory biomarker used in clinical practice in children with asthma because of its correlation with the activity of the afferent nerve endings in the airways.

# Standardization of clinical outcomes used in allergen immunotherapy in allergic asthma: An EAACI position paper

Jasper Kappen [1] [2], Zuzana Diamant [3] [4] [5] [6], Ioana Agache [7], Matteo Bonini [2] [8] [9], Jean Bousquet [10], G Walter Canonica [11], Stephen R Durham [2] [12], George V Guibas [13] [14], Eckard Hamelmann [15], Marek Jutel [16] [17], Nikolaos G Papadopoulos [18], Graham Roberts [19] [20] [21], Mohamed H Shamji [2] [12], Petra Zieglmayer [22], Roy Gerth van Wijk [23], Oliver Pfaar [24]

Affiliations expand

- PMID: 37449468


- DOI: 10.1111/all.15817

## Abstract

**Introduction:** In allergic asthma patients, one of the more common phenotypes might benefit from allergen immunotherapy (AIT) as add-on intervention to pharmacological treatment. AIT is a treatment with disease-modifying modalities, the evidence for efficacy is based on controlled clinical trials following standardized endpoint measures. However, so far there is a lack of a consensus for asthma endpoints in AIT trials. The aim of a task force

(TF) of the European Academy of Allergy and Clinical Immunology (EAACI) is evaluating several outcome measures for AIT in allergic asthma.

**Methods:** The following domains of outcome measures in asthmatic patients have been evaluated for this position paper (PP): (i) exacerbation rate, (ii) lung function, (iii) ICS withdrawal, (iv) symptoms and rescue medication use, (v) questionnaires (PROMS), (vi) bronchial/nasal provocation, (vii) allergen exposure chambers (AEC) and (viii) biomarkers.

**Results:** Exacerbation rate can be used as a reliable objective primary outcome; however, there is limited evidence due to different definitions of exacerbation. The time after ICS withdrawal to first exacerbation is considered a primary outcome measure. Besides, the advantages and disadvantages and clinical implications of further domains of asthma endpoints in AIT trials are elaborated in this PP.

**Conclusion:** This EAACI-PP aims to highlight important aspects of current asthma measures by critically evaluating their applicability for controlled trials of AIT.

- 133 references

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# Decreasing Goal Oxygen Saturations in Bronchiolitis Is Associated With Decreased Length of Stay

Shivani Briggs [1], Vedant Gupta [2], Nehal Thakkar [2], Jamie Librizzi [2], Hamy Temkit [2], Richard Engel [2]

Affiliations expand

- PMID: 37449328


- DOI: 10.1542/hpeds.2022-007020

## Abstract

**Objectives:** For patients hospitalized with bronchiolitis, many hospitals have implemented clinical practice guidelines to decrease variability in care. Our hospital updated its bronchiolitis clinical pathway by lowering goal oxygen saturation from 90% to 88%. We compared clinical outcomes before and after this change within the context of the pathway update.

**Methods:** This was a retrospective analysis of patients <24 months old admitted to a pediatric tertiary care center from 2019 to 2021 with bronchiolitis. Patients with congenital heart disease, asthma, home oxygen, or admitted to an ICU were excluded. The data were stratified for patients admitted before and after the clinical pathway update. Statistical methods consisted of 2 group comparisons using the $\chi$-square test for categorical variables, the Wilcoxon rank-sum test for continuous variables, and multiple regression analysis.

**Results:** A total of 1386 patients were included, 779 preupdate and 607 postupdate. There was no statistically significant difference in the admission rate of patients presenting to the emergency department with bronchiolitis between the 2 groups (P value .60). The median time to room air was 40.0 hours preupdate versus 30.0 hours postupdate (P value < .001). The median length of stay was 48.0 hours preupdate versus 41.0 hours postupdate (P value < .001). Readmission rate was 2.7% within 7 days of discharge preupdate, and 2.1% postupdate (P value .51).

**Conclusions:** Decreasing goal oxygen saturation to 88% was associated with a statistically significant decrease in time spent on oxygen and length of stay for patients admitted with bronchiolitis with no increase in readmissions.

# Conflict of interest statement

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# Impact of benralizumab on asthma exacerbation–related medical healthcare resource utilization and medical costs: results from the ZEPHYR 2 study

Yen Chung [1], Diego J Maselli [2], Fan Mu [3], Erin E Cook [3], Danni Yang [3], Joshua A Young [3], Keith A Betts [4], Eduardo Genofre [1], Donna Carstens [1]

Affiliations expand

- PMID: 37441729

- DOI: 10.1080/13696998.2023.2236867

# Abstract

**Background and Aim:** Benralizumab is a biologic add-on treatment for severe eosinophilic asthma that can reduce the rate of asthma exacerbations, but data on the

associated medical utilization are scarce. This retrospective study evaluated the economic value of benralizumab by analyzing healthcare resource utilization (HRU) and medical costs in a large patient population in the US.**Methods:** Insurance claims data (11/2016-6/2020) were analyzed. A pre-post design was used to compare asthma exacerbation rates, medical HRU and medical costs in the 12 months pre vs. post index (day after benralizumab initiation). Patients were aged ≥12 years, with ≥2 records of benralizumab and ≥2 asthma exacerbations pre index, and constituted non-mutually exclusive cohorts: biologic-naïve, biologic-experienced (switched from omalizumab or mepolizumab to benralizumab), or with extended follow-up (18 or 24 months).**Results:** In all cohorts (mean age 51-53 years; 67%-70% female; biologic-naïve, N = 1,292; biologic-experienced, N = 349; 18-month follow-up, N = 419; 24-month follow-up, N = 156), benralizumab treatment reduced the rate of asthma exacerbation by 53%-68% (p < 0.001). In the biologic-naïve cohort, inpatient admissions decreased by 58%, emergency department visits by 54%, and outpatient visits by 58% post index (all p < 0.001), with similar reductions in exacerbation-related medical HRU in other cohorts. Exacerbation-related mean total medical costs decreased by 51% in the biologic-naïve cohort ($4691 pre-index, $2289 post-index), with cost differences ranging from 16% to 64% across other cohorts (prior omalizumab: $2686 to $1600; prior mepolizumab: $5990 to $5008; 18-month: $3636 to $1667; 24-month: $4014 to $1449; all p < 0.001). Medical HRU and cost reductions were durable, decreasing by 64% in year 1 and 66% in year 2 in the 24 month follow-up cohort.**Conclusion:** Patients treated with benralizumab with prior exacerbations experienced reductions in asthma exacerbations and exacerbation-related medical HRU and medical costs regardless of prior biologic use, with the benefits observed for up to 24 months after treatment initiation.

**Keywords:** Benralizumab; Biologic treatment; Healthcare resource utilization; I; I1; I10; I11; I19; Medical costs; Severe eosinophilic asthma; Value-based medicine.

# Plain language summary

Benralizumab is a biologic approved as an add-on treatment for severe eosinophilic asthma. Previous real-world studies and clinical trials have shown that benralizumab can reduce the rate of asthma exacerbations and systemic corticosteroid use. However, there is little information on the economic value of benralizumab in real-world patient populations. This study showed that patients with severe asthma in the United States had lower rates of asthma exacerbations after starting treatment with benralizumab. The patients also had fewer asthma exacerbation-related hospitalizations, emergency department visits, and outpatient visits as well as lower medical costs related to asthma exacerbations compared with before the treatment. These benefits were observed in patients who had never taken and those who had been previously treated with biologic therapies, and for up to 24 months after starting benralizumab treatment. These results show that the clinical value of benralizumab translates into reduced medical utilization for patients with severe asthma.

Proceed to details

Cite

# Poorly controlled asthma and psychological health in African American young adults: Why is phenotyping necessary? Suggestions from a multidisciplinary "Stress-Asthma Working Group"

Gennaro Liccardi [1], Matteo Martini [2][3], Maria Beatrice Bilò [2][3], Manlio Milanese [4], Ilaria Baiardini [5][6], Maria Vittoria Liccardi [7], Paola Rogliani [1][8]

Affiliations expand

- PMID: 37439793


- DOI: 10.1080/02770903.2023.2236704

*No abstract available*

**Keywords:** African American; anticholinergics; anxiety; asthma phenotype; bronchial asthma; increased cholinergic tone; long-acting muscarinic antagonists; poorly controlled asthma; severe asthma; stress; tiotropium; young adults.

Proceed to details

Cite

# Real-world outcomes of mepolizumab treatment in severe eosinophilic asthma patients – retrospective cohort study in Slovakia

Milos Jesenak [1][2][3], Vaclav Vanecek [4], Martina Ondrusova [5][6], Veronika Urdova [2][7], Katarina Dostalova [8], Ludek Hochmuth [7]

Affiliations expand

- PMID: 37439266


- DOI: 10.5507/bp.2023.029

## Abstract

**Aims:** Mepolizumab, a fully-humanized recombinant IgG1 kappa monoclonal antibody directed against IL-5, has shown improved asthma control and lung function in randomised controlled trials. The aim of this study was to evaluate real-world clinical experience in patients with severe eosinophilic asthma treated with mepolizumab in Slovakia.

**Methods:** A retrospective, non-interventional study based on medical records of all adult asthma patients initiating mepolizumab between November 1, 2017 and January 31, 2019, completing 12 months of treatment. At baseline, general and clinical profile data were recorded 12 months prior to treatment. Primary and secondary endpoints described the results of mepolizumab use at 2, 6, and 12 months after the initiation and compared to baseline. Statistical testing of individual change (in each patient) in selected parameters was performed.

**Results:** The cohort included 17 patients with particularly severe asthma at baseline, with frequent severe exacerbations (SE, median 5 [IQR 4-6]/patient/year), high blood eosinophil counts (median $0.6 \times 10^9$/L), frequent oral corticosteroid (OCS) dependence (82.35%), median dose 15 (IQR 7.5-20) mg/day, impaired lung function, and a spectrum of comorbidities. In a one-year follow-up, the data showed reductions in median SE (0 [IQR 0-1] patient/year, eosinophilia (median $0.175 \times 10^9$/L) and OCS maintenance dose (median 6.25 [IQR 2.5-20] mg/day), all statistically significant after 12 months on mepolizumab. Improved and stabilised lung functions throughout the cohort and a reduced incidence of nasal polyposis were observed.

**Conclusions:** The results provide clinical evidence of mepolizumab efficacy in a real sample of patients with severe asthma when administered in routine care settings in Slovakia.

**Keywords:** Slovakia; exacerbations; mepolizumab; real world evidence; severe eosinophilic asthma.

## Conflict of interest statement

The authors report no conflicts of interest in this work.
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# Development of theoretically informed audit and feedback: An exemplar from a complex implementation strategy to

# improve asthma self-management in UK primary care

Kirstie McClatchey [1], Aimee Sheldon [1], Liz Steed [2], Jessica Sheringham [3], Steve Holmes [4], Megan Preston [5], Francis Appiagyei [5 6], David Price [6 7], Stephanie J C Taylor [2], Hilary Pinnock [1]; IMP2ART Programme Group

Affiliations expand

## Abstract

**Rationale:** Audit and feedback is an evidence-based implementation strategy, but studies reporting the use of theory to guide design elements are limited.

**Aims and objectives:** Within the context of a programme of research aiming to improve the implementation of supported asthma self-management in UK primary care (IMPlementing IMProved Asthma self-management as RouTine [IMP$^2$ ART]), we aimed to design and develop theoretically-informed audit and feedback that highlighted supported asthma self-management provision and areas for improvement in primary care general practices.

**Method:** Aligned with the Medical Research Council (MRC) complex intervention framework, the audit and feedback was developed in three phases: (1) Development: literature and theory exploration, and prototype audit and feedback design; (2) Feasibility: eliciting feedback on the audit and feedback from general practice staff (n = 9); (3) Prepiloting: delivering the audit and feedback within the IMP$^2$ ART implementation strategy (incorporating patient and professional resources and an asthma review template) and eliciting clinician feedback (n = 9).

**Results:** Audit and feedback design was guided by and mapped to existing literature suggestions and theory (e.g., Theoretical Domains Framework, Behaviour Change Technique Taxonomy). Feedback on the prototype audit and feedback confirmed feasibility but identified some refinements (a need to highlight supporting self-management and importance of asthma action plans). Prepiloting informed integration with other IMP$^2$ ART programme strategies (e.g., patient resources and professional education).

**Conclusion:** We conclude that a multistage development process including theory exploration and mapping, contributed to the design and delivery of the audit and

feedback. Aligned with the MRC framework, the IMP$^2$ART strategy (incorporating the audit and feedback) is now being tested in a UK-wide cluster randomised controlled trial.

**Keywords:** asthma; audit and feedback; clinical audit; primary care; self-management.

- <u>32 references</u>

SUPPLEMENTARY INFO

Grant supportexpand

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# Natural killer cells in the lung: potential role in asthma and virus-induced exacerbation?

<u>Florian Lepretre</u>[1], <u>Delphine Gras</u>[1], <u>Pascal Chanez</u>[1][2], <u>Catherine Duez</u>[3]

Affiliations expand

- PMID: 37437915

# Abstract

Asthma is a chronic inflammatory airway disorder whose pathophysiological and immunological mechanisms are not completely understood. Asthma exacerbations are mostly driven by respiratory viral infections and characterised by worsening of symptoms. Despite current therapies, asthma exacerbations can still be life-threatening. Natural killer (NK) cells are innate lymphoid cells well known for their antiviral activity and are present in the lung as circulating and resident cells. However, their functions in asthma and its exacerbations are still unclear. In this review, we will address NK cell activation and functions, which are particularly relevant for asthma and virus-induced asthma exacerbations. Then, the role of NK cells in the lungs at homeostasis in healthy individuals will be described, as well as their functions during pulmonary viral infections, with an emphasis on those associated with asthma exacerbations. Finally, we will discuss the involvement of NK cells in asthma and virus-induced exacerbations and examine the effect of asthma treatments on NK cells.

# Conflict of interest statement

Conflict of interest: C. Duez reports grants from Société Française d'allergologie and Fondation du Souffle outside the submitted work. Conflict of interest: P. Chanez reports grants, consultancy fees, lecture fees, travel support and advisory board participation from ALK, Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Menarini, Novartis and Sanofi-Aventis, outside the submitted work. All other authors have nothing to disclose.

- 146 references
- 2 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Supplementary conceptsexpand

FULL TEXT LINKS

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# Sensitisation to House Dust Mite Component Der p 23 Is Associated with Severe Symptoms and Asthma in Allergic Rhinitis Patients

[Yunbo Gao](#) [1], [Jingyun Li](#) [1 2 3 4], [Xu Xu](#) [1 2 3 4], [Chengshuo Wang](#) [2 3], [Yuan Zhang](#) [1 2], [Luo Zhang](#) [1 2 3 4]

Affiliations expand

- PMID: 37437556


- DOI: [10.1159/000531244](#)

## Abstract

**Introduction:** House dust mite (HDM) is an important source of airborne allergens in China as it contains several allergenic components that can cause allergic rhinitis (AR) and other allergic diseases. This study aimed to determine the clinical characteristics and disease severity in AR patients sensitised to different allergenic HDM components.

**Methods:** This was a retrospective study, which examined 129 patients who were first diagnosed with only HDM-induced AR at the Department of Allergy of Beijing Tongren Hospital from December 2019 to April 2021. Clinical characteristics and disease severity of the patients were assessed based on the sensitisation to specific Dermatophagoides

pteronyssinus (Der p) and Dermatophagoides farinae (Der f) allergenic components, including Der p 1, Der p 2, Der p 23, Der f 1, and Der f 2, employing multiple correspondence analysis (MCA) with correspondence analysis chart of MCA.

**Results:** Among HDM-induced AR cases, the positive rate of Der p 1 was the highest (87.6%), followed by Der p 2 (78.3%), Der f 2 (76.64%), Der f 1 (68.2%), and Der p 23 (37.2%). Multiple correspondence analyses showed that sensitisation to Der p 23 was associated with severe AR symptoms and asthma; sensitisation to Der p 2, Der f 1, and Der f 2 was associated with moderate AR; and no sensitisation to Der p 23 was associated with mild AR.

**Conclusion:** Der p 23 sensitisation is prevalent in northern China and may be associated with severe symptoms and asthma in AR patients.

**Keywords:** Allergenic components; Allergic rhinitis; Der p 23; House dust mite.

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J Asthma

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. 2023 Jul 12;1-9.

doi: 10.1080/02770903.2023.2236696. Online ahead of print.

# Doxycycline may be more clinically effective in Type 2 chronic rhinosinusitis nasal polyp comorbid with asthma

[Gülden Paçaci Çetin](#) [1], [Bahar Arslan](#) [1], [İnsu Yilmaz](#) [1]

Affiliations expand

# Abstract

**Objective:** Chronic rhinosinusitis with nasal polyp (CRSwNP) is one of the major phenotypes of chronic rhinosinusitis (CRS) with a high symptom burden. Doxycycline can be used as add-on therapy in CRSwNP. We aimed to evaluate short-term efficacy of oral doxycycline on visual analog scale (VAS) and SNOT-22 (Sino-nasal outcome test) score for CRSwNP.

**Methods:** Visual analog score (VAS) for nasal symptoms and total SNOT-22 scores of 28 patients who applied with the diagnosis of CRSwNP and received 100 mg doxycycline for 21 days were analyzed in this retrospective cohort study. Doxycycline efficacy was also evaluated in subgroups determined according to asthma, presence of atopy, total IgE and eosinophil levels.

**Results:** After 21-day doxycycline treatment, there was a significant improvement in VAS score for post-nasal drip, nasal discharge, nasal congestion, and sneeze, and total SNOT-22 score ($p = 0.001$, $p < 0.001$, $p < 0.001$, $p < 0.001$, $p < 0.001$, respectively). No significant improvement was observed in VAS score for the loss of smell ($p = 0.18$). In the asthmatic subgroup, there were significant improvements in all VAS scores and total SNOT-22 score after doxycycline. In the non-asthmatic subgroup, there was no significant change in any of the VAS scores, but total SNOT-22 score was significantly improved (42 [21-78] vs. 18 [9-33]; $p = 0.043$). Improvement in VAS score for loss of smell is significant in only some subgroups like asthmatic patients, non-atopic patients, and patients with eosinophil >300 cell/µL.
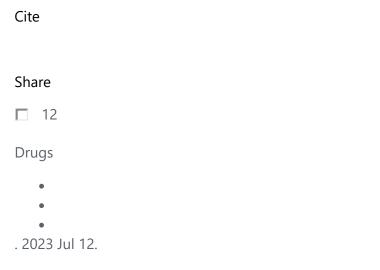
**Conclusions:** Doxycycline can be considered as an add-on treatment for symptom control in patients especially with CRSwNP comorbid with asthma.

**Keywords:** asthma; chronic rhinosinusitis; doxycycline; polyp; symptom score.

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# Omalizumab in Severe Asthma: Effect on Oral Corticosteroid Exposure and Remodeling. A Randomized Open-Label Parallel Study

Christian Domingo [# 1 2], Rosa M Mirapeix [# 3], Francisco-Javier González-Barcala [4 5 6 7], Carles Forné [8 9], Felip García [10]

Affiliations expand

- PMID: 37436680

- DOI: 10.1007/s40265-023-01905-5

## Abstract

**Introduction:** Data on the clinical efficacy and remodeling of omalizumab therapy in patients on oral corticosteroids (OC) are limited.

**Objective:** The purpose of the study is to show that in patients with corticosteroid-dependent asthma, omalizumab is a corticosteroid-sparing therapy able to inhibit airway remodeling and to reduce disease burden (lung function impairment, exacerbations).

**Methods:** This study is a randomised open-label study evaluating the addition of omalizumab to the standard of care in patients with severe asthma receiving oral corticosteroids. The primary endpoint was represented by the change in OC monthly dose

by the end of treatment and secondary endpoints included spirometry changes, airway inflammation (FeNO), number of exacerbations and airways remodelling assessed by bronchial biopsies studied by transmission electron microscopy. As a safety variable, adverse effects were recorded.

**Results:** Efficacy was assessed for 16 patients in the omalizumab group and 13 in the control group. The final cumulative mean monthly OC doses were 34.7 mg and 217 mg for the omalizumab and control group, respectively; the mean difference between groups adjusted for baseline was -148.1 [95% confidence interval (CI) -243.6, -52.5; p = 0.004]. OC withdrawal of 75% versus 7.7% (p = 0.001) was observed in the omalizumab and control group, respectively. Omalizumab provided a slowing of forced expiratory volume in one second ($FEV_1$) loss (70 mL versus 260 mL), a significant decrease in FeNO values and a reduction in the annual relative risk of clinically significant exacerbations of 54%. The treatment was well tolerated. The morphological study showed a significant decrease in basement membrane thickness in the omalizumab group (6.7 μm versus 4.6 μm) compared with controls (6.9 μm versus 7 μm) [mean difference between groups adjusted for baseline was -2.4 (95% CI -3.7, -1.2; p < 0.001], as well as a decrease in intercellular spaces (1.18 μm versus 0.62 μm and 1.21 μm versus 1.20 μm, p = 0.011, respectively). A qualitative improvement was also observed in the treated group.

**Conclusions:** Omalizumab showed a marked OC-sparing capacity and was associated with an improvement in clinical management that correlated with bronchial epithelial repair. In OC-dependent asthma, reversibility of remodelling is possible; the concepts that basement membrane enlargement is detrimental and that chronic airway obstruction is systematically irreversible are outdated (EudraCT: 2009-010914-31).

- [38 references]

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# Causal relationship between asthma-related diseases and the risk of COVID-19: A 2-sample mendelian randomization study

Shu Ran [1], XinHong Qiu [2], BaoLin Liu [3]

Affiliations expand

- PMID: 37436347


- DOI: 10.1016/j.jaci.2023.04.024

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Respirology

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

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

Affiliations expand

- PMID: 37434280


- DOI: 10.1111/resp.14553

## Abstract

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

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

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

**Conclusion:** Supranormal FEV$_1$ and/or FVC values occur in about 3% of the general population in different age bins and are associated with better health markers.

- 25 references

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# A systematic review of questionnaires measuring asthma control in children in a primary care population

Sara Bousema [1], Arthur M Bohnen [2], Patrick J E Bindels [2], Gijs Elshout [2]

## Abstract

Several questionnaires are used to measure asthma control in children. The most appropriate tool for use in primary care is not defined. In this systematic review, we evaluated questionnaires used to measure asthma control in children in primary care and determined their usefulness in asthma management. Searches were performed in the MEDLINE, Embase, Web of Science, Google Scholar and Cochrane databases with end date 24 June 2022. The study population comprised children aged 5-18 years with asthma. Three reviewers independently screened studies and extracted data. The methodological quality of the studies was assessed, using the COSMIN criteria for the measurement properties of health status questionnaires. Studies conducted in primary care were included if a minimum of two questionnaires were compared. Studies in secondary or tertiary care and studies of quality-of-life questionnaires were excluded. Heterogeneity precluded meta-analysis. Five publications were included: four observational studies and one sub-study of a randomized controlled trial. A total of 806 children were included (aged 5-18 years). We evaluated the Asthma Control Test (ACT), childhood Asthma Control Test (c-ACT), Asthma APGAR system, NAEPP criteria and Royal College of Physicians' '3 questions' (RCP3Q). These questionnaires assess different symptoms and domains. The quality of most of the studies was rated 'intermediate' or 'poor'. The majority of the evaluated questionnaires do not show substantial agreement with one another, which makes a comparison challenging. Based on the current review, we suggest that the Asthma APGAR system seems promising as a questionnaire for determining asthma control in children in primary care.

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## Conflict of interest statement

The authors declare no competing interests.

- 51 references

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Clinical Trial

# Non-randomised feasibility study testing a primary care intervention to promote engagement in an online health community for adults with troublesome asthma: protocol

Georgios Dimitrios Karampatakis [1], Helen E Wood [2], Chris J Griffiths [2], Stephanie J C Taylor [2], Veronica Toffolutti [2], Victoria J Bird [2], Nathan C Lea [3], Richard E Ashcroft [4], Bill Day [2], Neil S Coulson [5], Pietro Panzarasa [6], Xiancheng Li [6], Aziz Sheikh [7], Clare Relton [2], Nishanth Sastry [8], Jane S Watson [9], Viv Marsh [7], Jonathan Mant [10], Borislava Mihaylova [2], Neil Walker [2], Anna De Simoni [2]

Affiliations expand

# Abstract

**Introduction:** In the UK, approximately 4.3 million adults have asthma, with one-third experiencing poor asthma control, affecting their quality of life, and increasing their healthcare use. Interventions promoting emotional/behavioural self-management can improve asthma control and reduce comorbidities and mortality. Integration of online peer support into primary care services to foster self-management is a novel strategy. We aim to co-design and evaluate an intervention for primary care clinicians to promote engagement with an asthma online health community (OHC). Our protocol describes a 'survey leading to a trial' design as part of a mixed-methods, non-randomised feasibility study to test the feasibility and acceptability of the intervention.

**Methods and analysis:** Adults on the asthma registers of six London general practices (~3000 patients) will be invited to an online survey, via text messages. The survey will collect data on attitudes towards seeking online peer support, asthma control, anxiety, depression, quality of life, information on the network of people providing support with asthma and demographics. Regression analyses of the survey data will identify correlates/predictors of attitudes/receptiveness towards online peer support. Patients with troublesome asthma, who (in the survey) expressed interest in online peer support, will be invited to receive the intervention, aiming to reach a recruitment target of 50 patients. Intervention will involve a one-off, face-to-face consultation with a practice clinician to introduce online peer support, sign patients up to an established asthma OHC, and encourage OHC engagement. Outcome measures will be collected at baseline and 3 months post intervention and analysed with primary care and OHC engagement data. Recruitment, intervention uptake, retention, collection of outcomes, and OHC engagement will be assessed. Interviews with clinicians and patients will explore experiences of the intervention.

**Ethics and dissemination:** Ethical approval was obtained from a National Health Service Research Ethics Committee (reference: 22/NE/0182). Written consent will be obtained before intervention receipt and interview participation. Findings will be shared via dissemination to general practices, conference presentations and peer-reviewed publications.

**Trial registration number:** [NCT05829265](#).

## Conflict of interest statement

Competing interests: None declared.

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# Towards regional progress: APSR 2022 Big Five Lung Diseases Workshop

Paul N Reynolds[1], Sameera Ansari[2][3], Rosalyn Hernandez-Sebastian[4], Watchara Boonsawat[5], Shih-Yu Chen[6], Landy Lan[7][8], Dawei Yang[8], G M Monsur Habib[9], Jennifer Ann Mendoza-Wi[10], Hung-Ling Huang[11][12][13], Le Thi Tuyet Lan[14], Nguyen Nhu Vinh[14], Maria Lowella F De Leon[15], Anne B Chang[16][17]

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- PMID: 37433568

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# Is there a Best Strategy to Prevent Asthma Exacerbations in Inner City Asthmatics?

[Sandra E Zaeh](#) [1], [Geoffrey Chupp](#) [2], [Michelle N Eakin](#) [3]

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Allergy

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# Dupilumab sustains efficacy in patients with moderate-to-severe type 2 asthma regardless of ICS dose

Ian D Pavord [1], Arnaud Bourdin [2], Alberto Papi [3], Christian Domingo [4], Jonathan Corren [5], Arman Altincatal [6], Amr Radwan [7], Nami Pandit-Abid [8], Juby A Jacob-Nara [8], Yamo Deniz [7], Paul J Rowe [8], Elizabeth Laws [8], David J Lederer [7], Megan Hardin [6]

Affiliations expand

- PMID: 37431558

- DOI: 10.1111/all.15792

## Abstract

**Background:** Dupilumab, a human monoclonal antibody, blocks the shared receptor component for interleukins-4/13, key and central drivers of type 2 inflammation. The TRAVERSE (NCT02134028) open-label extension study demonstrated the long-term safety

and efficacy of dupilumab in patients ≥12 years who completed a previous dupilumab asthma study. The safety profile was consistent with that observed in the parent studies. Here, we assess whether dupilumab sustains long-term efficacy in patients regardless of inhaled corticosteroid (ICS) dose at parent study baseline (PSBL).

**Methods:** Patients from phase 2b (NCT01854047) or phase 3 (QUEST; NCT02414854) studies receiving high- or medium-dose ICS at PSBL and enrolled in TRAVERSE were included. We analyzed unadjusted annualized severe exacerbation rates, change from PSBL in pre-bronchodilator (BD) forced expiratory volume in 1 second ($FEV_1$), 5-item asthma control questionnaire, and type 2 biomarkers in patients with type 2 asthma at baseline (blood eosinophils ≥150 cells/μL or fractional exhaled nitric oxide [FeNO] ≥25 ppb), and subgroups defined by baseline blood eosinophils or FeNO.

**Results:** Of patients with type 2 asthma (n = 1666), 891 (53.5%) were receiving high-dose ICS at PSBL. In this subgroup, unadjusted exacerbation rates for dupilumab versus placebo were 0.517 versus 1.883 (phase 2b) and 0.571 versus 1.300 (QUEST) over the parent study (52 weeks) and remained low throughout TRAVERSE (0.313-0.494). Improvements in pre-BD $FEV_1$ were sustained throughout TRAVERSE. Similar clinical efficacy was observed among patients receiving medium-dose ICS at PSBL and biomarker subgroups.

**Conclusions:** Dupilumab showed sustained efficacy for up to 3 years in patients with uncontrolled, moderate-to-severe type 2 asthma on high- or medium-dose ICS.

**Keywords:** asthma control; exacerbations; inhaled corticosteroids; moderate-to-severe asthma; pre-bronchodilator FEV1.

- 32 references

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# Association between asthma and headache: Findings from the NHANES 2001–2004

Hok Leong Chin[1], Ka Kin Cheong[2]

Affiliations expand

- PMID: 37431155

- DOI: 10.1111/crj.13664

## Abstract

**Introduction:** With the adjustment of sociodemographic factors, our study aimed to explore the association between asthma control and headache using a representative sample in the United States.

**Methods:** A total of participants aged >20 years from the National Health and Nutrition Examination Survey (NHANES) cycles 2001-2004 were included. The presence of asthma and headache was determined by questionnaires. Multivariate logistic regression was performed.

**Results:** Participants with asthma had higher odds of suffering headaches (odds ratio = 1.62, 95% confidence interval: 1.30-2.02, $p < 0.001$). Those who had an asthma attack in the past year had higher odds of experiencing headaches than those who did not (odds ratio = 1.94, 95% confidence interval: 1.11-3.39, $p = 0.022$). No statistically significant association was found between participants who had emergency care visit for asthma in the past year and those who had not.

**Conclusion:** Patients with asthma attack in the past year were more likely to have a headache than those who without.

- 18 references

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Randomized Controlled Trial

# Airway and systemic biomarkers of health effects after short-term exposure to indoor ultrafine particles from cooking and candles - A randomized controlled double-blind crossover study among mild asthmatic subjects

Karin Rosenkilde Laursen [1], Nichlas Vous Christensen [2][3], Frans Aa Mulder [2][3], Jörg Schullehner [1][4], Hans Jürgen Hoffmann [5], Annie Jensen [6], Peter Møller [6], Steffen Loft [6], Anna-Carin

Olin [7], Berit B Rasmussen [3], Bernadette Rosati [3] [8], Bo Strandberg [9], Marianne Glasius [3], Merete Bilde [3], Torben Sigsgaard [10]; Climate Chamber Group

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## Abstract

**Background:** There is insufficient knowledge about the systemic health effects of exposure to fine ($PM_{2.5}$) and ultrafine particles emitted from typical indoor sources, including cooking and candlelight burning. We examined whether short-term exposure to emissions from cooking and burning candles cause inflammatory changes in young individuals with mild asthma. Thirty-six non-smoking asthmatics participated in a randomized controlled double-blind crossover study attending three exposure sessions (mean $PM_{2.5}$ µg/m$^3$; polycyclic aromatic hydrocarbons ng/m$^3$): (a) air mixed with emissions from cooking (96.1; 1.1), (b) air mixed with emissions from candles (89.8; 10), and (c) clean filtered air (5.8; 1.0). Emissions were generated in an adjacent chamber and let into a full-scale exposure chamber where participants were exposed for five hours. Several biomarkers were assessed in relation to airway and systemic inflammatory changes; the primary outcomes of interest were surfactant Protein-A (SP-A) and albumin in droplets in exhaled air - novel biomarkers for changes in the surfactant composition of small airways. Secondary outcomes included cytokines in nasal lavage, cytokines, C-reactive protein (CRP), epithelial progenitor cells (EPCs), genotoxicity, gene expression related to DNA-repair, oxidative stress, and inflammation, as well as metabolites in blood. Samples were collected before exposure start, right after exposure and the next morning.

**Results:** SP-A in droplets in exhaled air showed stable concentrations following candle exposure, while concentrations decreased following cooking and clean air exposure. Albumin in droplets in exhaled air increased following exposure to cooking and candles compared to clean air exposure, although not significant. Oxidatively damaged DNA and concentrations of some lipids and lipoproteins in the blood increased significantly following exposure to cooking. We found no or weak associations between cooking and candle exposure and systemic inflammation biomarkers including cytokines, CRP, and EPCs.

**Conclusions:** Cooking and candle emissions induced effects on some of the examined health-related biomarkers, while no effect was observed in others; Oxidatively damaged DNA and concentrations of lipids and lipoproteins were increased in blood after exposure to cooking, while both cooking and candle emissions slightly affected the small airways including the primary outcomes SP-A and albumin. We found only weak associations between the exposures and systemic inflammatory biomarkers. Together, the results show the existence of mild inflammation following cooking and candle exposure.

**Keywords:** Biomarkers; Candles; Cooking; Human exposure; Indoor air; Inflammation; Metabolomics; Oxidatively damaged DNA; SP-A; Ultrafine particles.

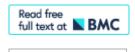# Conflict of interest statement

The authors declare no competing interests.

- 99 references
- 4 figures

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# Discharge criteria for inpatient paediatric asthma: a narrative systematic review

Aryanto Sudarmana [1], Joanna Lawrence [2][3][4], Neda So [5], Katherine Chen [5][3][4]

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- PMID: 37429700

## Abstract

**Introduction:** Criteria-led discharges (CLDs) and inpatient care pathways (ICPs) aim to standardise care and improve efficiency by allowing patients to be discharged on fulfilment of discharge criteria. This narrative systematic review aims to summarise the evidence for use of CLDs and discharge criteria in ICPs for paediatric inpatients with asthma, and summarise the evidence for each discharge criterion used.

**Methods:** Database search using keywords was performed using Medline, Embase and PubMed for studies published until 9 June 2022. Inclusion criteria included: paediatric patients <18 years old, admitted to hospital with asthma or wheeze and use of CLD, nurse-led discharge or ICP. Reviewers screened studies, extracted data and assessed study quality using the Quality Assessment with Diverse Studies tool. Results were tabulated. Meta-analysis was not performed due to heterogeneity of study designs and outcomes.

**Results:** Database search identified 2478 studies. 17 studies met the inclusion criteria. Common discharge criteria include bronchodilator frequency, oxygen saturation and respiratory assessment. Discharge criteria definitions varied between studies. Most definitions were associated with improvements in length of stay (LOS) without increasing re-presentation or readmission.

**Conclusion:** CLDs and ICPs in the care of paediatric inpatients with asthma are associated with improvements in LOS without increasing re-presentations or readmissions. Discharge criteria lack consensus and evidence base. Common criteria include bronchodilator frequency, oxygen saturations and respiratory assessment. This study was limited by a paucity of high-quality studies and exclusion of studies not published in English. Further research is necessary to identify optimal definitions for each discharge criterion.

## Conflict of interest statement

Competing interests: None declared.

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# Effect of bronchial thermoplasty on static and dynamic lung compliance and resistance in patients with severe persistent asthma

Ahmet Baydur [1], Richard Barbers [2], Darren May [2]

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- PMID: 37429559

# Abstract

**Rationale:** Bronchial thermoplasty (BT) reduces severity and frequency of bronchoconstriction and symptoms in severe, persistent asthmatics although it is usually not associated with change in spirometric variables. Other than spirometry. there are almost no data on changes in lung mechanics following BT.

**Objective:** To assess lung static (JAnau) and dynamic lung compliance (Cst,L and Cdyn,L, respectively) and static and dynamic lung resistance (Rst,L and Rdyn,L, respectively) before and after BT in severe asthmatics using the esophageal balloon technique.

**Methods:** Rdyn,L and Cdyn,L were measured at respiratory frequencies up to 145 breaths/min, using the esophageal balloon technique in 7 patients immediately before and 12-50 weeks after completing a series of 3 BT sessions.

**Results:** All patients experienced improved symptoms within a few weeks following completion of BT. Pre-BT, all patients exhibited frequency dependency of lung compliance, with mean Cdyn,L decreasing to 63% of Cst,L at maximum respiratory rates. Post-BT, Cst,L did not change significantly from pre-thermoplasty values, while Cdyn,L diminished to 62%% of Cst,L. In 4 of 7 patients, post-BT values of Cdyn,L were consistently higher than pre-BT over the range of respiratory rates. $R_L$ in 4 of 7 patients during quiet breathing and at higher respiratory frequencies decreased following BT.

**Conclusions:** Patients with severe persistent asthma exhibit increased resting lung resistance and frequency dependence of compliance, the magnitudes of which are ameliorated in some patients following bronchial thermoplasty and associated with variable change in frequency dependence of lung resistance. These findings are related to asthma severity and may be related to the heterogeneous and variable nature of airway smooth muscle modeling and its response to BT.

**Keywords:** Airway smooth muscle remodeling; Asthma; Bronchial thermoplasty; Esophageal balloon technique; Frequency dependence of compliance and resistance; Regional lung inhomogeneities.

# Conflict of interest statement

Declaration of competing interest None

FULL TEXT LINKS

# A case of biologic use in acute asthma exacerbation refractory to conventional management

Bo-Guen Kim [1], Dong Won Park [1], Tai Sun Park [1], Ji-Yong Moon [1], Tae-Hyung Kim [1], Sang-Heon Kim [1], Jang Won Sohn [1], Ho Joo Yoon [1], Hyun Lee [2]

Affiliations expand

- PMID: 37429420


- DOI: 10.1016/j.jaip.2023.06.064

*No abstract available*

# EMS Administration of Systemic Corticosteroids to Pediatric Asthma Patients: An Analysis by Severity and Transport Interval

Lauren Riney [1], Sam Palmer [2], Erik Finlay [2], Andrew Bertrand [3], Shannon Burcham [4], Phyllis Hendry [3], Manish Shah [5], Kathryn Kothari [5], David Ashby [5], Daniel Ostermayer [6], Olga Semenova [1], Benjamin N Abo [7][8][9], Benjamin Abes [7], Nichole Shimko [10], Emily Myers [9], Marshall Frank [8][9], Tim Turner [11], Mac Kemp [12], Kim Landry [12], Greg Roland [13], Jennifer Fishe [1]

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- PMID: 37428954
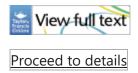

- DOI: 10.1080/10903127.2023.2234996

## Abstract

**Introduction:** Pediatric asthma exacerbations are a common cause of emergency medical services (EMS) encounters. Bronchodilators and systemic corticosteroids are mainstays of asthma exacerbation therapy, yet data on the efficacy of EMS administration of systemic corticosteroids are mixed. This study's objective was to assess the association between EMS administration of systemic corticosteroids to pediatric asthma patients on hospital admission rates based on asthma exacerbation severity and EMS transport intervals.**Methods:** This is a sub-analysis of the Early Administration of Steroids in the Ambulance Setting: An Observational Design Trial (EASI AS ODT). EASI AS ODT is a non-randomized, stepped wedge, observational study examining outcomes one year before and one year after seven EMS agencies incorporated an oral systemic corticosteroid option into their protocols for the treatment of pediatric asthma exacerbations. We included EMS encounters for patients ages 2 - 18 years confirmed by manual chart review to have asthma exacerbations. We compared hospital admission rates across asthma exacerbation

severities and EMS transport intervals using univariate analyses. We geocoded patients and created maps to visualize the general trends of patient characteristics.**Results:** A total of 841 pediatric asthma patients met inclusion criteria. While most patients were administered inhaled bronchodilators by EMS (82.3%), only 21% received systemic corticosteroids, and only 19% received both inhaled bronchodilators and systemic corticosteroids. Overall, there was no significant difference in hospitalization rates between patients who did and did not receive systemic corticosteroids from EMS (33% vs. 32%, p = 0.78). However, although not statistically significant, for patients who received systemic corticosteroids from EMS, there was an 11% decrease in hospitalizations for mild exacerbation patients and a 16% decrease in hospitalizations for patients with EMS transport intervals greater than 40 minutes.**Conclusion:** In this study, systemic corticosteroids were not associated with a decrease in hospitalizations of pediatric patients with asthma overall. However, while limited by small sample size and lack of statistical significance, our results suggest there may be a benefit in certain subgroups, particularly patients with mild exacerbations and those with transport intervals longer than 40 minutes. Given the heterogeneity of EMS agencies, EMS agencies should consider local operational and pediatric patient characteristics when developing standard operating protocols for pediatric asthma.

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# Omalizumab rescue therapy in refractory status asthmaticus

Sanjana Chetana Shanmukhappa [1], Arun Kumar [2], Akash Dey [2], Janani J V S [2], Srivatsa Lokeshwaran [3], Sunil Kumar K [3], Prakash Doraiswamy [4], Shashank M R [4], Lakshmi Gayathri [2]

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## Abstract

**Introduction:** Refractory status asthmaticus (RSA) is a severe, life-threatening form of asthma exacerbation that persists despite aggressive treatment with systemic corticosteroids, bronchodilators, and other supportive measures. Omalizumab, a monoclonal antibody that targets IgE, has been approved for treating severe allergic asthma and is effective in reducing the frequency of exacerbations and improving asthma control. Limited evidence exists regarding the use of Omalizumab in RSA, but some studies have suggested that it may have a role in its management.

**Case:** A 39-year-old male with a decade-long history of asthma presented to the emergency department intubated and unresponsive to pharmacological therapy. The patient's IgE levels were elevated, and Omalizumab was administered after a comprehensive evaluation. The patient made a dramatic recovery and was successfully weaned off the ventilator within 24 h of receiving Omalizumab. He made an uneventful recovery and was discharged home on Omalizumab once every two weeks with regular follow-ups.

**Discussion and conclusion:** Per our literature search, only 3 cases have been reported where Omalizumab was administered to patients with RSA to wean them off ventilatory support successfully. This case study adds to the existing data on the potential benefits of Omalizumab in managing RSA. It suggests it may be a valuable treatment option for patients who do not respond to standard therapy. However, further research is needed to determine the efficacy and safety of Omalizumab in this population.

**Keywords:** Omalizumab; RSA; Refractory status asthmaticus; allergic asthma.

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# Could we co-opt the cannabinoid system for asthma therapy?

Oscar Palomares [1]

Affiliations expand

- PMID: 37420178

- DOI: 10.1080/1744666X.2023.2235082

*No abstract available*

**Keywords:** Asthma; cannabinoid receptors; cannabinoids; immunomodulation; therapeutic agents.

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

Katja Warm [1], Linnea Hedman [2], Caroline Stridsman [1], Anne Lindberg [1], Eva Rönmark [2], Helena Backman [2]

Affiliations expand

- PMID: 37405375

- DOI: 10.1080/02770903.2023.2231078

## Abstract

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

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

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

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

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

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# Asthma disparities among U.S. children and adults

Cynthia A Pate [1], Xiaoting Qin [1], Carol Johnson [1], Hatice S Zahran [1]

Affiliations expand

## Abstract

**Objective:** To assess factors that are associated with asthma prevalence and asthma attacks among children (0-17 years) and adults (18 years and over) in the United States of America.

**Methods:** The 2019-2021 National Health Interview Survey data were analyzed using multivariable logistic regression models to determine associations between health outcomes (i.e. current asthma and asthma attacks) and demographic and socioeconomic factors. Each health outcome was regressed over each characteristic variable, adjusting for age, sex, and race/ethnicity for adults and sex and race/ethnicity for children.

**Results:** Asthma was more common among children who were male, blacks, parental education less than bachelor's, or had public health insurance, and among adults who had less than a bachelor's degree, do not own a home, or not in the workforce. Persons in families facing difficulty paying medical bills were more likely to have current asthma (children: aPR = 1.62[1.40-1.88]; adults: aPR = 1.67[1.55-1.81]) and asthma attacks (children: aPR = 1.34[1.15-1.56]; adults: aPR = 1.31[1.20-1.43]). Persons with family income <100% federal poverty threshold (FPT) (children: aPR = 1.39[1.17-1.64]; adults: aPR = 1.64[1.50-1.80]) or adults 100-199% FPT (aPR = 1.28[1.19-1.39]) were more likely to have current asthma. Children and adults with family income <100% FPT and adults 100-199% FPT were also more likely to have asthma attacks. Having asthma attacks was common among adults not in the workforce as well (aPR = 1.17[1.07-1.27]).

**Conclusions:** Asthma affects certain groups disproportionately. The findings of this paper suggesting asthma disparities continue to persist may increase public health programs awareness to better deliver effective and evidence-based interventions.

**Keywords:** Survey research; disparities; health outcomes; prevention; respiratory diseases; socioeconomic factors.

Editorial

# Finding the Right Biological: Eosinophil Subset Differences in Asthma and Chronic Obstructive Pulmonary Disease

Christine M Freeman [1][2][3], Jeffrey L Curtis [1][2][4], Annette T Hastie [5]

Affiliations expand

- PMID: 37311240


- DOI: 10.1164/rccm.202305-0811ED

*No abstract available*

# Comment on

- [Eosinophil Subtypes in Adults with Asthma and Adults with Chronic Obstructive Pulmonary Disease.](#)
  Cabrera López C, Sánchez Santos A, Lemes Castellano A, Cazorla Rivero S, Breña Atienza J, González Dávila E, Celli B, Casanova Macario C.Am J Respir Crit Care Med. 2023 Jul 15;208(2):155-162. doi: 10.1164/rccm.202301-0149OC.PMID: 37071848

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

[Brian Lipworth](#)[1], [Rory Chan](#)[1]

Affiliations expand

- PMID: 37279364

*No abstract available*

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# Oral Microbiota and Pediatric Asthma Phenotype: A New Window for Biomarkers?

Elodie Ghedin [1], Yvonne J Huang [2]

Affiliations expand

- PMID: 37276885

*No abstract available*

# Comment on

- [Oropharyngeal Microbiota Clusters in Children with Asthma or Wheeze Associate with Allergy, Blood Transcriptomic Immune Pathways, and Exacerbation Risk.](#)
Abdel-Aziz MI, Thorsen J, Hashimoto S, Vijverberg SJH, Neerincx AH, Brinkman P, van Aalderen W, Stokholm J, Rasmussen MA, Roggenbuck-Wedemeyer M, Vissing NH, Mortensen MS, Brejnrod AD, Fleming LJ, Murray CS, Fowler SJ, Frey U, Bush A, Singer F, Hedlin G, Nordlund B, Shaw DE, Chung KF, Adcock IM, Djukanovic R, Auffray C, Bansal AT, Sousa AR, Wagers SS, Chawes BL, Bønnelykke K, Sørensen SJ, Kraneveld AD, Sterk PJ, Roberts G, Bisgaard H, Maitland-van der Zee AH; U-BIOPRED Study Group.Am J Respir Crit Care Med. 2023 Jul 15;208(2):142-154. doi: 10.1164/rccm.202211-2107OC.PMID: 37163754

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# Longitudinal Asthma Phenotypes from Childhood to Middle-Age: A Population-based Cohort Study

Daniel J Tan [1], Caroline J Lodge [1], E Haydn Walters [1][2], Adrian J Lowe [1], Dinh S Bui [1], Gayan Bowatte [1][3], Jonathan Pham [1][4], Bircan Erbas [5], Jennie Hui [6], Garun S Hamilton [7][8], Paul S Thomas [9], Mark Hew [3][10], George Washko [11], Richard Wood-Baker [2], Michael J Abramson [9], Jennifer L Perret [1][12], Shyamali C Dharmage [1]

Affiliations expand

# Abstract

**Rationale:** Asthma is a heterogeneous condition, and longitudinal phenotyping may provide new insights into the origins and outcomes of the disease. **Objectives:** We aimed to characterize the longitudinal phenotypes of asthma between the first and sixth decades of life in a population-based cohort study. **Methods:** Respiratory questionnaires were collected at seven time points in the TAHS (Tasmanian Longitudinal Health Study) when participants were aged 7, 13, 18, 32, 43, 50, and 53 years. Current-asthma and ever-asthma status was determined at each time point, and group-based trajectory modeling was used to characterize distinct longitudinal phenotypes. Linear and logistic regression models were fitted to investigate associations of the longitudinal phenotypes with childhood factors and adult outcomes. **Measurements and Main Results:** Of 8,583 original participants, 1,506 had reported ever asthma. Five longitudinal asthma phenotypes were identified: early-onset adolescent-remitting (40%), early-onset adult-remitting (11%), early-onset persistent (9%), late-onset remitting (13%), and late-onset persistent (27%). All phenotypes were associated with chronic obstructive pulmonary disease at age 53 years, except for late-onset remitting asthma (odds ratios: early-onset adolescent-remitting, 2.00 [95% confidence interval (CI), 1.13-3.56]; early-onset adult-remitting, 3.61 [95% CI, 1.30-10.02]; early-onset persistent, 8.73 [95% CI, 4.10-18.55]; and late-onset persistent, 6.69 [95% CI, 3.81-11.73]). Late-onset persistent asthma was associated with the greatest comorbidity at age 53 years, with increased risk of mental health disorders and cardiovascular risk factors. **Conclusions:** Five longitudinal asthma phenotypes were identified between the first and sixth decades of life, including two novel remitting phenotypes. We found differential effects of these phenotypes on risk of chronic obstructive pulmonary disease and nonrespiratory comorbidities in middle age.

**Keywords:** asthma phenotypes; chronic obstructive pulmonary disease; comorbidities; longitudinal phenotypes; trajectories.

# Comment in

- Lung Function as a Biomarker of Health: An Old Concept Rediscovered.

SUPPLEMENTARY INFO

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# Oropharyngeal Microbiota Clusters in Children with Asthma or Wheeze Associate with Allergy, Blood Transcriptomic Immune Pathways, and Exacerbation Risk

Mahmoud I Abdel-Aziz [1][2][3][4], Jonathan Thorsen [5][6], Simone Hashimoto [1][7][2][3], Susanne J H Vijverberg [1][2][3], Anne H Neerincx [1][2][3], Paul Brinkman [1][2][3], Wim van Aalderen [7], Jakob Stokholm [5][8], Morten Arendt Rasmussen [5][8], Michael Roggenbuck-Wedemeyer [9][10], Nadja H Vissing [5], Martin Steen Mortensen [9], Asker Daniel Brejnrod [11], Louise J Fleming [12][13], Clare S Murray [14][15], Stephen J Fowler [14][15], Urs Frey [16], Andrew Bush [12][13], Florian Singer [17][18], Gunilla Hedlin [19][20], Björn Nordlund [19][20], Dominick E Shaw [21], Kian Fan Chung [12][13], Ian M Adcock [12][13], Ratko Djukanovic [22], Charles Auffray [23], Aruna T Bansal [24], Ana R Sousa [25], Scott S Wagers [26], Bo Lund

Chawes [6], Klaus Bønnelykke [6], Søren Johannes Sørensen [9], Aletta D Kraneveld [27], Peter J Sterk [1 2], Graham Roberts [22], Hans Bisgaard [5], Anke H Maitland-van der Zee [1 7 23]; U-BIOPRED Study Group

Collaborators, Affiliations expand

# Abstract

**Rationale:** Children with preschool wheezing or school-age asthma are reported to have airway microbial imbalances. **Objectives:** To identify clusters in children with asthma or wheezing using oropharyngeal microbiota profiles. **Methods:** Oropharyngeal swabs from the U-BIOPRED (Unbiased Biomarkers for the Prediction of Respiratory Disease Outcomes) pediatric asthma or wheezing cohort were characterized using 16S ribosomal RNA gene sequencing, and unsupervised hierarchical clustering was performed on the Bray-Curtis $\beta$-diversity. Enrichment scores of the Molecular Signatures Database hallmark gene sets were computed from the blood transcriptome using gene set variation analysis. Children with severe asthma or severe wheezing were followed up for 12-18 months, with assessment of the frequency of exacerbations. **Measurements and Main Results:** Oropharyngeal samples from 241 children (age range, 1-17 years; 40% female) revealed four taxa-driven clusters dominated by *Streptococcus*, *Veillonella*, *Rothia*, and *Haemophilus*. The clusters showed significant differences in atopic dermatitis, grass pollen sensitization, $FEV_1\%$ predicted after salbutamol, and annual asthma exacerbation frequency during follow-up. The *Veillonella* cluster was the most allergic and included the highest percentage of children with two or more exacerbations per year during follow-up. The oropharyngeal clusters were different in the enrichment scores of TGF-$\beta$ (transforming growth factor-$\beta$) (highest in the *Veillonella* cluster) and Wnt/$\beta$-catenin signaling (highest in the *Haemophilus* cluster) transcriptomic pathways in blood (all $q$ values <0.05). **Conclusions:** Analysis of the oropharyngeal microbiota of children with asthma or wheezing identified four clusters with distinct clinical characteristics (phenotypes) that associate with risk for exacerbation and transcriptomic pathways involved in airway remodeling. This suggests that further exploration of the oropharyngeal microbiota may lead to novel pathophysiologic insights and potentially new treatment approaches.

**Keywords:** asthma; microbiota; phenotype; precision medicine; wheezing.

# Comment in

- Oral Microbiota and Pediatric Asthma Phenotype: A New Window for Biomarkers?

Ghedin E, Huang YJ.Am J Respir Crit Care Med. 2023 Jul 15;208(2):119-121. doi: 10.1164/rccm.202305-0856ED.PMID: 37276885 No abstract available.

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# The associations between personality traits and mental health in people with and without asthma

Weixi Kang [1]

Affiliations expand

- PMID: 37075823

**Free article**

# Abstract

**Objective:** The aim of the current study is to investigate the associations between personality traits and mental health in people with asthma and compare it with people without asthma.

**Methods:** Data came from UKHLS with 3929 patients with asthma with a mean age of 49.19 (S.D. = 15.23) years old (40.09 % males) and 22,889 healthy controls (42.90 % males) with a mean age of 45.60 (S.D. = 17.23) years old. First, the current study investigated the difference in Big Five personality traits and mental health between people with and without asthma using a predictive normative modeling approach with one-sample t-tests. Second, a hierarchical regression accompanied by two multiple regressions was used to determine how personality traits may relate to people with and without asthma differently.

**Results:** The current study found asthma patients have significantly higher Neuroticism, higher Openness, lower Conscientiousness, higher Extraversion, and worse mental health. Asthma status significantly moderated the association between Neuroticism and mental health with this relationship being stronger in people with asthma. Moreover, Neuroticism was positively related to worse mental health and Conscientiousness and Extraversion were negatively associated with worse mental health in people with and without asthma. However, Openness was negatively associated with worse mental health in people without asthma but not in people with asthma.

**Limitations:** The limitations of the current study include cross-sectional designs, self-reported measured, and limited generalizability to other countries.

**Conclusion:** Clinicians and health professionals should use findings from the current study to come up with prevention and interaction programs that promote mental health based on personality traits in asthma patients.

**Keywords:** Asthma; Big Five; GHQ-12; Mental health; Neuroticism; Personality.

# Conflict of interest statement

Conflict of interest The author declares that there are no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

# Eosinophil Subtypes in Adults with Asthma and Adults with Chronic Obstructive Pulmonary Disease

Carlos Cabrera López [1], Alejandra Sánchez Santos [2], Angelina Lemes Castellano [3], Sara Cazorla Rivero [2][4], Joaquín Breña Atienza [5], Enrique González Dávila [6], Bartolomé Celli [7], Ciro Casanova Macario [8]

Affiliations expand

- PMID: 37071848

- DOI: [10.1164/rccm.202301-0149OC](10.1164/rccm.202301-0149OC)

## Abstract

**Rationale:** There is a differential response to eosinophilic modulation between patients with asthma and those with chronic obstructive pulmonary disease (COPD). There is also evidence of different subtypes of eosinophils in murine models. However, no study has compared eosinophil subtypes in individuals with COPD and in those with asthma. **Objectives:** Study the differences in eosinophils subtypes based in the surface protein expression in COPD patients and asthmatic patients. **Methods:** We studied 10 stable subjects in each of four groups: subjects with COPD, subjects with asthma, smokers

without COPD, and healthy volunteers. Subjects with COPD and those with asthma were matched by age, sex, and $FEV_1$% predicted. The following variables were determined: anthropometrics, smoking, exacerbation history, medication use, lung function, and comorbidities. Using flow cytometry and confocal microscopy from blood samples, we determined differences in eosinophil surface proteins and classified them as *1*) resident eosinophils (Siglec-8+CD62L+IL-3R$^{lo}$) or *2*) inflammatory eosinophils (iEos; Siglec-8+CD62L$^{lo}$IL-3R$^{hi}$). IL-5 receptor was also determined. Findings were validated in 59 patients with COPD and in 17 patients with asthma. **Measurements and Main Results:** Patients with asthma had a higher proportion of iEos (25 ± 15%) compared with those with COPD (0.5 ± 1%), smokers without COPD (0.14 ± 0.24%), and healthy volunteers (0.67 ± 1.72%). In patients with asthma, the proportion of iEos was independent of total eosinophil number. iEos had more IL-5 receptors than resident eosinophils (777.02 ± 124.55 vs. 598.35 ± 318.69; $P < 0.01$). In patients with COPD, there was no relation between iEos number and inhaled corticosteroid use, disease severity, or exacerbations rate. The findings in patients with COPD and those with asthma were confirmed in validation cohorts. **Conclusions:** There are differences in the subtypes of circulating eosinophils between patients with asthma and those with COPD. This could have clinical implications in the interpretation of eosinophil significance and the approach to therapy in these patients.

**Keywords:** COPD; asthma; eosinophils; subtypes.

# Comment in

- [Finding the Right Biological: Eosinophil Subset Differences in Asthma and Chronic Obstructive Pulmonary Disease.](#)
  Freeman CM, Curtis JL, Hastie AT.Am J Respir Crit Care Med. 2023 Jul 15;208(2):121-123. doi: 10.1164/rccm.202305-0811ED.PMID: 37311240 No abstract available.

SUPPLEMENTARY INFO

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Review

# Can individual protective measures safeguard cardiopulmonary health from air pollution? A systematic review and meta-analysis

Surabhi Shah [1], Eunji Kim [2], Kyoung-Nam Kim [3], Eunhee Ha [4]

Affiliations expand

- PMID: 36940818


- DOI: 10.1016/j.envres.2023.115708

## Abstract

Evidence supporting the effect of individual protective measures (IPMs) on air pollution is relatively scarce. In this study, we performed a systematic review and meta-analysis to investigate the effects of air purifiers, air-purifying respirators, and cookstove changes on cardiopulmonary health outcomes. We searched PubMed, Scopus, and Web of Science until December 31, 2022, 90 articles and 39,760 participants were included. Two authors independently searched and selected the studies, extracted information, and assessed each study's quality and risk of bias. We performed meta-analyses when three or more studies were available for each IPMs, with comparable intervention and health outcome. Systematic review showed that IPMs were beneficial in children and elderly with asthma along with healthy individuals. Meta-analysis results showed a reduction in cardiopulmonary inflammation using air purifiers than in control groups (with sham/no filter) with a decrease in interleukin 6 by -0.247 μg/mL (95% confidence intervals [CI] = -0.413, -0.082). A sub-group analysis for air purifier as an IPMs in developing counties reduced fractional exhaled nitric oxide by -0.208 ppb (95% confidence intervals [CI] = -0.394, -0.022). However, evidence describing the effects of air purifying respirator and cook stove changes on cardiopulmonary outcomes remained insufficient. Therefore, air purifiers

can serve as efficient IPMs against air pollution. The beneficial effect of air purifiers is likely to have a greater effect in developing countries than in developed countries.

**Keywords:** Air pollution; Air purifier; Air-purifying respirator; Cardiopulmonary health.

# Conflict of interest statement

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

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

ELSEVIER
FULL-TEXT ARTICLE

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

# Long–term treatment outcomes in refractory rhinitis medicamentosa managed with nasal surgery

William Li [1], Shibalik Misra [1], Richard John Harvey [1 2], Larry Kalish [1 3]

Affiliations expand

- PMID: 37449456

# Abstract

**Background:** Limited treatment options exist for refractory Rhinitis Medicamentosa (RM). The role of surgery after failed medical management is not well defined. Mucosal contact points and restricted airflow often perpetuate decongestant use. This study assessed the long-term outcomes of nasal surgery in patients with refractory RM.

**Methods:** A prospective cohort study of refractory RM treated with nasal surgery was performed with ≥12m follow-up. Refractory RM was defined as nasal decongestant use once/day continuously for ≥4 weeks despite medical therapy. Patients with concomitant sinus disease and non-rhinitis conditions were excluded. Sino-nasal Outcome Test (SNOT22), Nasal Symptom Score (NSS) and nasal medication use were assessed. Patients who ceased decongestants were compared to ongoing users.

**Results:** 56 patients (age 48.4 (5.0) years, 50% female) were assessed. Median follow-up was 3.4[1.6-6.2] years. Total cessation of decongestants was achieved in 91.1%, while 5.4% had intermittent use, and 3.6% reported daily use. Ongoing users had higher odds of concomitant asthma (40.0% v 3.9%; OR, 16.33 (1.7 to 159.75); p = 0.036), reduced symptom improvement (ΔSNOT22, -4.6 (15.7) v 27.1 (17), p = 0.009 and ΔNSS, -1.0 (4.2) v -6.6 (5.1), p = 0.025), greater ongoing use of nasal corticosteroid (60.0% v 5.9%; OR 24.0[2.8-203.1]) and saline sprays (40% v 3.9%; OR 16.3[1.7-159.8]) but showed no difference in allergy status (OR, 0.7[0.1-7.1]), previous surgery (OR, 1.0[0.1-10.2]), gastroesophageal reflux (OR 1.0[0.1-10.2] or underlying anxiety/depression (OR 6.1[0.8-45.9]) compared to those who ceased.

**Conclusion:** Surgically re-establishing a nasal airway was associated with long-term decongestant cessation and symptom improvement in medically refractory RM. This article is protected by copyright. All rights reserved.

**Keywords:** decongestive agent; nose surgery; rhinitis; sino-nasal outcome test-22.

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Review

# An Updated Review on Atrophic Rhinitis and Empty Nose Syndrome

Ibrahim Ali Sumaily [1], Nouf Adel Hakami [1], Anwar Dhawi Almutairi [2], Abdulrahman Abdullah Alsudays [3], Ebrahim Mohammed Abulqusim [1], Mohammed Maki Abualgasem [1], Abdulrahman Ahmad Alghulikah [4], Abdulrahman Awad Alserhani [5]

Affiliations expand

- PMID: 37449389


- DOI: 10.1177/01455613231185022

## Abstract

**Objective:** Atrophic rhinitis (AR) is a rare clinical condition affecting the nasal mucosa. It is characterized by progressive nasal congestion and thick, bothersome nasal secretions. In this narrative review, pathogenesis, differences between the 2 types of AR, new management modalities, and the impact of management on lifestyle have been highlighted. **Materials and Methods:** An extensive literature search was conducted using PubMed, Web of Science, Google Scholar, and Saudi Digital Library databases. The articles were investigated to extract information on the pathogenesis, types, new treatment modalities, and the impact of management on lifestyle. **Results:** AR has primary and secondary types that affect different populations and have specific clinical presentations. Primary AR is common in women and countries with long, warm seasons. Secondary AR is the most common disease in the industrialized world. It is more common among adults who have systemic disease, have undergone extensive nasal surgery, and have experienced nasal trauma. Certain infections, autoimmune disorders, chronic sinusitis, hormonal imbalance, poor nutritional condition, and iron deficiency anemia have been suggested as etiological factors. Conservative treatment is safe, inexpensive, and effective. Hygiene, a well-balanced diet, smoking cessation, and early detection and treatment of nasal pathology can help prevent AR. Some interventions shown to improve quality of life was explained in detail. **Conclusions:** This paper reviewed published relevant literature on AR

related to pathogenesis, types, new treatment modalities, and the impact of treatment on lifestyle, thus, providing a comprehensive view of the management and prevention of AR.

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# The ratio of total IgE level at week 16 to baseline significantly correlated with the clinical response to omalizumab in moderate to severe allergic rhinitis patients

Zhan Zhao [1], Yuqin Deng [1], Lei Xiang [1], Jin Chen [1], Jing Wan [1], Jinli Sun [1], Yonggang Kong [1], Qingquan Hua [2]

Affiliations expand

# Abstract

**Objective:** To analyze whether the ratio of total IgE level at week 16 to baseline could be used as an indicator to evaluate clinical efficacy of patients treated with omalizumab.

**Methods:** We retrospectively analyzed the clinical characteristics of 62 patients with moderate-to-severe allergic rhinitis treated with omalizumab, and compared the pre-and post-treatment nasal visual analog scale (n-VAS) scores, the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ), Rhinitis Control Assessment Test (RCAT), improvement in nasal congestion, number of acute episodes of rhinitis, and total IgE levels in serum. The relationship between the efficacy of treatment with omalizumab and the change in total IgE levels before and after treatment was further analyzed.

**Results:** This study included 62 patients with moderate-to-severe allergic rhinitis, of which 48 demonstrated significant improvement after 16 weeks of omalizumab therapy; the results of 16 weeks' omalizumab treatment in 14 patients did not show significant improvements in allergic rhinitis symptoms based on RACT scores. After 16 weeks of omalizumab treatment, the RQLQ score decreased from (36.6 ± 13.7) at baseline level to (9.1 ± 12.6) after 16 weeks treatment.The ratio of total IgE at week 16 to total IgE levels at baseline was (2.9 ± 1.4) KU/L in 62 patients. And the ratio of total IgE levels at week 16 to total IgE levels at baseline was (3.3 ± 1.4) KU/L for responders and (1.6 ± 0.5) KU/L for non-responders.

**Conclusion:** The ratio of total IgE level at week 16 to baseline significantly correlated with the clinical response to omalizumab in moderate to severe allergic rhinitis patients, when the ratio of total IgE level at week 16 to baseline was ≥2.0. Omalizumab effectively treated patients with moderate-to-severe allergic rhinitis, and improved their quality of life.

**Keywords:** Allergic rhinitis; Free IgE; IgE-omalizumab complex; Omalizumab; Total IgE.

# Conflict of interest statement

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

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# Post COVID‑19 symptoms are common, also among young adults in the general population

Ida Mogensen [#] [1] [2], Sandra Ekström [#] [3] [4] [5], Jenny Hallberg [6] [7], Antonios Georgelis [2] [6], Erik Melén [1] [6] [7], Anna Bergström [2] [6], Inger Kull [1] [7]

Affiliations expand

## Abstract

Post coronavirus disease‑19 (post COVID‑19) is mainly studied in clinical populations and less is known about post COVID‑19 in a young general population. The aim of the study is to investigate the prevalence and symptoms of post COVID‑19 and its potential risk factors in young adults. Participants from the Swedish population‑based birth cohort BAMSE were included (n = 2022, mean age 26.5 years). Post COVID‑19 was assessed through a questionnaire and defined as symptoms after confirmed COVID‑19 (registry‑based or self‑reported positive test) lasting for ≥ 2 months. In total, 681 participants had had confirmed COVID‑19. Among them, 112 (16.5%) fulfilled the definition of post COVID‑19 (17.8% in females, 14.5% in males, p = 0.26). The most common post COVID‑19 symptoms were altered smell and taste (68.8%), dyspnea (33.7%) and fatigue (30.4%). Overall, no major risk factors for post COVID‑19 were identified except for being bedbound during COVID‑19. However, asthma and rhinitis were associated with the post COVID‑19 symptom dyspnea, migraine with altered smell and taste, and lower self‑rated health with fatigue. In conclusion, post COVID‑19 symptoms are common, also among young adults in the

general population. Although not life-threatening, it could have a considerable impact on public health due to the high prevalence and long-term symptoms.

## Conflict of interest statement

The authors declare no competing interests.

- 50 references
- 4 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

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# Sensitisation to House Dust Mite Component Der p 23 Is Associated with Severe Symptoms and Asthma in Allergic Rhinitis Patients

Yunbo Gao [1], Jingyun Li [1][2][3][4], Xu Xu [1][2][3][4], Chengshuo Wang [2][3], Yuan Zhang [1][2], Luo Zhang [1][2][3][4]

Affiliations expand

- PMID: 37437556

# Abstract

**Introduction:** House dust mite (HDM) is an important source of airborne allergens in China as it contains several allergenic components that can cause allergic rhinitis (AR) and other allergic diseases. This study aimed to determine the clinical characteristics and disease severity in AR patients sensitised to different allergenic HDM components.

**Methods:** This was a retrospective study, which examined 129 patients who were first diagnosed with only HDM-induced AR at the Department of Allergy of Beijing Tongren Hospital from December 2019 to April 2021. Clinical characteristics and disease severity of the patients were assessed based on the sensitisation to specific Dermatophagoides pteronyssinus (Der p) and Dermatophagoides farinae (Der f) allergenic components, including Der p 1, Der p 2, Der p 23, Der f 1, and Der f 2, employing multiple correspondence analysis (MCA) with correspondence analysis chart of MCA.

**Results:** Among HDM-induced AR cases, the positive rate of Der p 1 was the highest (87.6%), followed by Der p 2 (78.3%), Der f 2 (76.64%), Der f 1 (68.2%), and Der p 23 (37.2%). Multiple correspondence analyses showed that sensitisation to Der p 23 was associated with severe AR symptoms and asthma; sensitisation to Der p 2, Der f 1, and Der f 2 was associated with moderate AR; and no sensitisation to Der p 23 was associated with mild AR.

**Conclusion:** Der p 23 sensitisation is prevalent in northern China and may be associated with severe symptoms and asthma in AR patients.

**Keywords:** Allergenic components; Allergic rhinitis; Der p 23; House dust mite.

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# Prevalence of Atopic Diseases Among Sexually Diverse Adults in the US

Katelyn J Rypka [1 2 3], Abel Woldu [3], Markus D Boos [4], Sheilagh M Maguiness [5], Matthew D Mansh [1]

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## Plain language summary

This cross-sectional study assesses the prevalence of asthma, allergic rhinitis, or atopic dermatitis among sexually diverse adults compared with heterosexual adults in the US.

## Conflict of interest statement

FULL TEXT LINKS

FULL TEXT
JAMA Dermatology

# Global, regional, and national burden of allergic disorders and their risk factors in 204 countries and territories, from 1990 to 2019: A systematic analysis for the Global Burden of Disease Study 2019

Youn Ho Shin [1][2], Jimin Hwang [3][4], Rosie Kwon [5], Seung Won Lee [6], Min Seo Kim [7][8]; GBD 2019 Allergic Disorders Collaborators; Jae Il Shin [9], Dong Keon Yon [5][10]

Collaborators, Affiliations expand

# Abstract

**Background:** Asthma and atopic dermatitis (AD) are chronic allergic conditions, along with allergic rhinitis and food allergy and cause high morbidity and mortality both in children and adults. This study aims to evaluate the global, regional, national, and temporal trends of the burden of asthma and AD from 1990 to 2019 and analyze their associations with geographic, demographic, social, and clinical factors.

**Methods:** Using data from the Global Burden of Diseases (GBD), Injuries, and Risk Factors Study 2019, we assessed the age-standardized prevalence, incidence, mortality, and disability-adjusted life years (DALYs) of both asthma and AD from 1990 to 2019, stratified by geographic region, age, sex, and socio-demographic index (SDI). DALYs were calculated as the sum of years lived with disability and years of life lost to premature mortality. Additionally, the disease burden of asthma attributable to high body mass index, occupational asthmagens, and smoking was described.

**Results:** In 2019, there were a total of 262 million [95% uncertainty interval (UI): 224-309 million] cases of asthma and 171 million [95% UI: 165-178 million] total cases of AD globally; age-standardized prevalence rates were 3416 [95% UI: 2899-4066] and 2277 [95% UI: 2192-2369] per 100,000 population for asthma and AD, respectively, a 24.1% [95% UI: -27.2 to -20.8] decrease for asthma and a 4.3% [95% UI: 3.8-4.8] decrease for AD compared to baseline in 1990. Both asthma and AD had similar trends according to age, with age-specific prevalence rates peaking at age 5-9 years and rising again in adulthood. The prevalence and incidence of asthma and AD were both higher for individuals with higher SDI; however, mortality and DALYs rates of individuals with asthma had a reverse trend, with higher mortality and DALYs rates in those in the lower SDI quintiles. Of the three risk factors, high body mass index contributed to the highest DALYs and deaths due to asthma, accounting for a total of 3.65 million [95% UI: 2.14-5.60 million] asthma DALYs and 75,377 [95% UI: 40,615-122,841] asthma deaths.

**Conclusions:** Asthma and AD continue to cause significant morbidity worldwide, having increased in total prevalence and incidence cases worldwide, but having decreased in age-standardized prevalence rates from 1990 to 2019. Although both are more frequent at younger ages and more prevalent in high-SDI countries, each condition has distinct temporal and regional characteristics. Understanding the temporospatial trends in the disease burden of asthma and AD could guide future policies and interventions to better manage these diseases worldwide and achieve equity in prevention, diagnosis, and treatment.

**Keywords:** asthma; atopic dermatitis; disability-adjusted life years; eczema; epidemiology; global burden; mortality.

- 41 references

SUPPLEMENTARY INFO

Grant supportexpand

FULL TEXT LINKS

WILEY Full Text Article

# Identification of key genes and the pathophysiology associated with allergen–specific immunotherapy for allergic rhinitis

Kai Fan [# 1 2], Shican Zhou [# 1 2], Ling Jin [1 2], Shiwang Tan [1 2], Ju Lai [1 2], Zimu Zhang [1 2], Jingwen Li [1 2], Xiayue Xu [1 2], Chunyan Yao [1 2], Zhiqiang Yan [3], Shaoqing Yu [4 5]

Affiliations expand

## Abstract

**Background:** Allergen-specific immunotherapy (AIT) is a causative treatment in allergic rhinitis (AR), comprising long-term allergen administration and over three years of

treatment. This study is carried out for revealing the mechanisms and key genes of AIT in AR.

**Methods:** The present study utilized online Gene Expression Omnibus (GEO) microarray expression profiling dataset GSE37157 and GSE29521 to analyze the hub genes changes related to AIT in AR. Based on limma package, differential expression analysis for the two groups (samples of allergic patients prior to AIT and samples of allergic patients undergoing AIT) was performed to obtain differentially expressed genes (DEGs). Gene Ontology (GO) analysis and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis of DEGs were conducted using DAVID database. A Protein-Protein Interaction network (PPI) was built and a significant network module was acquired by using Cytoscape software (Cytoscape, 3.7.2). Utilizing the miRWalk database, we identified potential gene biomarkers, constructed interaction networks of target genes and microRNAs (miRNAs) using Cytoscape software, and explore the cell type-specific expression patterns of these genes in peripheral blood using publicly available single-cell RNA sequencing data (GSE200107). Finally, we are using PCR to detect changes in the hub genes that are screened using the above method in peripheral blood before and after AIT treatment.

**Results:** GSE37157 and GSE29521 included 28 and 13 samples, respectively. A total of 119 significantly co-upregulated DEGs and 33 co-downregulated DEGs were obtained from two datasets. The GO and KEGG analyses demonstrated that protein transport, positive regulation of apoptotic process, Natural killer cell mediated cytotoxicity, T cell receptor signaling pathway, TNF signaling pathway, B cell receptor signaling pathway and Apoptosis may be potential candidate therapeutic targets for AIT of AR. From the PPI network, 20 hub genes were obtained. Among them, the PPI sub-networks of CASP3, FOXO3, PIK3R1, PIK3R3, ATF4, and POLD3 screened out from our study have been identified as reliable predictors of AIT in AR, especially the PIK3R1.

**Conclusion:** Our analysis has identified novel gene signatures, thereby contributing to a more comprehensive understanding of the molecular mechanisms underlying AIT in the treatment of AR.

**Keywords:** Allergen-specific immunotherapy; Allergic rhinitis; Bioinformatics analysis; Differentially expressed genes; microRNAs..

# Conflict of interest statement

The authors declare no competing interests.

- 45 references
- 5 figures

SUPPLEMENTARY INFO

# Correlation of Multiple Allergen Simultaneous Test with Nasal Provocation Test of House Dust Mite

Kyung Soo Kim [1], Hyun Jin Min [1]

Affiliations expand

## Abstract

**Objectives:** Compared with the skin prick test, relationship between the multiple allergen simultaneous test (MAST) and nasal provocation test (NPT) has rarely been evaluated. We evaluated the relationship between the results of the MAST and NPT against house dust

mites in the Korean population. **Methods:** Medical records of patients who underwent both MAST and NPT were reviewed. Positive MAST was diagnosed when the levels of immunoglobulin E (IgE) specific for *Dermatophagoides farinae* (DF) and *Dermatophagoides pteronyssinus* (DP) were ≥2 positivity or ≥0.70 IU/ml. During the NPT, changes in subjective symptoms, including nasal obstruction, rhinorrhea, sneezing, itching, ocular discomfort, and peak nasal inspiratory flow (PNIF), were measured. The correlation between NPT and MAST results was statistically analyzed. **Results:** A total of 96 participants were enrolled in this study: 26 were assigned to the MAST-positive group, and 70 were assigned to the MAST-negative group. Changes in subjective symptoms before and after the nasal allergen challenge were significantly associated with the MAST results. Changes in PNIF before and after the nasal allergen challenge were also significantly associated with the MAST results. We found that a cutoff value of "a subjective total nasal symptom change" of more than 17.5 had a sensitivity of 68.6% and a specificity of 69.2%, while a cutoff value of "a PNIF change" of more than 6.51 had a sensitivity of 67.1% and a specificity of 69.2%. **Conclusion:** NPT was significantly associated with MAST, and further studies regarding the relationship between NPT using various allergen conditions and MAST are warranted.

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# Age-related differences in associations between uncontrolled asthma,

# comorbidities and biomarkers in adult-onset asthma

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

Affiliations expand

- PMID: 37405375


- DOI: [10.1080/02770903.2023.2231078](#)

## Abstract

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

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

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

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

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# Effects of pollen concentration on allergic rhinitis in children: A retrospective study from Beijing, a Chinese megacity

Yuxin Zhao [1], Zhaobin Sun [2], Li Xiang [3], Xingqin An [4], Xiaoling Hou [5], Jing Shang [6], Ling Han [7], Caihua Ye [8]

Affiliations expand

- PMID: 37080269

- DOI: 10.1016/j.envres.2023.115903

# Abstract

With global climate change and rapid urbanization, the prevalence of allergic diseases caused by pollen is rising dramatically worldwide with unprecedented complexity and

severity, especially for children in mega-cities. However, because of the lack of long time-series pollen concentrations data, the accurate evaluation of the impact of pollen on allergic rhinitis (AR) was scarce in the Chinese metropolis. A generalized additive model was used to assess the effect of pollen concentration on pediatric AR outpatient visits in Beijing from 2014 to 2019. A stratified analysis of 10 pollen species and age-gender-specific groups was also conducted during the spring and summer-autumn peak pollen periods separately. Positive associations between pollen concentration and pediatric AR varied with the season and pollen species were detected. Although the average daily pollen concentration is higher during the spring tree pollen peak, the influence was stronger at the summer-autumn weed pollen peak with the maximum relative risk 1.010 (95% CI 1.009, 1.011), which was higher than the greatest relative risk, 1.003 (95% CI 1.002, 1.004) in the spring peak. The significant adverse effects can be sustained to lag10 during the study period, and longer in the summer-autumn peak (lag13) than in the spring peak (lag8). There are thresholds for the health effects and they varied between seasons. The significant effect appeared when the pollen concentration was higher than $3.74 \times 10^5$ grain·m$^{-2}$·d$^{-1}$ during the spring tree pollen peaks and $4.70 \times 10^4$ grain·m$^{-2}$·d$^{-1}$ during the summer-autumn weed pollen peaks. The stratified results suggested that the species-specific effects were heterogeneous. It further highlights that enough attention should be paid to the problem of pollen allergy in children, especially school-aged children aged 7-18 years and weed pollen in the summer-autumn peak pollen period. These findings provide a more accurate reference for the rational coordination of medical resources and improvement of public health.

**Keywords:** Allergic rhinitis; Children's health; Generalized additive model; Pollen concentration.

# Conflict of interest statement

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

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

ELSEVIER
FULL-TEXT ARTICLE

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

# Microbiology sampling in non-cystic fibrosis bronchiectasis cases from northern Alberta

Mitchell J Wagner[1], Monette Dimitrov[1], Grace Y Lam[1][2], Winnie Leung[1][2], Gregory J Tyrrell[1][3], Dilini Vethanayagam[1][2]

Affiliations expand

- PMID: 37450508


- DOI: 10.1371/journal.pone.0288704

## Abstract

Non-cystic fibrosis bronchiectasis (NCFB) is a chronic respiratory disease resulting in chronic cough, thick sputum, and lower airway microbial colonization, akin to patients with cystic fibrosis (CF). NCFB is a common, yet under recognized entity which inflicts significant morbidity and mortality particularly to older individuals, with a rising prevalence in the developed world. Given that sputum cultures are a non-invasive method to characterize the lower airway microbiota in NCFB patients, for which pathogenic organisms are associated with worsened outcomes, we sought to characterize the microbiological pattern and clinical outcomes associated with sputum culture in a cohort of NCFB patients from Western Canada. A total of 20 subjects were prospectively recruited from various bronchiectasis clinics across the Greater Edmonton area. A retrospective chart review and a symptoms questionnaire was performed, gathering information not limited to symptoms, comorbidities, exacerbations, hospitalizations, sputum production, and sputum culture results over the prior 5 years. Subjects reported frequent hospitalization alongside a significant burden of symptoms. A large majority of sputum cultures grew pathogenic

organisms such as Haemophilus influenzae and Pseudomonas aeruginosa. We also note the considerable waste and inefficiency associated with sputum cultures, outlining areas for which this important diagnostic modality can be improved. Accurate characterization of the airway microbiota alongside efficient delivery of health services are key to ensuring the proper treatment of individuals with NCFB, given their high disease burden and frequent hospitalization.

## Conflict of interest statement

The authors have declared that there are no competing interests.
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# Association of selected inflammatory biomarkers with cough reflex sensitivity in asthmatic children

P Kunč[1], J Fábry, M Grendár, P Ferenc, T Strachan, K Ištvánková, T Hurtová, R Péčová

Affiliations expand

- PMID: 37449748

## Abstract

Bronchial asthma is the most common chronic respiratory disease of childhood. Cough is one of its defining symptoms. This study investigated the associations between selected

inflammatory biomarkers and cough reflex sensitivity after capsaicin inhalation in children with mild and moderate well-controlled type 2 endotype asthma compared with non-asthmatic probands. Sensitivity to the cough reflex was measured by recording the cough response after capsaicin inhalation. The sandwich ELISA method was used to measure serum concentrations of the investigated potential inflammatory biomarkers (interleukin 13, interleukin 1beta, eosinophil-derived neurotoxin). The acquired data were statistically evaluated according to descriptive analyses for summarization and comparison between cough reflex sensitivity parameters and individual biomarker values in the observed and control groups modeled by a simple linear regression model. Statistical significance was defined as $p < 0.05$. We showed a statistically significant association (p-value 0.03) between cough reflex sensitivity - C2 value (capsaicin concentration required for two cough responses) and interleukin 1beta serum concentrations in the asthma group compared with the control group of non-asthmatic children. Our results support the possibility of interleukin 1beta as a potential additive inflammatory biomarker used in clinical practice in children with asthma because of its correlation with the activity of the afferent nerve endings in the airways.

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# The Severity of Chronic Cough Diary (SCCD): development and content validation of a novel patient-reported outcome instrument for evaluating the symptom experience of chronic cough

Margarita de la Orden Abad [1], Claudia Haberland [2], Hayley Karn [3], Anne Skalicky [4], Asha Hareendran [3][5]

# Abstract

**Background:** Refractory chronic cough (RCC), a cough lasting longer than 8 weeks with an unexplained underlying etiology and unresponsive to conventional treatment, can have substantial effects on patients' quality of life. For assessment of the efficacy of antitussive medication in clinical trials in RCC, patient-reported outcome (PRO) instruments should be fit for purpose with appropriate content validity. Here we describe the qualitative testing of a newly developed PRO instrument: the Severity of Chronic Cough Diary (SCCD).

**Methods:** The SCCD was developed to assess patients' symptom experience of cough in patients with RCC. A preliminary version was tested and refined based on an iterative process in a qualitative study. In total, three rounds of interviews were conducted with adult participants diagnosed with RCC in the USA (n = 19) and UK (n = 10). Rounds 1-3 consisted of hybrid concept elicitation (CE) interviews and cognitive interviews (CIs), with Round 3 also including interviews in a subset of participants (n = 5) about the usability of the SCCD as administered on an electronic handheld device.

**Results:** The CE interviews identified concepts important to patients' experiences related to RCC that were broadly in line with the concepts in the preliminary version of the SCCD. Participants provided positive feedback on the draft SCCD across all CI rounds, reporting the instrument to be relevant and straightforward to complete, and containing a comprehensive set of concepts to evaluate their symptom experience of RCC. Participants demonstrated a good understanding of proposed item wording, response options, and the 24-hour recall period, and thought completion of the SCCD on the electronic device was easy. Following revisions based on results from each interview round, the SCCD at the end of this qualitative research study had 14 items assessing the concepts of: cough symptoms (five items), symptoms related to cough (four items), disruption to activities due to cough (three items), and disruption to sleep due to cough (two items).

**Conclusions:** The results of this study provide qualitative evidence supporting the content validity of the SCCD as a PRO instrument for evaluating outcomes of therapies for RCC in clinical trials.

## Conflict of interest statement

MdlOA and CH are employees of Bayer AG. HK and AS are employees of Evidera, which was contracted by Bayer AG to conduct the study. AH was an employee of Evidera at the time of the study and is now an employee of UCB.

- 24 references
- 2 figures

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

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

1
PLoS One

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. 2023 Jul 14;18(7):e0288704.

 doi: 10.1371/journal.pone.0288704. eCollection 2023.

# Microbiology sampling in non–cystic fibrosis bronchiectasis cases from northern Alberta

[Mitchell J Wagner](#) [1], [Monette Dimitrov](#) [1], [Grace Y Lam](#) [1 2], [Winnie Leung](#) [1 2], [Gregory J Tyrrell](#) [1 3], [Dilini Vethanayagam](#) [1 2]

Affiliations expand

# Abstract

Non-cystic fibrosis bronchiectasis (NCFB) is a chronic respiratory disease resulting in chronic cough, thick sputum, and lower airway microbial colonization, akin to patients with cystic fibrosis (CF). NCFB is a common, yet under recognized entity which inflicts significant morbidity and mortality particularly to older individuals, with a rising prevalence in the developed world. Given that sputum cultures are a non-invasive method to characterize the lower airway microbiota in NCFB patients, for which pathogenic organisms are associated with worsened outcomes, we sought to characterize the microbiological pattern and clinical outcomes associated with sputum culture in a cohort of NCFB patients from Western Canada. A total of 20 subjects were prospectively recruited from various bronchiectasis clinics across the Greater Edmonton area. A retrospective chart review and a symptoms questionnaire was performed, gathering information not limited to symptoms, comorbidities, exacerbations, hospitalizations, sputum production, and sputum culture results over the prior 5 years. Subjects reported frequent hospitalization alongside a significant burden of symptoms. A large majority of sputum cultures grew pathogenic organisms such as Haemophilus influenzae and Pseudomonas aeruginosa. We also note the considerable waste and inefficiency associated with sputum cultures, outlining areas for which this important diagnostic modality can be improved. Accurate characterization of the airway microbiota alongside efficient delivery of health services are key to ensuring the proper treatment of individuals with NCFB, given their high disease burden and frequent hospitalization.

# Conflict of interest statement

The authors have declared that there are no competing interests.

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Chest

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# Phenotypic features of pediatric bronchiectasis exacerbations associated with symptom resolution after 14-days of oral antibiotic treatment

Vikas Goyal [1], Stephanie T Yerkovich [2], Keith Grimwood [3], Julie M Marchant [4], Catherine A Byrnes [5], Ian Brent Masters [6], Anne B Chang [7]

Affiliations expand

# Abstract

**Background:** Respiratory exacerbations in children and adolescents with bronchiectasis are treated with antibiotics. However, antibiotics can have variable inter-individual effects when treating exacerbations.

**Research question:** Can phenotypic features associated with symptom resolution after a 14-day course of oral antibiotics for a non-severe exacerbation of bronchiectasis be identified?

**Study design and methods:** Combining data from two multicenter randomized controlled trials, we identified 217 children with bronchiectasis assigned to at least 14-days of oral antibiotics to treat non-severe (non-hospitalized) exacerbations. Univariable and then

multivariable logistic regression were used to identify factors associated with symptom resolution within 14-days of commencing antibiotics. Identified associations were re-evaluated by mediation analysis.

**Results:** Of the 217 study participants (52% males), 41% were Indigenous (Australian First Nations, New Zealand Māori or Pacific Islanders). The median age was 6.6-years (interquartile range 4.0-10.1). By Day-14, symptoms had resolved in 130 children (responders), but persisted in the remaining 87 (non-responders). Multivariable analysis found those who were Indigenous (adjusted odds ratio [$OR_{adjusted}$]=3.59, 95% confidence interval [CI] 1.35-9.54) or had new abnormal auscultatory findings ($OR_{adjusted}$=3.85, 95%CI 1.56-9.52) were more likely to be responders, while those with multiple bronchiectatic lobes at diagnosis ($OR_{adjusted}$=0.66, 95%CI 0.46-0.95) or higher cough-scores when starting exacerbation treatment ($OR_{adjusted}$=0.55, 95%CI 0.34-0.90) were more likely to be non-responders. Detecting a respiratory virus at the beginning of an exacerbation was not associated with antibiotic failure at 14-days.

**Interpretation:** Children with Indigenous ethnicity, milder bronchiectasis, mild exacerbations (low reported cough scores) or new abnormal auscultatory signs are more likely to respond to appropriate oral antibiotics than those without these features. These patient and exacerbation phenotypes may assist clinical management and development of biomarkers to identify those whose symptoms are more likely to resolve following 14-days of oral antibiotics. Australian New Zealand Clinical Trials Registry (ACTRN12612000011886 and ACTRN12612000010897).

**Keywords:** Bronchiectasis exacerbation; pediatric; phenotype; response to antibiotics.

FULL TEXT LINKS

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# Etiology and clinical characteristics of a non-cystic fibrosis bronchiectasis cohort in a middle eastern population

Irfan Shafiq [1], Ali Saeed Wahla [2], Mateen Haider Uzbeck [2], Zaid Zoumot [2], Mohamed Abuzakouk [2], Shuayb Elkhalifa [2], Govinda Bodi [2], Khalaf Mohamed Almazrouei [2], Kashyap Bodi [2], Said Isse [2]

Affiliations expand

## Abstract

**Background:** Bronchiectasis is a widely prevalent airway disease characterized by airway dilatation and recurrent infections, that can lead to respiratory failure in severe cases. The etiology of bronchiectasis varies geographically, but there is a lack of published data examining its etiology specifically within the Middle Eastern population.

**Methods:** We conducted a retrospective analysis of our bronchiectasis patient registry, extracting clinical and demographic characteristics from electronic medical records. Quantitative variables were presented as the median and interquartile range (IQR), while categorical variables were expressed as numbers and percentages. Statistical comparisons for continuous characteristics were performed using the t-test, and significance was determined by a p-value less than 0.05.

**Results:** In total we analysed 260 records (63% female, 37% male), with median age of 58 years (interquartile range (IQR) 38-71), Body Mass Index (BMI) 25.8(IQR 22-30), forced expiratory volume in the first second (FEV1) %predicted 65 (IQR 43-79) and FEV1/forced vital capacity (FVC) 0.76 (0.67-0.86). Sixty-five cases (25%) were post-infectious in aetiology (excluding post-TB - n:27 10.4%). Forty-eight (18.5%) patients were labelled idiopathic, while Primary Ciliary Dyskinesia (PCD) accounted for 23 (8.8%) cases. Pseudomonas

aeruginosa was the most common colonizing organism (32.7%), followed by Haemophilus influenzae (9.2%) and Methicillin-Sensitive Staphylococcus aureus(6.9%). At the time of review, 11 patients had died (median age, FEV %predicted, and bronchiectasis severity index (BSI) 59 years, 38% and 15.5 respectively), all due to respiratory failure, and as expected, all were classed severe on BSI. The BSI score was available for 109 patients, of which 31(28%) were classed mild, 29(27%) were moderate, and 49 (45%) were classed severe. The median BSI score was 8 (IQR 4-11). On dividing the patients according to obstructive vs. restrictive spirometry, we found that patients with FEV1/FVC < 0.70 had significantly higher BSI (10.1 vs. 6.9, p-value < 0.001) and that 8 out of the 11 deceased patients had FEV1/FVC < 70%.

**Conclusions:** In our study, post-infectious, idiopathic, and PCD were identified as the most common etiologies of bronchiectasis. Additionally, patients with obstructive spirometry appeared to have a worse prognosis compared to those with restrictive spirometry.

**Keywords:** Aetiology; Bronchiectasis; Obstructive lung disease; Post-infectious.
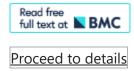
# Conflict of interest statement

The authors declare no competing interests.

- 23 references
- 3 figures

SUPPLEMENTARY INFO

MeSH termsexpand

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Case Reports

# [Endovascular embolization hemoptysis in a patient with coronary artery as non-bronchial systemic artery: a case report]

[Article in Chinese]

X Q Li [1], X J Yang [2]

Affiliations expand

- PMID: 37402663


- DOI: 10.3760/cma.j.cn112147-20221128-00930

## Abstract

in English, Chinese

The coronary artery as a responsible vessel for hemoptysis is very rare. This patient was admitted to the hospital with bronchiectasis and hemoptysis, and the right coronary artery was found to be one of the non-bronchial systemic arteries by computed tomography angiography, and the hemoptysis stopped immediately after successful embolization of all bronchial arteries and non-bronchial systemic arteries by bronchial artery embolization. However, the patient had a recurrence of a small amount of hemoptysis 1 month and 3 months after surgery. The patient underwent lobectomy of the lesion after multidisciplinary discussion and did not have any hemoptysis after surgery.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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