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Considerato il crescente interesse sull'argomento, abbiamo aggiunto una sezione su (premature birth) AND (pulmonary obstructive disease), ed in questo numero abbiamo incluso tutti gli articoli risultati dalla ricerca, dal prossimo verranno inseriti solo i settimanali

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

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Int J Cardiovasc Imaging



. 2023 Dec 1.

doi: 10.1007/s10554-023-03027-1. Online ahead of print.

COPD: pulmonary vascular volume associated with cardiac structure and function

[Lisa Steen Duus](#)^{1,2}, [Ditte Vesterlev](#)³, [Anne Bjerg Nielsen](#)^{3,4}, [Mats Højbjerg Lassen](#)³, [Pradeesh Sivapalan](#)⁵, [Charlotte Suppli Ulrik](#)⁶, [Therese Lapperre](#)^{7,8,9}, [Andrea Browatzki](#)¹⁰, [Rubén San José Estépar](#)⁴, [Pietro Nardelli](#)⁴, [Jens-Ulrik Staehr Jensen](#)⁵, [Raúl San José Estépar](#)^{#11}, [Tor Biering-Sørensen](#)^{#3,12}

Affiliations expand

- PMID: 38040946
- DOI: [10.1007/s10554-023-03027-1](https://doi.org/10.1007/s10554-023-03027-1)

Abstract

Background: Early recognition of cardiac dysfunction in patients with chronic obstructive pulmonary disease (COPD) may prevent future cardiac impairment and improve prognosis. Quantitative assessment of subsegmental and segmental vessel volume by Computed Tomographic (CT) imaging can provide a surrogate of pulmonary vascular remodeling. We aimed to examine the relationship between lung segmental- and subsegmental vessel volume, and echocardiographic measures of cardiac structure and function in patients with COPD.

Methods: We studied 205 participants with COPD, included in a large cohort study of cardiovascular disease in COPD patients. Participants had an available CT scan and echocardiogram. Artificial intelligence (AI) algorithms calculated the subsegmental vessel fraction

as the vascular volume in vessels below 10 mm² in cross-sectional area, indexed to total intrapulmonary vessel volume. Linear regressions were conducted, and standardized β -coefficients were calculated. Scatterplots were created to visualize the continuous correlations between the vessel fractions and echocardiographic parameters.

Results: We found that lower subsegmental vessel fraction and higher segmental vessel volume were correlated with higher left ventricular (LV) mass, LV diastolic dysfunction, and inferior vena cava (IVC) dilatation. Subsegmental vessel fraction was correlated with right ventricular (RV) remodeling, while segmental vessel fraction was correlated with higher pulmonary pressure. Measures of LV mass and right atrial pressure displayed the strongest correlations with pulmonary vasculature measures.

Conclusion: Pulmonary vascular remodeling in patients with COPD, may negatively affect cardiac structure and function. AI-identified remodeling in pulmonary vasculature may provide a tool for early identification of COPD patients at higher risk for cardiac impairment.

Keywords: Artificial intelligence; COPD; Cardiac structure and function: computed tomography; Echocardiography.

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[Review](#)

Adv Drug Deliv Rev

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. 2023 Nov 29:115146.

doi: 10.1016/j.addr.2023.115146. Online ahead of print.

Long-acting inhaled medicines: Present and future

[Chengqian Zhang](#)¹, [Davide D'Angelo](#)², [Francesca Buttini](#)³, [Mingshi Yang](#)⁴

Affiliations expand

- PMID: 38040120
- DOI: [10.1016/j.addr.2023.115146](https://doi.org/10.1016/j.addr.2023.115146)

Abstract

Inhaled medicines continue to be an essential part of treatment for respiratory diseases such as asthma, chronic obstructive pulmonary disease, and cystic fibrosis. In addition, inhalation technology, which is an active area of research and innovation to deliver medications via the lung to the bloodstream, offers potential advantages such as rapid onset of action, enhanced bioavailability, and reduced side effects for local treatments. Certain inhaled macromolecules and particles can also end up in different organs via lymphatic transport from the respiratory epithelium. While the majority of research on inhaled medicines is focused on the delivery technology, particle engineering, combination therapies, innovations in inhaler devices, and digital health technologies, researchers are also exploring new pharmaceutical technologies and strategies to prolong the duration of action of inhaled drugs. This is because, in contrast to most inhaled medicines that exert a rapid onset and short duration of action, long-acting inhaled medicines (LAIM) improve not only improve patient compliance by reducing the dosing frequency, but also the effectiveness and convenience of inhaled therapies to better manage patients' conditions. This paper reviews the advances in LAIM, the pharmaceutical technologies and strategies for developing LAIM, and emerging new inhaled modalities that possess a long-acting nature and potential in the treatment and prevention of various diseases. The challenges in the development of the future LAIM are also discussed where active research and innovations are taking place.

Keywords: Inhaled medicines; Long-acting effects; New inhaled modalities; Pulmonary drug delivery.

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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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Editorial

Ann Am Thorac Soc

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. 2023 Dec;20(12):1703-1704.

doi: 10.1513/AnnalsATS.202309-833ED.

All the Lonely People: Social Isolation and Loneliness in Chronic Obstructive Pulmonary Disease

[Lauren E Ferrante](#)¹, [Andrew B Cohen](#)^{2,3}

Affiliations expand

- PMID: 38038602
- DOI: [10.1513/AnnalsATS.202309-833ED](https://doi.org/10.1513/AnnalsATS.202309-833ED)

No abstract available

Comment on

- [National Prevalence of Social Isolation and Loneliness in Adults with Chronic Obstructive Pulmonary Disease.](#)

Suen AO, Iyer AS, Cenzer I, Farrand E, White DB, Singer J, Sudore R, Kotwal A. *Ann Am Thorac Soc*. 2023 Dec;20(12):1709-1717. doi: 10.1513/AnnalsATS.202304-288OC.PMID: 37463307

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Editorial

Ann Am Thorac Soc

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. 2023 Dec;20(12):1707-1708.

doi: 10.1513/AnnalsATS.202308-745ED.

The Price Is Right: Cost-Effectiveness of Long-Term Azithromycin for Chronic Obstructive Pulmonary Disease

[Brice Taylor](#)¹, [Stephen Chiang](#)², [Stephanie Taylor](#)^{2,3}

Affiliations [expand](#)

- PMID: 38038601
- DOI: [10.1513/AnnalsATS.202308-745ED](https://doi.org/10.1513/AnnalsATS.202308-745ED)

No abstract available

Comment on

- [A Cost-Effectiveness Analysis of Azithromycin for the Prevention of Acute Exacerbations of Chronic Obstructive Pulmonary Disease.](#)

Ahmadian S, Johnson KM, Ho JK, Sin DD, Lynd LD, Harrison M, Sadatsafavi M. *Ann Am Thorac Soc.* 2023 Dec;20(12):1735-1742. doi: 10.1513/AnnalsATS.202304-301OC.PMID: 37703432

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J Med Case Rep

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. 2023 Dec 1;17(1):497.

doi: 10.1186/s13256-023-04256-7.

[Superior vena cava syndrome induced by lung hyperinflation in chronic obstructive pulmonary disease: a case report](#)

[Nobuhiro Kanaji](#)¹, [Naoki Watanabe](#)², [Takuya Inoue](#)², [Hitoshi Mizoguchi](#)², [Kosuke Sakamoto](#)³, [Yuta Komori](#)², [Kosuke Kawada](#)², [Norimitsu Kadowaki](#)²

Affiliations [expand](#)

- PMID: 38037127

- DOI: [10.1186/s13256-023-04256-7](https://doi.org/10.1186/s13256-023-04256-7)

Abstract

Background: Superior vena cava syndrome is rarely attributed to chronic obstructive pulmonary disease.

Case presentation: We present the case of an 82-year-old Japanese man who experienced gradually progressive dyspnea on exertion. His physical examination revealed small vascular dilatations on his chest and upper abdominal skin characterized by blood flow from head to leg, indicating superior vena cava syndrome. Radiographic findings included lung hyperinflation with a drop-like heart on chest X-ray, and emphysematous changes on computed tomography. The superior vena cava appeared extremely narrow and slit-like, with no adjacent mass or giant bulla. Pulmonary function testing indicated a forced expiratory volume in 1 second of 0.82L (44.4% of predicted value) and a forced expiratory volume in 1 second/forced vital capacity of 31.29%. A diagnosis of chronic obstructive pulmonary disease was made. We discuss how longitudinal forces can narrow the superior vena cava, particularly when it protrudes toward the lung field due to its anatomical location in the upper mediastinum. The absence of mediastinal adipose tissue may render the superior vena cava susceptible to compression, resulting in a loss of its typical columnar structure. The protrusion of the superior vena cava toward the lung field may be a contributing factor to superior vena cava narrowing in chronic obstructive pulmonary disease.

Conclusion: This case represents the first reported instance of superior vena cava syndrome associated with chronic obstructive pulmonary disease, characterized by lung hyperinflation, in the absence of a giant bulla.

Keywords: Case report; Chronic obstructive pulmonary disease; Emphysema; Superior vena cava syndrome.

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- [7 references](#)

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J Physiother

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. 2023 Nov 29:S1836-9553(23)00115-7.

doi: 10.1016/j.jphys.2023.10.009. Online ahead of print.

Critically appraised paper: In adults with chronic obstructive pulmonary disease, long-term telerehabilitation and unsupervised home-based treadmill training reduced hospitalisations and emergency department presentations compared with usual care [synopsis]

[Vinicius Cavalheri](#) ¹

Affiliations expand

- PMID: 38036400
- DOI: [10.1016/j.jphys.2023.10.009](https://doi.org/10.1016/j.jphys.2023.10.009)

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Review

The potential roles and mechanisms of Chitinase-3-like-1 in the pathogenesis of type 2-biased airway diseases

[Yian Zhou](#)¹, [Zheng Liu](#)², [Yang Liu](#)³

Affiliations expand

- PMID: 38036279
- DOI: [10.1016/j.clim.2023.109856](https://doi.org/10.1016/j.clim.2023.109856)

Abstract

The immune modulation in the epithelium is a protective feature of the epithelial function in the mucosal airways. Dysfunction of the epithelium can lead to chronic allergic airway inflammatory diseases, such as chronic rhinosinusitis with nasal polyps (CRSwNP), allergic rhinitis (AR), and allergic asthma. Chitinase-3-like-1 (CHI3L1) is a key modulator in the epithelium against irritants, pathogens, and allergens and is involved in cancers, autoimmune diseases, neurological disorders, and other chronic diseases. Induction of epithelial cell-derived CHI3L1 is also confirmed to be implicated in the pathogenesis of Th2-related airway diseases like CRSwNP, AR, and allergic asthma, triggering a cascade of subsequent inflammatory reactions leading to the disease development. The techniques that block the biological function of CHI3L1 include small interfering RNA, neutralizing antibodies, and microRNAs and these methods proved to be successful in preclinical and clinical investigation in cancers, autoimmune diseases, asthma, and chronic obstructive pulmonary disease. Therefore, treatment with CHI3L1-blocking methods could open up therapeutic options for allergic airway diseases. This review article discusses the role of epithelial cell-derived CHI3L1 in the development of CRSwNP, AR, and allergic asthma and examines the use of CHI3L1 as a potential therapeutic agent for allergic airway diseases.

Keywords: Allergic rhinitis; Asthma; Biologic; Chitinase-3-like-1; Nasal polyps; Rhinosinusitis.

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Conflict of interest statement

Declaration of Competing Interest The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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BMJ Open Respir Res



. 2023 Nov 30;10(1):e001454.

doi: 10.1136/bmjresp-2022-001454.

Characteristics of inflammatory phenotypes in patients with chronic obstructive pulmonary disease: a cross-sectional study

[Xiang Wen](#)^{#1,2}, [Zhishan Deng](#)^{#1}, [Jieqi Peng](#)^{#1,3}, [Huajing Yang](#)^{#1}, [Fan Wu](#)^{1,3}, [Cuiqiong Dai](#)¹, [Youlan Zheng](#)¹, [Ningning Zhao](#)¹, [Zihui Wang](#)¹, [Shan Xiao](#)^{1,4}, [Jianwu Xu](#)¹, [Lifei Lu](#)¹, [Xiaohui Wu](#)¹, [Kunning Zhou](#)¹, [Jianwei Dai](#)⁵, [Bing Li](#)⁵, [Pixin Ran](#)^{6,3}, [Yumin Zhou](#)⁶

Affiliations [expand](#)

- PMID: 38035712
- DOI: [10.1136/bmjresp-2022-001454](https://doi.org/10.1136/bmjresp-2022-001454)

Abstract

Background: The relationship between airway inflammation in chronic obstructive pulmonary disease (COPD) and clinical characteristics remains unclear. This study aimed to investigate the airway inflammatory phenotypes in COPD and their association with clinical characteristics.

Methods: 895 patients with COPD were recruited from Guangdong Province, China in this study. Each patient underwent questionnaire interviews, spirometry testing, CT scans and induced sputum examination. Classification of airway inflammation phenotypes was based on sputum inflammatory cell counts. Covariance analysis was applied to assess associations with airway inflammation phenotypes.

Results: In this study, we found that neutrophilic phenotype (NP, 58.0%) was the most common airway inflammation phenotype in patients with COPD, followed by mixed granulocytic phenotype (MGP, 32.6%), eosinophilic phenotype (EP, 5.4%) and paucigranulocytic phenotype (PP, 4.0%). Compared with NP patients, those with MGP exhibited more frequent chronic respiratory symptoms, and a higher proportion of individuals classified under Global Initiative for Chronic Obstructive Lung Disease stages 3 and 4. After adjusting for confounding factors, MGP patients had lower lung function, and more severe emphysema and air trapping. On the contrary, patients with PP had the best pulmonary function and less emphysema and air trapping.

Conclusions: NP was the most common airway inflammation phenotype in patients with COPD. Patients with MGP had more respiratory symptoms, greater loss of lung function, and more severe emphysema and gas trapping compared with those with NP. Meanwhile, PP may be a phenotype of mild damage to lung structure in patients with COPD.

Keywords: COPD epidemiology; Emphysema.

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Conflict of interest statement

Competing interests: None declared.

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Am J Respir Crit Care Med



. 2023 Nov 30.

doi: 10.1164/rccm.202309-1709LE. Online ahead of print.

Is This Really a New START in COPD?

[J Alberto Neder](#)¹

Affiliations expand

- PMID: 38033314
- DOI: [10.1164/rccm.202309-1709LE](https://doi.org/10.1164/rccm.202309-1709LE)

No abstract available

Keywords: DYSPNEA; PULMONARY FUNCTION TESTS; SPIROMETRY.

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Am J Respir Crit Care Med



. 2023 Nov 30.

doi: 10.1164/rccm.202310-1761LE. Online ahead of print.

Use FEV₁/FVC Z-Score Staging to Minimize Sex and Age Bias in Staging Chronic Obstructive Pulmonary Disease

[Brian L Graham](#) ¹

Affiliations expand

- PMID: 38033313
- DOI: [10.1164/rccm.202310-1761LE](https://doi.org/10.1164/rccm.202310-1761LE)

No abstract available

Keywords: COPD staging; z-scores.

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Am J Respir Crit Care Med

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. 2023 Nov 30.

doi: 10.1164/rccm.202310-1739LE. Online ahead of print.

Novel FEV₁/FVC-based Diagnosis and Severity Classification of Chronic Obstructive Pulmonary Disease: How About FEV₁ Percent Predicted Basing?

[Hiroaki Ogata](#)¹, [Yasuyoshi Washio](#)², [Makoto Yoshida](#)³

Affiliations expand

- PMID: 38033312
- DOI: [10.1164/rccm.202310-1739LE](https://doi.org/10.1164/rccm.202310-1739LE)

No abstract available

Keywords: COPD; FEV₁ percent predicted; FEV₁/FVC; PRISm.

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BMC Pulm Med



. 2023 Nov 29;23(1):481.

doi: [10.1186/s12890-023-02771-3](https://doi.org/10.1186/s12890-023-02771-3).

[Sex differences in comorbidities and mortality risk among patients with chronic obstructive pulmonary disease: a study based on NHANES data](#)

[Na Li](#)^{#1}, [Xiaoli Li](#)^{#1}, [Minjie Liu](#)^{#1}, [Yakang Wang](#)², [Junning Wang](#)³

Affiliations expand

- PMID: 38031050

- PMID: [PMC10687794](#)
- DOI: [10.1186/s12890-023-02771-3](#)

Abstract

Background: Patients with chronic obstructive pulmonary disease (COPD) commonly have coexisting comorbidities that contribute to higher exacerbation frequency, poorer health status, and increased all-cause mortality; however, there are only a few studies available on the sex discrepancy in the comorbidity distribution and outcomes among COPD patients, and there is limited information about the discrepancy in all-cause mortality between men and women.

Methods: Based on data from the U.S. National Health and Nutrition Examination Survey conducted between 2007 and 2012, we compared participants aged 40-79 years with spirometry-defined COPD to compare the prevalence of comorbidities between men and women. The survival of the subjects was documented, and the sex discrepancy was determined using Kaplan-Meier analysis. Comorbidities and all-cause mortality were analyzed by using a Cox proportional hazards model to determine their strength of association in different sex groups.

Results: Compared to men, women had a significantly higher prevalence of asthma (OR 1.93, 95% CI 1.46 to 2.57, $p < 0.001$) and arthritis (OR 1.77, 95% CI 1.39 to 2.24, $p < 0.001$). Women had a significantly lower prevalence of coronary heart disease (OR 0.48, 95% CI 0.27 to 0.87, $p = 0.015$) and gout (OR 0.42, 95% CI 0.25 to 0.67, $p = 0.001$). Kaplan-Meier analysis revealed that compared with that of the female group, the survival rate of the male group was significantly lower ($p < 0.001$). Among men, the presence of anemia (HR 2.38, [95% CI 1.52-3.73], $p < 0.001$), gout (HR 1.55, [95% CI 1.04-2.30], $p = 0.029$) and congestive heart failure comorbidities (HR 1.85, [95% CI 1.12-3.04] $p = 0.016$) was associated with a higher risk of mortality; among women, the presence of anemia (HR 2.21, [95% CI 1.17-4.20], $p = 0.015$) and stroke (HR 2.04, [95% CI 1.07-3.88], $p = 0.031$) comorbidities was associated with a higher risk of mortality after adjusting for age, race/Hispanic status, BMI, smoking status, FEV1% predicted and prevalent comorbidities.

Conclusions: COPD-related comorbidities and all-cause mortality were discrepant between men and women, and men had poorer survival than women in the nationally representative data that were analyzed.

Keywords: COPD; Comorbidities; Sex differences; Survival.

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Conflict of interest statement

The authors declare no competing interests.

- [37 references](#)
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SUPPLEMENTARY INFO

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Lancet Respir Med



. 2023 Dec;11(12):1041-1043.

doi: 10.1016/S2213-2600(23)00436-8.

[Chronic obstructive pulmonary disease: hiding in plain sight, a Statement from the COPD Foundation Medical and Scientific Advisory Committee](#)

[Surya P Bhatt](#)¹, [Richard Casaburi](#)², [Alvar Agusti](#)³, [Bartolome R Celli](#)⁴, [Bruce E Miller](#)⁵, [Nirupama Putcha](#)⁶, [Jean Rommes](#)⁷, [Mark T Dransfield](#)⁸; [Medical and Scientific Advisory Committee of the COPD Foundation](#)

Affiliations expand

- PMID: 38030371
- DOI: [10.1016/S2213-2600\(23\)00436-8](https://doi.org/10.1016/S2213-2600(23)00436-8)

No abstract available

Conflict of interest statement

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Ingelheim; honorarium from Integrity Continuing Education for continued medical education. AA declares grants from GSK, AstraZeneca, Chiesi, Sanofi, and Menarini; and consulting or advisory board fees from GSK, AstraZeneca, Chiesi, Menarini, Cipla, Zambon, Sanofi, and Regeneron. BRC reports consulting or advisory board fees or honoraria from GSK, AstraZeneca, Menarini, Sanofi, Axios, and Chiesi; and fees for participation in data safety monitoring boards from AstraZeneca, Sanofi, and Vertex. BEM serves as a contractor and consultant for the COPD Foundation. NP reports grants from the National Institutes of Health; and fees for participation on data safety monitoring boards for CSL Behring, GSK, and Pharmacosmos. NP reports grants from the National Institutes of Health, the American Lung Association, and the Department of Defense; royalties from Up To Date; serves on the Board of Directors of the COPD Foundation (unpaid); and consulting fees from AstraZeneca, Genentech, GSK, Novartis, Pulmonx, and Teva. All other authors declare no competing interests.

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Editorial

Lancet Respir Med

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. 2023 Dec;11(12):1035.

doi: 10.1016/S2213-2600(23)00433-2.

Changing how we see COPD

[The Lancet Respiratory Medicine](#)

- PMID: 38030370

- DOI: [10.1016/S2213-2600\(23\)00433-2](https://doi.org/10.1016/S2213-2600(23)00433-2)

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Observational Study

BMJ

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. 2023 Nov 29;383:e077784.

doi: 10.1136/bmj-2023-077784.

[Air pollution deaths attributable to fossil fuels: observational and modelling study](#)

[Jos Lelieveld](#)^{1,2}, [Andy Haines](#)³, [Richard Burnett](#)⁴, [Cathryn Tonne](#)^{5,6}, [Klaus Klingmüller](#)⁷, [Thomas Münzel](#)⁸, [Andrea Pozzer](#)^{7,2}

Affiliations expand

- PMID: 38030155
- PMCID: [PMC10686100](#)

- DOI: [10.1136/bmj-2023-077784](https://doi.org/10.1136/bmj-2023-077784)

Free PMC article

Abstract

Objectives: To estimate all cause and cause specific deaths that are attributable to fossil fuel related air pollution and to assess potential health benefits from policies that replace fossil fuels with clean, renewable energy sources.

Design: Observational and modelling study.

Methods: An updated atmospheric composition model, a newly developed relative risk model, and satellite based data were used to determine exposure to ambient air pollution, estimate all cause and disease specific mortality, and attribute them to emission categories.

Data sources: Data from the global burden of disease 2019 study, observational fine particulate matter and population data from National Aeronautics and Space Administration (NASA) satellites, and atmospheric chemistry, aerosol, and relative risk modelling for 2019.

Results: Globally, all cause excess deaths due to fine particulate and ozone air pollution are estimated at 8.34 million (95% confidence interval 5.63 to 11.19) deaths per year. Most (52%) of the mortality burden is related to cardiometabolic conditions, particularly ischaemic heart disease (30%). Stroke and chronic obstructive pulmonary disease both account for 16% of mortality burden. About 20% of all cause mortality is undefined, with arterial hypertension and neurodegenerative diseases possibly implicated. An estimated 5.13 million (3.63 to 6.32) excess deaths per year globally are attributable to ambient air pollution from fossil fuel use and therefore could potentially be avoided by phasing out fossil fuels. This figure corresponds to 82% of the maximum number of air pollution deaths that could be averted by controlling all anthropogenic emissions. Smaller reductions, rather than a complete phase-out, indicate that the responses are not strongly non-linear. Reductions in emission related to fossil fuels at all levels of air pollution can decrease the number of attributable deaths substantially. Estimates of avoidable excess deaths are markedly higher in this study than most previous studies for these reasons: the new relative risk model has implications for high income (largely fossil fuel intensive) countries and for low and middle income countries where the use of fossil fuels is increasing; this study accounts for all cause mortality in addition to disease specific mortality; and the large reduction in air pollution from a fossil fuel phase-out can greatly reduce exposure.

Conclusion: Phasing out fossil fuels is deemed to be an effective intervention to improve health and save lives as part the United Nations' goal of climate neutrality by 2050. Ambient air pollution would no longer be a leading, environmental health risk factor if the use of fossil fuels were superseded by equitable access to clean sources of renewable energy.

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Conflict of interest statement

Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/disclosure-of-interest/ and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

- [46 references](#)
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Am J Respir Crit Care Med

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. 2023 Nov 29.

doi: 10.1164/rccm.202308-1436OC. Online ahead of print.

[Prevalence, Diagnostic Utility and Associated Characteristics of Bronchodilator Responsiveness](#)

[Richard Beasley](#)¹, [Rod Hughes](#)², [Alvar Agusti](#)³, [Peter Calverley](#)⁴, [Bradley Chipps](#)⁵, [Ricardo Del Olmo](#)⁶, [Alberto Papi](#)⁷, [David Price](#)^{8,9,10}, [Helen Reddel](#)^{11,12}, [Hana Mullerova](#)², [Eleni Rapsomaniki](#)²

Affiliations [expand](#)

- PMID: 38029294

- DOI: [10.1164/rccm.202308-1436OC](https://doi.org/10.1164/rccm.202308-1436OC)

Abstract

Background: The prevalence and diagnostic utility of bronchodilator responsiveness (BDR) in a real-life setting is unclear. We explored this uncertainty in patients aged ≥ 12 years with physician-assigned diagnoses of asthma, asthma and COPD, or COPD in NOVELTY, a prospective cohort study in primary and secondary care in 18 countries.

Methods: The proportion of patients with a positive BDR test in each diagnostic category was calculated using 2005 (ΔFEV_1 or $\Delta\text{FVC} \geq 12\%$ and $\geq 200\text{mL}$) and 2021 (ΔFEV_1 or $\Delta\text{FVC} > 10\%$ predicted) ERS/ATS criteria.

Results: We studied 3,519 patients with physician-assigned diagnosis of asthma, 833 with asthma+COPD, and 2,436 with COPD. The prevalence of BDR was 19.7% (asthma), 29.6% (asthma+COPD) and 24.7% (COPD) using 2005 criteria; 18.1%, 23.3% and 18.0% respectively using 2021 criteria. Using 2021 criteria, in patients diagnosed with asthma, BDR was associated with higher FeNO, lower lung function, higher symptom burden, more frequent hospital admissions, greater use of triple therapy, oral corticosteroids or biologics; in patients diagnosed with COPD, BDR (2021) was associated with lower lung function and higher symptom burden.

Conclusions: BDR prevalence in patients with chronic airway diseases on treatment ranges from 18-30%, being modestly lower with the 2021 compared with 2005 ERS/ATS criteria, and is associated with lower lung function and greater symptom burden. These observations question the validity of BDR as a key diagnostic tool for asthma managed in clinical practice or as a standard inclusion criterion for clinical trials of asthma, and instead suggest BDR be considered a treatable trait for chronic airways disease.

Keywords: asthma; bronchodilator responsiveness; chronic obstructive pulmonary disease; diagnosis.

FULL TEXT LINKS



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. 2023 Nov 26;15(11):e49430.

Role of Screening Lung Function Tests in a Routine Health Checkup

[Shankar Iyer](#)¹, [S P Raj](#)¹, [Sumeet Singhania](#)¹, [Caroline Simon](#)¹

Affiliations expand

- PMID: 38024041
- PMCID: [PMC10679964](#)
- DOI: [10.7759/cureus.49430](#)

Abstract

Background and objectives The lung function test is a gold standard, guideline-recommended test to detect obstructive airway diseases like asthma and COPD. It is of considerable value in detecting the presence and severity of airflow obstruction in patients with respiratory symptoms. However, the role of spirometry in a routine health checkup is controversial. Spirometry, when used in routine health checkup settings as a case-finding tool for all adults with persistent respiratory symptoms or having a history of exposure to risk factors, is likely to label a relatively large proportion of individuals as diseased with airflow obstruction. Conversely, spirometry is normal in a relatively large percentage of adults who report respiratory symptoms including dyspnea, the respiratory symptom having the greatest impact on quality of life. The objective of this study is to determine the utility of spirometry as a screening test to detect airflow obstruction in otherwise healthy subjects undergoing a routine health checkup. **Methods** This observational study was conducted with 538 health checkup individuals aged 18 and over. A brief history was taken prior to the test. Lung function tests were performed and interpreted as per the Global Initiative for Chronic Obstructive Lung Disease criteria. The anthropometric and spirometric data obtained were compared to other population-based spirometric studies to compare the prevalence of airflow limitation, the risk factors, and smoking history. **Results** Of the total 538 subjects incorporated in the study, 305 (57%) were males and 233 (43%) were females aged between 18 to 80 years with a mean age of 45 years. The male-to-female ratio was 1.3:1 with a mean BMI of 25.9. The overall yield from lung function tests in detecting airflow obstruction was 63 subjects (11.7%), of which 36 (11.8%) were males and 27 (11.5%) were females. Seventy-three subjects (13.5%) were classified as having a small airway obstruction, of which 34 were males (46.6%), and 39 were females (53.4%). The distribution of airflow obstruction by age was with eight subjects (5.4%) in the 18-35 group, 21 subjects (7.8%) in the 36-55 group, and 34 (25%) in the elderly (>55) age group. Although overall smoking history showed no significant association with developing airflow obstruction, significant association with smoking was found in the elderly (>55) age group. **Interpretation and conclusions** The results of the study suggest that lung function tests should be included in routine health checkups in the subset of individuals greater than 35 years of age with or without a history of smoking, in all age groups with a family history of asthma, in individuals with

respiratory symptoms and in individuals greater than 55 years of age with a moderate history of smoking.

Keywords: "spirometry"; air flow obstruction; health checkup; lung function test; obstructive airway diseases; smoking.

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Conflict of interest statement

The authors have declared that no competing interests exist.

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

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. 2023 Nov 27;9(6):00686-2023.

doi: 10.1183/23120541.00686-2023. eCollection 2023 Nov.

Exhaled nitric oxide, eosinophils and current smoking in COPD patients

[Andrew Higham](#)¹, [Augusta Beech](#)^{1,2}, [James Dean](#)^{1,2}, [Dave Singh](#)^{1,2}

Affiliations expand

- PMID: 38020571

- PMCID: [PMC10680026](#)

- DOI: [10.1183/23120541.00686-2023](https://doi.org/10.1183/23120541.00686-2023)

Abstract

High F_{ENO} can occur despite low blood eosinophil counts in ex-smokers, while a minority of current smokers have elevated F_{ENO} that is not related to eosinophil counts. F_{ENO} levels may be related to noneosinophilic mechanisms in a subgroup of COPD. <https://bit.ly/3PSWvM2>.

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Conflict of interest statement

Conflict of interest: A. Higham has received personal fees from Chiesi. Conflict of interest: D. Singh has received personal fees from Aerogen, AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, CSL Behring, Epidendo, Genentech, GlaxoSmithKline, Glenmark, Gossamerbio, Kinaset, Menarini, Novartis, Orion, Pulmatrix, Sanofi, Synairgen, Teva, Theravance and Verona. Conflict of interest: A. Beech and J. Dean have no conflicts of interest to declare.

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

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. 2023 Nov 27;9(6):00548-2023.

doi: 10.1183/23120541.00548-2023. eCollection 2023 Nov.

Systematic review and meta-analysis of prevalence of undiagnosed major cardiac comorbidities in COPD

[Joseph Kibbler^{1,2}](#), [Clare Wade³](#), [Grace Mussell¹](#), [David P Ripley¹](#), [Stephen C Bourke^{1,2}](#), [John Steer^{1,3}](#)

Affiliations expand

- PMID: 38020568
- PMCID: [PMC10680032](#)
- DOI: [10.1183/23120541.00548-2023](#)

Abstract

Background: It is often stated that heart disease is underdiagnosed in COPD. Evidence for this statement comes from primary studies, but these have not been synthesised to provide a robust estimate of the burden of undiagnosed heart disease.

Methods: A systematic review of studies using active diagnostic techniques to establish the prevalence of undiagnosed major cardiac comorbidities in patients with COPD was carried out. MEDLINE, Embase, Scopus and Web of Science were searched for terms relating to heart failure (specifically, left ventricular systolic dysfunction (LVSD), coronary artery disease (CAD) and atrial fibrillation), relevant diagnostic techniques and COPD. Studies published since 1980, reporting diagnosis rates using recognised diagnostic criteria in representative COPD populations not known to have heart disease were included. Studies were classified by condition diagnosed, diagnostic threshold used and whether participants had stable or exacerbated COPD. Random-effects meta-analysis of prevalence was conducted where appropriate.

Results: In general, prevalence estimates for undiagnosed cardiac comorbidities in COPD had broad confidence intervals, with significant study heterogeneity. Most notably, a prevalence of undiagnosed LVSD of 15.8% (11.1-21.1%) was obtained when defined as left ventricular ejection fraction <50%. Undiagnosed CAD was found in 2.3-18.0% of COPD patients and atrial fibrillation in 1.4% (0.3-3.5%).

Conclusion: Further studies using recent diagnostic advances, and investigating therapeutic interventions for patients with COPD and heart disease are needed.

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Conflict of interest statement

Conflict of interest: The authors have nothing to disclose.

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

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Review

J Med Internet Res

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. 2023 Nov 29:25:e49639.

doi: 10.2196/49639.

[Consideration of Sex, Gender, or Age on Outcomes of Digital Technologies for Treatment and Monitoring of Chronic Obstructive Pulmonary Disease: Overview of Systematic Reviews](#)

[Katja Matthias](#)¹, [Ivonne Honekamp](#)², [Monique Heinrich](#)¹, [Karina Karolina De Santis](#)³

Affiliations expand

- PMID: 38019578
- DOI: [10.2196/49639](https://doi.org/10.2196/49639)

Abstract

Background: Several systematic reviews have addressed digital technology use for treatment and monitoring of chronic obstructive pulmonary disease (COPD).

Objective: This study aimed to assess if systematic reviews considered the effects of sex, gender, or age on the outcomes of digital technologies for treatment and monitoring of COPD through an overview of such systematic reviews. The objectives of this overview were to (1) describe the definitions of sex or gender used in reviews; (2) determine whether the consideration of sex, gender, or age was planned in reviews; (3) determine whether sex, gender, or age was reported in review results; (4) determine whether sex, gender, or age was incorporated in implications for clinical practice in reviews; and (5) create an evidence map for development of individualized clinical recommendations for COPD based on sex, gender, or age diversity.

Methods: MEDLINE, the Cochrane Library, Epistemonikos, Web of Science, and the bibliographies of the included systematic reviews were searched to June 2022. Inclusion was based on the PICOS framework: (1) population (COPD), (2) intervention (any digital technology), (3) comparison (any), (4) outcome (any), and (5) study type (systematic review). Studies were independently selected by 2 authors based on title and abstract and full-text screening. Data were extracted by 1 author and checked by another author. Data items included systematic review characteristics; PICOS criteria; and variables related to sex, gender, or age. Systematic reviews were appraised using A Measurement Tool to Assess Systematic Reviews, version 2 (AMSTAR 2). Data were synthesized using descriptive statistics.

Results: Of 1439 records, 30 systematic reviews published between 2010 and 2022 were included in this overview. The confidence in the results of 25 of the 30 (83%) reviews was critically low according to AMSTAR 2. The reviews focused on user outcomes that potentially depend on sex, gender, or age, such as efficacy or effectiveness (25/30, 83%) and acceptance, satisfaction, or adherence (3/30, 10%) to digital technologies for COPD. Reviews reported sex or gender (19/30 systematic reviews) or age (25/30 systematic reviews) among primary study characteristics. However, only 1 of 30 reviews included age in a subgroup analysis, and 3 of 30 reviews identified the effects of sex, gender, or age as evidence gaps.

Conclusions: This overview shows that the effects of sex, gender, or age were rarely considered in 30 systematic reviews of digital technologies for COPD treatment and monitoring. Furthermore, systematic reviews did not incorporate sex, gender, nor age in their implications for clinical practice. We recommend that future systematic reviews should (1) evaluate the effects of sex, gender, or age on the outcomes of digital technologies for treatment and monitoring of COPD and (2) better adhere to reporting guidelines to improve the confidence in review results.

Trial registration: PROSPERO CRD42022322924;
https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=322924.

International registered report identifier (irrid): RR2-10.2196/40538.

Keywords: AMSTAR 2; COPD; age; chronic disease; chronic illness; chronic obstructive pulmonary disease; critical appraisal; digital intervention; digital technologies; gender; monitoring; outcome reporting; overview; review methodology; sex; systematic review; treatment.

©Katja Matthias, Ivonne Honekamp, Monique Heinrich, Karina Karolina De Santis. Originally published in the Journal of Medical Internet Research (<https://www.jmir.org>), 29.11.2023.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Clin Cardiol

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. 2023 Nov 29.

doi: 10.1002/clc.24189. Online ahead of print.

Factors associated with disease progression in patients with atrial fibrillation and heart failure anticoagulated with rivaroxaban

[Nicolás Manito](#)¹, [José María Cepeda-Rodrigo](#)², [Nuria Farré](#)³, [Miguel Castillo Orive](#)⁴, [Enrique Galve](#)⁵, [Javier Jiménez-Candil](#)⁶, [José M García-Pinilla](#)^{7,8,9,10}, [Eduardo Sebastián López Sánchez](#)¹¹, [Carles Rafols](#)¹², [Juan José Gómez Doblas](#)^{7,8,9,10}

Affiliations expand

- PMID: 38018889
- DOI: [10.1002/clc.24189](https://doi.org/10.1002/clc.24189)

Free article

Abstract

Background: Patients with atrial fibrillation (AF) and heart failure (HF) have a high risk of thromboembolism and other outcomes and anticoagulation is recommended.

Hypothesis: This study was aimed to explore the risk factors associated with HF worsening in patients with AF and HF taking rivaroxaban in Spain.

Methods: Multicenter, prospective, observational study that included adults with AF and chronic HF, receiving rivaroxaban ≥ 4 months before entering. HF worsening was defined as first hospitalization or emergency visit because of HF exacerbation.

Results: A total of 672 patients from 71 Spanish centers were recruited, of whom 658 (97.9%) were included in the safety analysis and 552 (82.1%) in the per protocol analysis. At baseline, mean age was 73.7 ± 10.9 years, 64.9% were male, CHA₂ DS₂ -VASc was 4.1 ± 1.5 , HAS-BLED was 1.6 ± 0.9 and 51.3% had HF with preserved ejection fraction. After 24 months of follow-up, 24.9% of patients developed HF worsening, 11.6% died, 2.9% had a thromboembolic event, 3.1% a major bleeding, 0.5% an intracranial bleeding and no patient had a fatal hemorrhage. Older age, the history of chronic obstructive pulmonary disease, the previous use of vitamin K antagonists, and restrictive or infiltrative cardiomyopathies, were independently associated with HF worsening. Only 6.9% of patients permanently discontinued rivaroxaban treatment.

Conclusions: Approximately one out of four patients with HF and AF treated with rivaroxaban developed a HF worsening episode after 2 years of follow-up. The identification of those factors that increase the risk of HF worsening could be helpful in the comprehensive management of this population.

Keywords: anticoagulation; atrial fibrillation; direct oral anticoagulant; heart failure; rivaroxaban; worsening heart failure.

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- [40 references](#)

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Grants and fundingexpand

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Clinical Utility of Chest Sonography in COPD Patients with a Focus on Diaphragmatic Measurements

[Hend M Esmaeel¹](#), [Kamal A Atta¹](#), [Safiya Khalaf¹](#), [Doaa Gadallah¹](#)

Affiliations expand

- PMID: 38018039
- DOI: [10.4046/trd.2023.0030](https://doi.org/10.4046/trd.2023.0030)

Free article

Abstract

Background: There are many methods of evaluating diaphragmatic function, such as trans-diaphragmatic pressure measurements, which are considered the key rule of diagnosis, we studied the clinical usefulness of chest ultrasonography in evaluating stable COPD patients and those in exacerbation, we focus on diaphragmatic measurements and their correlation to spirometry and other clinical parameters.

Methods: In a prospective case control study, we enrolled 100 COPD patients divided into 40 stable COPD patients and 60 patients with exacerbation. The analysis included 20 age-matched controls. In addition to the clinical assessment of the study population, radiological evaluation included chest radiographs and chest computed tomography. Transthoracic ultrasonography (TUS) was done for all included subjects.

Results: Multiple A lines (more than 3) were more frequent in COPD exacerbation than in stable patients, the same for B Lines. TUS significantly showed high specificity, negative predictive value (NPV), positive predictive value (PPV), and accuracy in detecting pleural effusion, consolidation, pneumothorax, and lung mass. Diaphragmatic measurements were significantly lower among stable COPD subjects than healthy controls. Diaphragmatic thickness and excursion illustrated a significant negative correlation with BMI and dyspnea scale and a positive correlation with spirometry measures. Patients in GOLD group D showed lower diaphragmatic measurements (thickness and excursion).

Conclusion: The TUS of COPD patients both in stable and exacerbated conditions and the assessment of diaphragm excursion and thickness by TUS in COPD patients and their correlations to disease-related factors proved informative and paved the way for the better management of COPD patients.

Keywords: COPD; chest ultrasound; diaphragm excursion; diaphragm thickness.

FULL TEXT LINKS



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Respir Res



. 2023 Nov 28;24(1):299.

doi: 10.1186/s12931-023-02611-2.

[Deep learning parametric response mapping from inspiratory chest CT scans: a new approach for small airway disease screening](#)

[Bin Chen](#) ^{#12}, [Ziyi Liu](#) ^{#345}, [Jinjuan Lu](#) ^{#6}, [Zhihao Li](#) ³⁴⁵, [Kaiming Kuang](#) ⁷⁸, [Jiancheng Yang](#) ⁷⁹, [Zengmao Wang](#) ³⁴⁵, [Yingli Sun](#) ¹², [Bo Du](#) ¹⁰¹¹¹², [Lin Qi](#) ¹³¹⁴, [Ming Li](#) ¹⁵¹⁶

Affiliations expand

- PMID: 38017476

- PMCID: [PMC10683250](#)

- DOI: [10.1186/s12931-023-02611-2](https://doi.org/10.1186/s12931-023-02611-2)

Free PMC article

Abstract

Objectives: Parametric response mapping (PRM) enables the evaluation of small airway disease (SAD) at the voxel level, but requires both inspiratory and expiratory chest CT scans. We hypothesize that deep learning PRM from inspiratory chest CT scans can effectively evaluate SAD in individuals with normal spirometry.

Methods: We included 537 participants with normal spirometry, a history of smoking or secondhand smoke exposure, and divided them into training, tuning, and test sets. A cascaded generative adversarial network generated expiratory CT from inspiratory CT, followed by a UNet-like network predicting PRM using real inspiratory CT and generated expiratory CT. The performance of the prediction is evaluated using SSIM, RMSE and dice coefficients. Pearson correlation evaluated the correlation between predicted and ground truth PRM. ROC curves evaluated predicted PRM^{fSAD} (the volume percentage of functional small airway disease, fSAD) performance in stratifying SAD.

Results: Our method can generate expiratory CT of good quality (SSIM 0.86, RMSE 80.13 HU). The predicted PRM dice coefficients for normal lung, emphysema, and fSAD regions are 0.85, 0.63, and 0.51, respectively. The volume percentages of emphysema and fSAD showed good correlation between predicted and ground truth PRM ($|r|$ were 0.97 and 0.64, respectively, $p < 0.05$). Predicted PRM^{fSAD} showed good SAD stratification performance with ground truth PRM^{fSAD} at thresholds of 15%, 20% and 25% (AUCs were 0.84, 0.78, and 0.84, respectively, $p < 0.001$).

Conclusion: Our deep learning method generates high-quality PRM using inspiratory chest CT and effectively stratifies SAD in individuals with normal spirometry.

Keywords: Computed tomography; Deep learning; Parametric response mapping; Small airways.

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Conflict of interest statement

The authors declare that they have no competing interests.

- [45 references](#)
- [6 figures](#)

SUPPLEMENTARY INFO

MeSH terms, Supplementary concepts, Grants and fundingexpand

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Review

J Aerosol Med Pulm Drug Deliv

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. 2023 Nov 28.

doi: 10.1089/jamp.2023.29104.ajh. Online ahead of print.

Dry Powder Inhalers: An Overview

[Anthony J Hickey](#)¹

Affiliations expand

- PMID: 38016133
- DOI: [10.1089/jamp.2023.29104.ajh](https://doi.org/10.1089/jamp.2023.29104.ajh)

Abstract

Dry powder inhaler products have played an important role in the treatment and prevention of asthma and more recently chronic obstructive pulmonary disease. The considerations that go into formulation development to support these products cover a unique range of disciplines including analytical and physical chemistry, aerosol physics, device technology, process engineering and industrial design. An enormous research effort has been expended in the last half century to provide understanding of this complex dosage form. The guiding principles in considering the development of dry powder inhaler products encompass requirements for disease therapy, advantages and limitations of adopting certain technological approaches, and desirable features to facilitate patient use, which are all embodied in the target product profile.

Keywords: aerosol; dose-metering systems; drug formulation; inhalation devices; inhaler design; milling; spray drying.

SUPPLEMENTARY INFO

Publication typesexpand

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Review

Rev Environ Health



. 2023 Nov 29.

doi: 10.1515/reveh-2023-0135. Online ahead of print.

Prevalence of chronic obstructive pulmonary disease in Indian nonsmokers: a systematic review & meta-analysis

[Tejas M Suri](#)¹, [Tamoghna Ghosh](#)², [Saurabh Mittal](#)¹, [Vijay Hadda](#)¹, [Karan Madan](#)¹, [Anant Mohan](#)¹

Affiliations expand

- PMID: 38016010
- DOI: [10.1515/reveh-2023-0135](https://doi.org/10.1515/reveh-2023-0135)

Abstract

Introduction: Nonsmokers with chronic obstructive pulmonary disease (COPD) are neglected despite constituting half of all cases in studies from the developed world. Herein, we systematically reviewed the prevalence of COPD among nonsmokers in India.

Content: We searched Embase, Scopus, and PubMed databases for studies examining the prevalence of COPD among nonsmokers in India. We used the Joanna Briggs Institute (JBI) checklist to assess included studies' quality. Meta-analysis was performed using random-effects model.

Summary: Seven studies comprising 6,903 subjects were included. The quality of the studies ranged from 5/9 to 8/9. The prevalence of COPD varied between 1.6 and 26.6 %. Studies differed considerably in demographics and biomass exposure profiles of subjects. Among the four studies that enrolled both middle-aged and elderly Indian nonsmokers not screened based on biomass fuel exposure, the pooled prevalence of COPD was 3 % (95 % CI, 2-3 %; $I^2=50.52$ %, $p=0.11$). The pooled prevalence of COPD among biomass fuel-exposed individuals was 10 % (95 % CI, 2-18 %; $I^2=98.8$ %, $p<0.001$).

Outlook: Limited evidence suggests a sizable burden of COPD among nonsmokers and biomass fuel-exposed individuals in India. More epidemiological studies of COPD in nonsmokers are needed from low and middle-income countries.

Keywords: India; biomass fuel; chronic obstructive pulmonary disease; epidemiology; nonsmoker; prevalence.

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NPJ Digit Med

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. 2023 Nov 27;6(1):222.

Wearable technology interventions in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis

[Amar J Shah](#)^{1,2}, [Malik A Althobiani](#)^{2,3}, [Anita Saigal](#)^{1,2}, [Chibueze E Ogbonnaya](#)⁴, [John R Hurst](#)^{1,2}, [Swapna Mandal](#)^{5,6}

Affiliations expand

- PMID: 38012218
- PMCID: [PMC10682416](#)
- DOI: [10.1038/s41746-023-00962-0](#)

Free PMC article

Abstract

Chronic obstructive pulmonary disease (COPD) is the third leading cause of death and is associated with multiple medical and psychological comorbidities. Therefore, future strategies to improve COPD management and outcomes are needed for the betterment of patient care. Wearable technology interventions offer considerable promise in improving outcomes, but prior reviews fall short of assessing their role in the COPD population. In this systematic review and meta-analysis we searched ovid-MEDLINE, ovid-EMBASE, CINAHL, CENTRAL, and IEEE databases from inception to April 2023 to identify studies investigating wearable technology interventions in an adult COPD population with prespecified outcomes of interest including physical activity promotion, increasing exercise capacity, exacerbation detection, and quality-of-life. We identified 7396 studies, of which 37 were included in our review. Meta-analysis showed wearable technology interventions significantly increased: the mean daily step count (mean difference (MD) 850 (494-1205) steps/day) and the six-minute walk distance (MD 5.81 m (1.02-10.61 m)). However, the impact was short-lived. Furthermore, wearable technology coupled with another facet (such as health coaching or pulmonary rehabilitation) had a greater impact than wearable technology alone. Wearable technology had little impact on quality-of-life measures and had mixed results for exacerbation avoidance and prediction. It is clear that wearable technology interventions may have the potential to form a core part of future COPD management plans, but further work is required to translate this into meaningful clinical benefit.

Conflict of interest statement

A.J.S. and S.M. have received grants from Acurable Ltd. The payments have been made to their institutions. These grants are not linked to the current manuscript. J.R.H. has received support to attend meetings, personal payment and payment to his institution from pharmaceutical companies that make medicines to treat COPD. All other authors have no conflicts of interest to declare.

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

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nature portfolio [UNIMORE](#) 

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PLoS One

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. 2023 Nov 27;18(11):e0289373.

doi: 10.1371/journal.pone.0289373. eCollection 2023.

[Route of administration significantly affects particle deposition and cellular recruitment](#)

[Keziyah Yisrael](#)^{1,2}, [Ryan W Drover](#)^{3,4}, [Malia L Shapiro](#)^{1,2}, [Martha Anguiano](#)¹, [Nala Kachour](#)^{1,2}, [Qi Li](#)^{3,4}, [Emily Tran](#)¹, [David R Cocker 3rd](#)^{3,4}, [David D Lo](#)^{1,2,5}

Affiliations [expand](#)

- PMID: 38011140
- PMCID: [PMC10681169](#)

- DOI: [10.1371/journal.pone.0289373](https://doi.org/10.1371/journal.pone.0289373)

Free PMC article

Abstract

Lung exposures to dusts, pollutants, and other aerosol particulates are known to be associated with pulmonary diseases such as asthma and Chronic Obstructive Pulmonary Disease. These health impacts are attributed to the ability of aerosol components to induce pulmonary inflammation, which promotes tissue remodeling, including fibrosis, tissue degradation, and smooth muscle proliferation. Consequently, the distribution of these effects can have a significant impact on the physiologic function of the lung. In order to study the impact of distribution of inhaled particulates on lung pathogenesis, we compared the effect of different methods of particle delivery. By comparing intranasal versus aerosol delivery of fluorescent microspheres, we observed strikingly distinct patterns of particle deposition; intranasal delivery provided focused deposition concentrated on larger airways, while aerosol delivery showed uniform deposition throughout the lung parenchyma. Recognizing that the impacts of inflammatory cells are contingent upon their recruitment and behavior, we postulate that these variations in distribution patterns can result in significant alterations in biological responses. To elucidate the relevance of these findings in terms of biological representation, we subsequently conducted an investigation into the responses elicited by the administration of endotoxin (bacterial Lipopolysaccharide, or LPS) in a transgenic neutrophil reporter mouse model. As with the microsphere results, patterns of recruited neutrophil inflammatory responses matched the delivery method; that is, despite the active migratory behavior of neutrophils, inflammatory histopathology patterns were either focused on large airways (intranasal administration) or diffusely throughout the parenchyma (aerosol). These results demonstrate the importance of modes of aerosol delivery as different patterns of inflammation and tissue remodeling will have distinct impacts on lung physiology.

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Conflict of interest statement

The authors have declared that no competing interests exist.

- [17 references](#)
- [10 figures](#)

SUPPLEMENTARY INFO

MeSH terms, Substances, Grants and funding [expand](#)

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Review

J Comp Eff Res

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. 2023 Dec;12(12):e230136.

doi: 10.57264/cer-2023-0136. Epub 2023 Nov 24.

Rational use of inhaled corticosteroids for the treatment of COPD: a plain language summary

[Amnon Ariel](#)¹, [Peter J Barnes](#)², [Tiago Maricoto](#)^{3,4,5}, [Miguel Román-Rodríguez](#)⁶, [Andy Powell](#)⁷, [Jennifer K Quint](#)²

Affiliations expand

- PMID: 38009437
- DOI: [10.57264/cer-2023-0136](https://doi.org/10.57264/cer-2023-0136)

Free article

Abstract

What is this summary about?: Inhaled corticosteroids (ICS) are a type of medication delivered via an inhaler device that are commonly used in the treatment of asthma. ICS can also be used to treat chronic obstructive pulmonary disease (COPD), a progressive respiratory condition in which the lungs become worse over time. However, unlike in asthma, ICS are only effective in a small proportion of people with COPD. ICS can cause significant side effects in people with COPD, including pneumonia. Because of this, guidelines written by COPD experts recommend that ICS should largely be prescribed to people with COPD whose symptoms flare up frequently and become difficult to manage (episodes known as exacerbations). Despite this guidance, records collected from routine clinical practice suggest that many healthcare professionals prescribe ICS to people with COPD who do not have frequent exacerbations, putting them at unnecessary risk of side

effects. The over-prescription of ICS in COPD may partly be due to the recent introduction of single-inhaler combination therapies, which combine ICS with other medicines (bronchodilators). This 'one inhaler for all' approach is a concerning trend as it goes against global COPD treatment guidelines, which recommend ICS use in only a small proportion of people. This is a plain language summary of a review article originally published in the journal *NPJ Primary Care Respiratory Medicine*. In this review, we investigate the benefits and risks of ICS use in COPD. Using data from both randomized controlled trials (RCTs) and observational studies, we explain which people benefit from ICS use, and why health regulatory bodies have concluded that ICS do not help people with COPD to live longer. Lastly, we provide practical guidance for doctors and people with COPD regarding when ICS should be prescribed and when they should be withdrawn.

Keywords: ICS; LAMA/LABA; chronic obstructive pulmonary disease COPD; inhaled corticosteroids; lay summary; long-acting bronchodilators; observational study; plain language summary; randomized controlled trial; real-world evidence; treatment guidelines.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Editorial

Respir Care

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. 2023 Dec;68(12):1775-1778.

doi: 10.4187/respcare.11573.

[What Are We Aiming for in Chronic Hypercapnic Respiratory Failure?](#)

[Brian W Locke](#)¹, [Jeanette Brown](#)²

Affiliations expand

- PMID: 38007234
- PMCID: PMC10676247 (available on 2024-12-01)
- DOI: [10.4187/respcare.11573](https://doi.org/10.4187/respcare.11573)

No abstract available

Conflict of interest statement

Dr Locke discloses relationships with American Thoracic Society, and the National Institutes of Health. Dr Brown has disclosed no conflicts of interest.

- [24 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Meta-Analysis

Lancet Digit Health

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- . 2023 Dec;5(12):e872-e881.
- doi: 10.1016/S2589-7500(23)00177-2.

Machine learning and deep learning predictive models for long-term prognosis in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis

[Luke A Smith](#)¹, [Lauren Oakden-Rayner](#)², [Alix Bird](#)², [Minyan Zeng](#)², [Minh-Son To](#)³, [Sutapa Mukherjee](#)⁴, [Lyle J Palmer](#)²

Affiliations [expand](#)

- PMID: 38000872
- DOI: [10.1016/S2589-7500\(23\)00177-2](https://doi.org/10.1016/S2589-7500(23)00177-2)

Free article

Abstract

Background: Machine learning and deep learning models have been increasingly used to predict long-term disease progression in patients with chronic obstructive pulmonary disease (COPD). We aimed to summarise the performance of such prognostic models for COPD, compare their relative performances, and identify key research gaps.

Methods: We conducted a systematic review and meta-analysis to compare the performance of machine learning and deep learning prognostic models and identify pathways for future research. We searched PubMed, Embase, the Cochrane Library, ProQuest, Scopus, and Web of Science from database inception to April 6, 2023, for studies in English using machine learning or deep learning to predict patient outcomes at least 6 months after initial clinical presentation in those with COPD. We included studies comprising human adults aged 18-90 years and allowed for any input modalities. We reported area under the receiver operator characteristic curve (AUC) with 95% CI for predictions of mortality, exacerbation, and decline in forced expiratory volume in 1 s (FEV₁). We reported the degree of interstudy heterogeneity using Cochran's Q test (significant heterogeneity was defined as $p \leq 0.10$ or $I^2 > 50\%$). Reporting quality was assessed using the TRIPOD checklist and a risk-of-bias assessment was done using the PROBAST checklist. This study was registered with PROSPERO (CRD42022323052).

Findings: We identified 3620 studies in the initial search. 18 studies were eligible, and, of these, 12 used conventional machine learning and six used deep learning models. Seven models analysed exacerbation risk, with only six reporting AUC and 95% CI on internal validation datasets (pooled AUC 0.77 [95% CI 0.69-0.85]) and there was significant heterogeneity (I^2 97%, $p < 0.0001$). 11 models analysed mortality risk, with only six reporting AUC and 95% CI on internal validation datasets (pooled AUC 0.77 [95% CI 0.74-0.80]) with significant degrees of heterogeneity (I^2 60%,

$p=0.027$). Two studies assessed decline in lung function and were unable to be pooled. Machine learning and deep learning models did not show significant improvement over pre-existing disease severity scores in predicting exacerbations ($p=0.24$). Three studies directly compared machine learning models against pre-existing severity scores for predicting mortality and pooled performance did not differ ($p=0.57$). Of the five studies that performed external validation, performance was worse than or equal to regression models. Incorrect handling of missing data, not reporting model uncertainty, and use of datasets that were too small relative to the number of predictive features included provided the largest risks of bias.

Interpretation: There is limited evidence that conventional machine learning and deep learning prognostic models demonstrate superior performance to pre-existing disease severity scores. More rigorous adherence to reporting guidelines would reduce the risk of bias in future studies and aid study reproducibility.

Funding: None.

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Conflict of interest statement

Declaration of interests LAS and AB are supported by GlaxoSmithKline. LO-R received stocks from Sirona Medical Imaging as a consultant on artificial intelligence development and implementation. All other authors declare no competing interests.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Am J Prev Med

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. 2023 Dec;65(6):1198-1199.

doi: 10.1016/j.amepre.2023.09.011.

Author Response to Issues for Studies on E-cigarettes and Chronic Obstructive Pulmonary Disorder

[Steven F Cook¹](#), [Nancy L Fleischer²](#), [Douglas A Arenberg³](#), [Rafael Meza⁴](#)

Affiliations expand

- PMID: 37981347
- DOI: [10.1016/j.amepre.2023.09.011](https://doi.org/10.1016/j.amepre.2023.09.011)

No abstract available

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Publication types, MeSH termsexpand

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32

Am J Prev Med

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. 2023 Dec;65(6):1196-1197.

doi: 10.1016/j.amepre.2023.09.009.

Issues for Studies on E-cigarettes and Chronic Obstructive Pulmonary Disorder

[Thomas A Wills](#)¹, [Wubin Xie](#)², [Andrew C Stokes](#)³

Affiliations expand

- PMID: 37981346
- DOI: [10.1016/j.amepre.2023.09.009](https://doi.org/10.1016/j.amepre.2023.09.009)

No abstract available

SUPPLEMENTARY INFO

Publication types, MeSH terms expand

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33

Review

Sleep Med

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. 2023 Dec;112:282-290.

doi: 10.1016/j.sleep.2023.10.034. Epub 2023 Nov 6.

[Prevalence and clinical characteristics of sleep disorders in chronic obstructive pulmonary disease: A systematic review and meta-analysis](#)

[Dongru Du](#)¹, [Guangyue Zhang](#)², [Dan Xu](#)³, [Lian Liu](#)³, [Xueru Hu](#)³, [Lei Chen](#)³, [Xiaoou Li](#)⁴, [Yongchun Shen](#)⁵, [Fuqiang Wen](#)³

Affiliations expand

- PMID: 37950939
- DOI: [10.1016/j.sleep.2023.10.034](https://doi.org/10.1016/j.sleep.2023.10.034)

Abstract

Background: Sleep disorders, including obstructive sleep apnea (OSA), restless leg syndrome (RLS) and insomnia, are present in chronic obstructive pulmonary disease (COPD) with varied prevalence. The aim of this systematic review and meta-analysis was to investigate prevalence of OSA, RLS and insomnia in patients with COPD and summarize their clinical characteristics.

Methods: We searched PubMed, Web of Science and Scopus for eligible articles reporting the prevalence of OSA, RLS, and insomnia in COPD patients. The Newcastle–Ottawa scale was applied for quality assessment. Odds ratios or mean differences with 95 % confidence intervals (CIs) were applied for the overall prevalence calculation and clinical characteristics assessment. Sensitivity analysis, subgroup analysis and meta-regression were conducted to evaluate the heterogeneity of the results.

Results: Sixty articles reporting the prevalence of sleep disorders in patients with COPD were included, and the prevalence of OSA, RLS, and insomnia reached 29.1 % (95%CI 27.2%-30.9 %), 21.6 % (95%CI 11.8%-33.3 %) and 29.5 % (95%CI 16.9%-44.0 %), respectively. COPD patients with OSA were characterized by male sex (OR 1.631 95 % CI: 1.231-2.161), obesity(kg/m²) (MD 4.435, 95 % CI 3.218-5.652), higher Epworth Sleepiness Scale (MD: 3.741, 95 % CI: 0.655-6.828, $p = 0.018$), better pulmonary function (MD 5.66, 95 % CI 3.546-7.774) and higher risks of hypertension (OR 1.933 95 % CI 1.382-2.70) and diabetes (OR 1.898 95 % CI 1.264-2.849). COPD patients with RLS were associated with a higher Epworth sleepiness scale (ESS) score (MD 3.444, 95 % CI 1.880-5.008) and a longer COPD duration(year) (MD: 3.656, 95 % CI: 2.209-5.103). COPD patients with insomnia were characterized by female sex(OR 0.556, 95%CI 0.545,0.567, $p < 0.001$).

Conclusion: Our study suggests that OSA, RLS and insomnia are common in COPD patients with specific clinical characteristics. Further studies are needed to explore the interactions between COPD and sleep disorders.

Keywords: Chronic obstructive pulmonary disease; Clinical characteristics; Insomnia; Obstructive sleep apnea; Prevalence; Restless leg syndrome.

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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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34

Cytokine

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. 2023 Dec:172:156404.

doi: 10.1016/j.cyto.2023.156404. Epub 2023 Nov 2.

Inflammation and comorbidities of chronic obstructive pulmonary disease: The cytokines put on a mask!

[Jian Long](#)¹, [Ping Xu](#)², [Jie Chen](#)³, [Jiangrong Liao](#)⁴, [Desheng Sun](#)³, [Zhongyong Xiang](#)⁵, [Hongchang Ma](#)⁵, [Haizhen Duan](#)⁶, [Mingliang Ju](#)⁷, [Yao Ouyang](#)⁸

Affiliations expand

- PMID: 37922621
- DOI: [10.1016/j.cyto.2023.156404](https://doi.org/10.1016/j.cyto.2023.156404)

Abstract

Objective: Chronic obstructive pulmonary disease (COPD) is a well-known complex multicomponent disease characterized by systemic inflammation that frequently coexists with other conditions. We investigated the relationship between some inflammatory markers and complications in COPD patients to explore the possible roles of inflammation in these comorbidities.

Methods: This study used cross-sectional and case-control methods. We included 336 hospitalized COPD patients, 64 healthy controls, and 42 major depression patients and evaluated all participants using the Hamilton Rating Scale. C-reactive protein (CRP), red blood cell distribution width (RDW), neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), monocyte/lymphocyte ratio (MLR), interleukin-1 β (IL-1 β) and interleukin-6 (IL-6) were collected and measured in the study population. Statistical methods were used to analyze the association of inflammatory markers with COPD comorbidities.

Results: Cor pulmonale and psychological comorbidities (depression and anxiety) were more common in this study on COPD patients. We found that MLR (OR = 2.054, 95 % CI 1.129-3.735, $p = 0.018$) and RDW (OR = 1.367, 95 % CI 1.178-1.586, $p = 0.000$) were related to COPD patients complicated with cor pulmonale, while IL-6 (OR = 1.026, 95 % CI 1.001-1.053, $p = 0.045$) and RDW (OR = 1.280, 95 % CI 1.055-1.552, $p = 0.012$) were related to depression symptoms.

Conclusion: MLR, RDW and IL-6 were closely related to cor pulmonale and depression in COPD patients. IL-1 β and IL-6 are closely related to depression in humans.

Keywords: Anxiety; COPD; Comorbidities; Depression; Inflammatory.

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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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Serum levels of biomarkers that may link chronic obstructive pulmonary disease and depressive disorder

[Elżbieta Małujło-Balcerska](#)¹, [Tadeusz Pietras](#)^{2,3}, [Witold Śmigieński](#)⁴

Affiliations expand

- PMID: 37921965
- PMCID: [PMC10661791](#)
- DOI: [10.1007/s43440-023-00548-3](#)

Free PMC article

Abstract

Background: Depressive disorder is a common comorbidity of chronic obstructive pulmonary disease (COPD); according to some studies, it occurs in approximately 80% of patients. The presence of depressive symptoms influences the quality of life and affects the course and treatment of this disease. The cause of depressive symptoms in COPD and the linking mechanism between COPD and depressive disorder have not been clearly elucidated, and more studies are warranted. Inflammation and inflammation-related processes and biomarkers are involved in the etiology of COPD and depressive disorder and may be an explanation for the potential occurrence of depressive disorder in patients diagnosed with COPD. The scope of this study was to measure and compare the profiles of IL-18, TGF- β , RANTES, ICAM-1, and uPAR among stable COPD patients, recurrent depressive disorder (rDD) patients, and healthy controls.

Methods: Inflammation and inflammation-related factors were evaluated in COPD patients, patients diagnosed with depressive disorder, and control individuals using enzyme-linked immunosorbent assays.

Results: Interleukin (IL)-18, transforming growth factor (TGF)- β , chemokine RANTES, and urokinase plasminogen activator receptor (uPAR) concentrations were higher in patients suffering

from COPD and depression than in control patients. Intercellular adhesive molecule (ICAM)-1 levels were significantly higher in COPD patients and lower in depressive disorder patients than in controls.

Conclusions: Higher levels of IL-18, TGF- β , RANTES, and uPAR in patients with COPD might indicate the presence of depressive disorder and suggest the need for further evaluation of the mental state of these patients.

Keywords: Chronic obstructive pulmonary disease; Depressive disorder; Inflammation.

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Conflict of interest statement

The authors declare no conflict of interest.

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

SUPPLEMENTARY INFO

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[Review](#)

J Psychosom Res

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. 2023 Dec;175:111537.

doi: 10.1016/j.jpsychores.2023.111537. Epub 2023 Oct 24.

Global prevalence and risk factors of depression in patients with chronic obstructive pulmonary disease: A systematic review and meta-analysis from 2000 to 2022

[Hongmei Xie¹](#), [Yunlan Jiang²](#), [Lu Liu³](#), [Hanmei Peng³](#), [Jie Li³](#), [Zengli Chen³](#)

Affiliations expand

- PMID: 37907038
- DOI: [10.1016/j.jpsychores.2023.111537](https://doi.org/10.1016/j.jpsychores.2023.111537)

Abstract

Objective: This study aims to assess the global and regional prevalence and the potential risk factors for depression among COPD patients.

Methods: Web of Science, EMBASE, PubMed, and PsycINFO databases were searched for the literature related to the prevalence and risk factors of depression in COPD. Random-effect models were performed to pool the global prevalence. Sub-group analysis and meta-regression were conducted to investigate the potential heterogeneity. Meta-analysis was performed only on the risk factors that have been reported in a minimum of three studies.

Results: A total of 79 studies from 25 countries were included. The pooled global prevalence of variably defined depression among COPD patients was 34.5% (95% CI: 30.9-38.1). The odds of depression in COPD patients were 3.53 times higher than in non-COPD participants (95% CI: 2.35-5.29). Meta-regression results showed that region, income level, and research setting are the main sources of heterogeneity. Female sex (OR=1.92), living alone (OR=2.29), BODE index (OR=1.48), dyspnea (OR=3.02), impaired quality of life (OR=1.26), and GOLD stage III~IV (OR=1.96) were found to be significant risk factors for depression in meta-analyses.

Conclusions: More than one-third of COPD patients experience depression, with marked variations in prevalence across countries and regions. This study further highlights the need for the consolidation of mental health considerations into COPD treatments. High-quality, longitudinal studies and further research are needed to gain a better understanding of risk and protective factors.

Keywords: Chronic obstructive pulmonary disease; Depression; Meta-regression; Prevalence; Risk factors.

Conflict of interest statement

Declaration of Competing Interest All authors have no conflicts of interest to disclose.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS



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Cite

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37

Br J Gen Pract

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. 2023 Nov 30;73(737):e876-e884.

doi: 10.3399/BJGP.2022.0565. Print 2023 Dec.

Early detection of chronic obstructive pulmonary disease in primary care: a randomised controlled trial

[Anthony Chapron¹](#), [Emilie Andres²](#), [Laure Fiquet²](#), [Fabienne Pelé³](#), [Emmanuel Allory²](#), [Estelle Le Pabic³](#), [Aurélie Veislinger²](#), [Lisa Le Guillou⁴](#), [Stéphanie Guillot⁴](#), [Bruno Laviolle⁵](#), [Stéphane Jouneau⁶](#)

Affiliations expand

- PMID: 37903640
- PMCID: [PMC10633669](#)
- DOI: [10.3399/BJGP.2022.0565](#)

Abstract

Background: Worldwide, chronic obstructive pulmonary disease (COPD) remains largely underdiagnosed.

Aim: To assess whether the use of Global Initiative for Chronic Obstructive Lung Disease (GOLD) questions and COPD coordination, either alone or combined, would detect new COPD cases in primary care.

Design and setting: GPs in Brittany, France, systematically enrolled patients aged 40-80 years over a 4-month period in this French multicentre cluster randomised controlled study.

Method: GPs were randomly allocated to one of four groups: control (standard of care), GOLD questions (adapted from symptoms and risk factors identified by GOLD), COPD coordination, and GOLD questions with COPD coordination. New cases of COPD were those confirmed by spirometry: post-bronchodilator forced expiratory volume in 1 second over forced vital capacity of <0.7 .

Results: In total, 11 430 consultations were conducted by 47 GPs, who enrolled 3162 patients who did not have prior diagnosed asthma or COPD. Among these, 802 (25%) were enrolled in the control, 820 (26%) in the GOLD questions, 802 (25%) in the COPD coordination, and 738 (23%) in the GOLD questions with COPD coordination groups. In the control group, COPD was not evoked, and no spirometry was prescribed. All new cases of COPD diagnosed ($n = 24$, 0.8%) were in the intervention groups, representing 6.8% of patients who performed spirometry. Statistically significantly more new cases of COPD were detected with COPD coordination ($P = 0.01$).

Conclusion: Interventions that can be easily implemented, such as the GOLD questions and COPD coordination, can identify new cases of COPD. Studies are needed to identify the most appropriate case-finding strategies for GPs to detect COPD in primary care for each country.

Keywords: GOLD questions; chronic obstructive pulmonary disease; early detection; general practice; primary care.

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Conflict of interest statement

The authors have declared no competing interests.

- [Cited by 1 article](#)
- [32 references](#)
- [3 figures](#)

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38

Respirology

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. 2023 Dec;28(12):1171-1172.

doi: 10.1111/resp.14616. Epub 2023 Oct 26.

In case you missed it

[Diane M Gray](#)¹

Affiliations expand

- PMID: 37882663
- DOI: [10.1111/resp.14616](https://doi.org/10.1111/resp.14616)

Free article

No abstract available

Keywords: COPD; asthma; improving care.

FULL TEXT LINKS



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Respirology

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2023 Dec;28(12):1166-1169.

doi: 10.1111/resp.14612. Epub 2023 Oct 25.

Lung function and exacerbations in patients with COPD escalated to triple therapy: The RETRIEVE real-world study

[Stavros Tryfon](#)¹, [Efthymia Papadopoulou](#)¹, [Maria Bertoli](#)², [Konstantinos Exarchos](#)³, [Alexandros Ginis](#)², [Konstantinos Kostikas](#)³

Affiliations expand

- PMID: 37879756
- DOI: [10.1111/resp.14612](https://doi.org/10.1111/resp.14612)

Free article

No abstract available

Keywords: COPD exacerbations; FEV1; chronic obstructive pulmonary disease; open triple therapy; salmeterol-fluticasone fixed-dose combination.

- [9 references](#)

SUPPLEMENTARY INFO

Grants and funding expand

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Review



The treatable traits approach to adults with obstructive airways disease in primary and secondary care

[Mike Thomas](#)¹, [Richard Beasley](#)^{2,3}

Affiliations expand

- PMID: 37877554
- DOI: [10.1111/resp.14610](https://doi.org/10.1111/resp.14610)

Free article

Abstract

The treatable traits approach is based on the recognition that the different clinical phenotypes of asthma and chronic obstructive airways disease (COPD) are a heterogeneous group of conditions with different underlying mechanisms and clinical manifestations, and that the identification and treatment of the specific clinical features or traits facilitates a personalised approach to management. Fundamentally, it recognises two important concepts. Firstly, that treatment for obstructive lung disease can achieve better outcomes if guided by specific clinical characteristics. Secondly, that in patients with a diagnosis of asthma, and/or COPD, poor respiratory health may also be due to numerous overlapping disorders that can present with symptoms that may be indistinguishable from asthma and/or COPD, comorbidities that might require treatment in their own right, and lifestyle or environmental factors that, if addressed, might lead to better control rather than simply increasing airways directed treatment. While these concepts are well accepted, how best to implement this personalised medicine approach in primary and secondary care within existing resource constraints remains uncertain. In this review, we consider the evidence base for this management approach and propose that the priority now is to assess different prototype templates for the identification and management of treatable traits in both asthma and COPD, in primary, secondary and tertiary care, to provide the evidence that will guide their use in clinical practice in different health care systems.

Keywords: COPD; asthma; obstructive airways disease; personalized medicine; primary care; secondary care; treatable traits.

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- [111 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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41

Am J Transplant

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. 2023 Dec;23(12):2000-2007.

doi: 10.1016/j.ajt.2023.10.010. Epub 2023 Oct 18.

Characteristics and Outcomes Among Adults Aged ≥ 60 Years Hospitalized with Laboratory-Confirmed Respiratory Syncytial Virus – RSV-NET, 12 States, July 2022–June 2023

[Fiona P Havers](#)¹, [Michael Whitaker](#)², [Michael Melgar](#)², [Bhoomija Chatwani](#)³, [Shua J Chai](#)⁴, [Nisha B Alden](#)⁵, [James Meek](#)⁶, [Kyle P Openo](#)⁷, [Patricia A Ryan](#)⁸, [Sue Kim](#)⁹, [Ruth Lynfield](#)¹⁰, [Yomei P Shaw](#)¹¹, [Grant Barney](#)¹², [Brenda L Tesini](#)¹³, [Melissa Sutton](#)¹⁴, [H Keipp Talbot](#)¹⁵, [Kristen P Olsen](#)¹⁶, [Monica E Patton](#)², [RSV-NET Surveillance Team](#)

Collaborators, Affiliations expand

- PMID: 37863432

- DOI: [10.1016/j.ajit.2023.10.010](https://doi.org/10.1016/j.ajit.2023.10.010)

Abstract

Respiratory syncytial virus (RSV) causes substantial morbidity and mortality in older adults. In May 2023, two RSV vaccines were approved for prevention of RSV lower respiratory tract disease in adults aged ≥ 60 years. In June 2023, CDC recommended RSV vaccination for adults aged ≥ 60 years, using shared clinical decision-making. Using data from the Respiratory Syncytial Virus-Associated Hospitalization Surveillance Network, a population-based hospitalization surveillance system operating in 12 states, this analysis examined characteristics (including age, underlying medical conditions, and clinical outcomes) of 3,218 adults aged ≥ 60 years who were hospitalized with laboratory-confirmed RSV infection during July 2022-June 2023. Among a random sample of 1,634 older adult patients with RSV-associated hospitalization, 54.1% were aged ≥ 75 years, and the most common underlying medical conditions were obesity, chronic obstructive pulmonary disease, congestive heart failure, and diabetes. Severe outcomes occurred in 18.5% (95% CI = 15.9%-21.2%) of hospitalized patients aged ≥ 60 years. Overall, 17.0% (95% CI = 14.5%-19.7%) of patients with RSV infection were admitted to an intensive care unit, 4.8% (95% CI = 3.5%-6.3%) required mechanical ventilation, and 4.7% (95% CI = 3.6%-6.1%) died; 17.2% (95% CI = 14.9%-19.8%) of all cases occurred in long-term care facility residents. These data highlight the importance of prioritizing those at highest risk for severe RSV disease and suggest that clinicians and patients consider age (particularly age ≥ 75 years), long-term care facility residence, and underlying medical conditions, including chronic obstructive pulmonary disease and congestive heart failure, in shared clinical decision-making when offering RSV vaccine to adults aged ≥ 60 years.

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42

Environ Pollut

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. 2023 Dec 1:338:122665.

Double trouble: The interaction of PM_{2.5} and O₃ on respiratory hospital admissions

Jiachen Li¹, Lirong Liang², Baolei Lyu³, Yutong Samuel Cai⁴, Yingting Zuo⁵, Jian Su⁶, Zhaohui Tong⁷

Affiliations expand

- PMID: 37806428
- DOI: [10.1016/j.envpol.2023.122665](https://doi.org/10.1016/j.envpol.2023.122665)

Free article

Abstract

The co-occurrence of fine particulate matter (PM_{2.5}) and ozone (O₃) pollution during the warm season has become a growing public health concern. The interaction between PM_{2.5} and O₃ and its contribution to disease burden associated with co-pollution has not been thoroughly examined. We collected data on hospital admissions for respiratory diseases from a city-wide hospital discharge database in Beijing between 2013 and 2019. City-wide 24-h mean PM_{2.5} and daily maximum 8-h mean O₃ were averaged from 35 monitoring stations across Beijing. Conditional Poisson regression was employed to estimate the interaction between warm-season PM_{2.5} and O₃ on respiratory admissions. A model incorporating a tensor product term was used to fit the non-linear interaction and estimate the number of respiratory admissions attributable to PM_{2.5} and O₃ pollution. From January 18, 2013 to December 31, 2019, 1,191,308 respiratory admissions were recorded. We observed multiplicative interactions between warm-season PM_{2.5} and O₃ on upper respiratory infections (P = 0.004), pneumonia (P = 0.002), chronic obstructive pulmonary disease (P = 0.041), and total respiratory disease (P < 0.001). PM_{2.5}-O₃ co-pollution during warm season exhibited a super-additive effect on respiratory admissions, with a relative excess risk due to interaction of 1.65% (95%CI: 0.46%-2.84%). There was a non-linear pattern of the synergistic effect between PM_{2.5} and O₃ on respiratory admissions. Based on the World Health Organization global air quality guidelines, 12,421 respiratory admissions would be reduced if both daily PM_{2.5} and O₃ concentrations had not exceeded the target (PM_{2.5} 15 µg/m³, O₃ 100 µg/m³). The number of respiratory admissions attributable to either PM_{2.5} or O₃ pollution decreased by 48.7% from 2013 to 2019. Prioritizing O₃ control during the warm season is a cost-effective strategy for Beijing. These findings underscore the significance of concurrently addressing both PM_{2.5} pollution and O₃ pollution during the warm season to alleviate the burden of respiratory diseases.

Keywords: Air pollution; Ozone; Particulate matter; Respiratory hospitalizations.

Conflict of interest statement

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

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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ESC Heart Fail

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. 2023 Dec;10(6):3612-3621.

doi: 10.1002/ehf2.14497. Epub 2023 Oct 3.

Epidemiology and treatment of heart failure with chronic obstructive pulmonary disease in Canadian primary care

[Nathaniel M Hawkins](#)^{1,2}, [Sandra Peterson](#)², [Samaneh Salimian](#)¹, [Catherine Demers](#)³, [Karim Keshavjee](#)⁴, [Sean A Virani](#)¹, [G B John Mancini](#)¹, [Sabrina T Wong](#)^{2,5}

Affiliations expand

- PMID: 37786365

- PMID: [PMC10682874](#)
- DOI: [10.1002/ehf2.14497](#)

Free PMC article

Abstract

Aims: Heart failure (HF) and chronic obstructive pulmonary disease (COPD) are largely managed in primary care, but their intersection in terms of disease burden, healthcare utilization, and treatment is ill-defined.

Methods and results: We examined a retrospective cohort including all patients with HF or COPD in the Canadian Primary Care Sentinel Surveillance Network from 2010 to 2018. The population size in 2018 with HF, COPD, and HF with COPD was 15 778, 27 927, and 4768 patients, respectively. While disease incidence declined, age-sex-standardized prevalence per 100 population increased for HF alone from 2.33 to 3.63, COPD alone from 3.44 to 5.96, and COPD with HF from 12.70 to 15.67. Annual visit rates were high and stable around 8 for COPD alone but declined significantly over time for HF alone (9.3-8.1, $P = 0.04$) or for patients with both conditions (14.3-11.9, $P = 0.006$). For HF alone, cardiovascular visits were common (29.4%), while respiratory visits were infrequent (3.5%), with the majority of visits being non-cardiorespiratory. For COPD alone, respiratory and cardiovascular visits were common (16.4% and 11.3%) and the majority were again non-cardiorespiratory. For concurrent disease, 39.0% of visits were cardiorespiratory. The commonest non-cardiorespiratory visit reasons were non-specific symptoms or signs, endocrine, musculoskeletal, and mental health. In patients with HF with and without COPD, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker/angiotensin receptor-neprilysin inhibitor use was similar, while mineralocorticoid receptor antagonist use was marginally higher with concurrent COPD. Beta-blocker use was initially lower with concurrent COPD compared with HF alone (69.3% vs. 74.0%), but this progressively declined by 2018 (74.5% vs. 73.5%).

Conclusions: The prevalence of HF and COPD continues to rise. Although patients with either or both conditions are high utilizers of primary care, the majority of visits relate to non-cardiorespiratory comorbidities. Medical therapy for HF was similar and the initially lower beta-blocker utilization disappeared over time.

Keywords: Chronic obstructive pulmonary disease; Epidemiology; Heart failure; Primary care.

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Conflict of interest statement

None declared.

- [33 references](#)
- [5 figures](#)

SUPPLEMENTARY INFO

MeSH terms, Grants and fundingexpand

FULL TEXT LINKS



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Review

Immunotherapy

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. 2023 Dec;15(18):1511-1519.

doi: 10.2217/imt-2023-0136. Epub 2023 Oct 2.

What role will ensifentrine play in the future treatment of chronic obstructive pulmonary disease patients? Implications from recent clinical trials

[Mario Cazzola¹](#), [Clive Page²](#), [Luigino Calzetta³](#), [Dave Singh⁴](#), [Paola Rogliani¹](#), [Maria Gabriella Matera⁵](#)

Affiliations expand

- PMID: 37779474
- DOI: [10.2217/imt-2023-0136](https://doi.org/10.2217/imt-2023-0136)

Abstract

Data from the phase III ENHANCE clinical trials provide compelling evidence that ensifentrine, an inhaled 'bifunctional' dual phosphodiesterase 3/4 inhibitor, can provide additional benefit to existing treatments in patients with chronic obstructive pulmonary disease and represents a 'first-in-class' drug having bifunctional bronchodilator and anti-inflammatory activity in a single molecule. Ensifentrine, generally well tolerated, can provide additional bronchodilation when added to muscarinic receptor antagonists or β_2 -agonists and reduce the exacerbation risk. This information allows us to consider better the possible inclusion of ensifentrine in the future treatment of chronic obstructive pulmonary disease. However, there is less information on whether it provides additional benefit when added to inhaled corticosteroid or 'triple therapy' and, therefore, when this drug is best utilized in clinical practice.

Keywords: COPD; anti-inflammatory activity; bronchodilation; combination therapy; ensifentrine; pivotal RCTs.

Plain language summary

Chronic obstructive pulmonary disease (COPD) is the name for a group of lung conditions that cause breathing difficulties/airflow limitations. The airflow limitation is not completely reversible and is associated with a state of chronic inflammation of lung tissue. Treatment of the disease is still heavily dependent on the use of medications called bronchodilators and corticosteroids. However, corticosteroids have little-to-no impact on the underlying inflammation in most COPD patients. Therefore, innovative anti-inflammatory approaches are required. In this context, single molecules that are capable of simultaneously inducing bronchodilation, relaxing the muscles in the lungs and widening the airways (bronchi), and anti-inflammatory activity are a highly intriguing possibility for treating COPD. One approach is to develop drugs that can simultaneously inhibit enzymes called phosphodiesterase (PDE)3 and PDE4. Enzymes are proteins that help speed up metabolism, or the chemical reactions in our bodies. PDE4 inhibitors are intracellular enzymes (work inside the cell) expressed in most inflammatory cells, even in neutrophils (a type of white blood cells), which are involved in the pathogenesis of COPD, where an infection turns into a disease. However, its inhibition does not produce severe bronchodilator effects, which is instead obtained by inhibiting PDE3, the PDE isoenzyme (a different form of the same enzyme) that is predominantly expressed in airway smooth muscle cells. A treatment called ensifentrine is a dual PDE3/4 inhibitor (inhibits both PDE3 and PDE4). Two recent phase III studies (ENHANCE-1 and ENHANCE-2) have shown that it induces significant bronchodilation and reduces the risk of COPD worsening, exerting an anti-inflammatory effect. Data from the ENHANCE studies also showed the benefit of adding ensifentrine to treatment with bronchodilators. Certainly, the drug represents a useful therapeutic option, but further clinical studies are needed to be able to correctly position ensifentrine in the context of regular COPD treatment.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Ann Am Thorac Soc

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. 2023 Dec;20(12):1743-1751.

doi: 10.1513/AnnalsATS.202305-458OC.

Lifestyle Intervention and Excess Weight in Chronic Obstructive Pulmonary Disease (COPD): INSIGHT COPD Randomized Clinical Trial

David H Au^{1,2}, Emily Gleason¹, Rachel Hunter-Merrill¹, Anna E Barón³, Margaret Collins¹, Corina Ronneberg⁴, Nan Lv⁴, Peter Rise¹, Travis Hee Wai¹, Robert Plumley¹, Stephen R Wisniewski⁵, Frank C Scirba⁶, Dong-Yun Kim⁷, Paul Simonelli⁸, Jerry A Krishnan⁴, Christine H Wendt⁹, Laura C Feemster¹², Gerard J Criner¹⁰, Veeranna Maddipati¹¹, Arjun Mohan¹¹, Jun Ma¹²

Affiliations expand

- PMID: 37769182
- DOI: [10.1513/AnnalsATS.202305-458OC](https://doi.org/10.1513/AnnalsATS.202305-458OC)

Abstract

Rationale: Being overweight or obese is common among patients with chronic obstructive pulmonary disease (COPD), but whether interventions targeted at weight loss improve functional impairments is unknown. **Objectives:** INSIGHT (Intervention Study in Overweight Patients with COPD) tested whether a pragmatic low-intensity lifestyle intervention would lead to better physical functional status among overweight or obese participants with COPD. **Methods:** The trial was a 12-month, multicenter, patient-level pragmatic clinical trial. Participants were recruited from April 2017 to August 2019 from 38 sites across the United States and randomized to receive usual care or usual care plus lifestyle intervention. The intervention was a self-directed video program delivering the Diabetes Prevention Program's Group Lifestyle Balance curriculum. **Results:** The primary outcome was 6-minute-walk test distance at 12 months. Priority secondary outcomes were postwalk modified Borg dyspnea at 12 months and weight at 12 months. Participants ($N = 684$; mean age, 67.0 ± 8.0 yr [standard deviation]; 41.2% female) on average were obese (body mass index, 33.0 ± 4.6 kg/m²) with moderate COPD (forced expiratory volume in 1 second % predicted, $58.1 \pm 15.7\%$).

At 12 months, participants randomized to the intervention arm walked farther (adjusted difference, 42.3 ft [95% confidence interval (CI), 7.9-76.7 ft]; $P = 0.02$), had less dyspnea at the end of the 6-minute-walk test (adjusted difference, -0.36 [95% CI, -0.63 to -0.09]; $P = 0.008$), and had greater weight loss (adjusted difference, -1.34 kg [95% CI, -2.33 to -0.34 kg]; $P = 0.008$) than control participants. The intervention did not improve the odds of achieving clinically meaningful thresholds of walk distance (98.4 ft) or dyspnea (1 unit) but did achieve meaningful thresholds of weight loss (3% and 5%). **Conclusions:** Among participants with COPD who were overweight or obese, a self-guided low-intensity video-based lifestyle intervention led to modest weight loss but did not lead to clinically important improvements in physical functional status and dyspnea. Clinical trial registered with www.clinicaltrials.gov ([NCT02634268](https://www.clinicaltrials.gov/ct2/show/study?term=NCT02634268)).

Keywords: COPD; exercise tolerance; obese; quality of life; randomized controlled trial.

SUPPLEMENTARY INFO

Associated data, Grants and funding expand

FULL TEXT LINKS



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Thorax

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. 2023 Dec;78(12):1240-1247.

doi: 10.1136/thorax-2023-220522. Epub 2023 Sep 27.

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

[Sara Souto-Miranda](#)^{1,2,3,4}, [Isabel Saraiva](#)⁵, [Martijn A Spruit](#)^{2,6}, [Alda Marques](#)^{7,8}

Affiliations expand

- PMID: 37758457

- DOI: [10.1136/thorax-2023-220522](https://doi.org/10.1136/thorax-2023-220522)

Abstract

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

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

Results: A total of 299 people (n=229 healthcare professionals/researchers/policy-makers; n=70 people with COPD and informal caregivers) participated in the survey (83% retention), which covered 29 countries/five continents. After the second round, six outcomes were included and three were added in the meeting. The final COS contains dyspnoea, fatigue, functional exercise capacity, health-related quality of life, health behaviours/lifestyle, knowledge about the disease, lower limb muscle function, personal goals and problematic activities of daily living.

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

Keywords: pulmonary rehabilitation; respiratory measurement.

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Published by BMJ.

Conflict of interest statement

Competing interests: None declared.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Am J Respir Crit Care Med



. 2023 Dec 1;208(11):1177-1195.

doi: 10.1164/rccm.202305-0924OC.

Activation of CD8⁺ T Cells in Chronic Obstructive Pulmonary Disease Lung

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Collaborators, Affiliations expand

- PMID: 37756440
- DOI: [10.1164/rccm.202305-0924OC](https://doi.org/10.1164/rccm.202305-0924OC)

Abstract

Rationale: Despite the importance of inflammation in chronic obstructive pulmonary disease (COPD), the immune cell landscape in the lung tissue of patients with mild-moderate disease has not been well characterized at the single-cell and molecular level. **Objectives:** To define the immune cell landscape in lung tissue from patients with mild-moderate COPD at single-cell resolution. **Methods:** We performed single-cell transcriptomic, proteomic, and T-cell receptor repertoire analyses on lung tissue from patients with mild-moderate COPD ($n = 5$, Global Initiative for Chronic Obstructive Lung Disease I or II), emphysema without airflow obstruction ($n = 5$), end-stage COPD ($n = 2$), control ($n = 6$), or donors ($n = 4$). We validated in an independent patient cohort ($N = 929$) and integrated with the *Hhip*^{+/-} murine model of COPD. **Measurements and Main Results:** Mild-moderate COPD lungs have increased abundance of two CD8⁺ T cell subpopulations: cytotoxic KLRG1⁺TIGIT⁺CX3CR1⁺ TEMRA (T effector memory CD45RA⁺) cells, and DNAM-1⁺CCR5⁺ T resident memory (T_{RM}) cells. These CD8⁺ T cells interact with myeloid and alveolar type II cells via *IFNG* and have hyperexpanded T-cell receptor clonotypes. In an independent cohort, the CD8⁺KLRG1⁺ TEMRA cells are increased in mild-moderate COPD lung compared with control or end-stage COPD lung. Human CD8⁺KLRG1⁺ TEMRA cells are similar to CD8⁺ T cells driving

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

Keywords: RNA sequence analysis; chronic obstructive pulmonary disease; memory T cells; multiomics; proteomics.

Comment in

- [Bad Neighbors or Bad Neighborhoods: Pathogenic Residency of T Cells in Chronic Obstructive Pulmonary Disease.](#)
Peng T. *Am J Respir Crit Care Med*. 2023 Dec 1;208(11):1148-1150. doi: 10.1164/rccm.202310-1760ED.PMID: 37855741 No abstract available.
- [Cited by 1 article](#)

SUPPLEMENTARY INFO

Grants and funding[expand](#)

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COPD

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. 2023 Dec;20(1):307-320.

doi: 10.1080/15412555.2023.2259224. Epub 2023 Sep 22.

Chest MRI and CT Predictors of 10-Year All-Cause Mortality in COPD

[Maksym Sharma](#)^{1,2}, [Paulina V Wyszkievicz](#)^{1,2}, [Alexander M Matheson](#)^{1,2}, [David G McCormack](#)³, [Grace Parraga](#)^{1,2,3,4}

Affiliations expand

- PMID: 37737132
- DOI: [10.1080/15412555.2023.2259224](https://doi.org/10.1080/15412555.2023.2259224)

Abstract

Pulmonary imaging measurements using magnetic resonance imaging (MRI) and computed tomography (CT) have the potential to deepen our understanding of chronic obstructive pulmonary disease (COPD) by measuring airway and parenchymal pathologic information that cannot be provided by spirometry. Currently, MRI and CT measurements are not included in mortality risk predictions, diagnosis, or COPD staging. We evaluated baseline pulmonary function, MRI and CT measurements alongside imaging texture-features to predict 10-year all-cause mortality in ex-smokers with ($n = 93$; 31 females; 70 ± 9 years) and without ($n = 69$; 29 females, 69 ± 9 years) COPD. CT airway and vessel measurements, helium-3 (^3He) MRI ventilation defect percent (VDP) and apparent diffusion coefficients (ADC) were quantified. MRI and CT texture-features were extracted using PyRadiomics (version 2.2.0). Associations between 10-year all-cause mortality and all clinical and imaging measurements were evaluated using multivariable regression model odds-ratios. Machine-learning predictive models for 10-year all-cause mortality were evaluated using area-under-receiver-operator-characteristic-curve (AUC), sensitivity and specificity analyses. DL_{CO} (% pred) (HR = 0.955, 95% CI: 0.934-0.976, $p < 0.001$), MRI ADC (HR = 1.843, 95% CI: 1.260-2.871, $p < 0.001$), and CT informational-measure-of-correlation (HR = 3.546, 95% CI: 1.660-7.573, $p = 0.001$) were the strongest predictors of 10-year mortality. A machine-learning model trained on clinical, imaging, and imaging textures was the best predictive model (AUC = 0.82, sensitivity = 83%, specificity = 84%) and outperformed the solely clinical model (AUC = 0.76, sensitivity = 77%, specificity = 79%). In ex-smokers, regardless of COPD status, addition of CT and MR imaging texture measurements to clinical models provided unique prognostic information of mortality risk that can allow for better clinical management. **Clinical Trial Registration:** [www.clinicaltrials.gov NCT02279329](https://www.clinicaltrials.gov/NCT02279329).

Keywords: Ex-smokers; computed tomography; hyperpolarized gas MRI; machine-learning; mortality; texture analysis.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated data, Grants and funding expand

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Curr Opin Support Palliat Care



. 2023 Dec 1;17(4):263-269.

doi: 10.1097/SPC.0000000000000674. Epub 2023 Oct 26.

Should opioids be used for breathlessness and in whom? A PRO and CON debate of the evidence

[Magnus Ekström](#)¹, [Daisy J A Janssen](#)^{2,3}

Affiliations expand

- PMID: 37720983
- PMCID: [PMC10597437](#)
- DOI: [10.1097/SPC.0000000000000674](#)

Free PMC article

Abstract

Purpose of review: The net clinical benefit of opioids for chronic breathlessness has been challenged by recent randomized clinical trials. The purpose was to review and weigh the evidence for and against opioid treatment for chronic breathlessness in people with serious disease.

Recent findings: Evidence to date on the efficacy and safety of opioids for chronic breathlessness was reviewed. Findings supporting a benefit from opioids in meta-analyses of earlier, mostly smaller trials were not confirmed by recent larger trials. Evidence pertains mostly to people with chronic obstructive pulmonary disease but also to people with pulmonary fibrosis, heart failure, and advanced cancer. Taken together, there is no consistent evidence to generally recommend opioids for severe breathlessness or to identify people who are more likely to benefit. Opioid treatment may be tested in patients with intractable breathlessness and limited other treatment options, such as in end-of-life care. Knowledge gaps were identified and recommendations were made for future research.

Summary:

Key Points

- Supportive findings of net benefit of opioids for chronic breathlessness in earlier trials have not been confirmed by recent larger randomized clinical trials.
- There is no evidence that the opioid treatment improves the person's exercise capacity or quality of life, and it increases the risk of adverse events.
- Evidence to date does not support that opioids should generally be recommended for treating breathlessness.
- In people with intractable symptoms and short expected survival, with few or no treatment options, it may still be reasonable to try opioid treatment with the aim to alleviate severe breathlessness.
- Research is needed to explore the potential benefit of opioids in selected patient groups.

Opioids cannot be generally recommended for treating breathlessness based on insufficient evidence for net clinical benefit.

Conflict of interest statement

M.E. reports no conflicts of interest. D.J.A.J. has received non-personal lecture fees from Abbott, Chiesi, and AstraZeneca in the previous 2 years.

- [48 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances[expand](#)

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Ann Am Thorac Soc

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. 2023 Dec;20(12):1735-1742.

doi: 10.1513/AnnalsATS.202304-301OC.

A Cost-Effectiveness Analysis of Azithromycin for the Prevention of Acute Exacerbations of Chronic Obstructive Pulmonary Disease

[Safa Ahmadian](#)^{1,2}, [Kate M Johnson](#)^{1,2,3,4}, [Joseph Khoa Ho](#)^{1,2}, [Don D Sin](#)^{3,4}, [Larry D Lynd](#)^{2,5}, [Mark Harrison](#)^{2,5}, [Mohsen Sadatsafavi](#)^{1,2,3,4}

Affiliations expand

- PMID: 37703432
- DOI: [10.1513/AnnalsATS.202304-301OC](https://doi.org/10.1513/AnnalsATS.202304-301OC)

Abstract

Rationale: Daily oral azithromycin therapy can reduce the risk of acute exacerbations of chronic obstructive pulmonary disease (COPD). However, given its adverse events and additional costs, it is not known whether adding long-term azithromycin as an adjunct therapy to inhaled pharmacotherapy is cost effective. **Objectives:** The objective of this study was to evaluate the cost-effectiveness of add-on azithromycin therapy in COPD as recommended by contemporary COPD management guidelines. **Methods:** We extended a previously validated Canadian COPD policy model to include azithromycin-related inputs and outcomes. The cost-effectiveness of azithromycin was evaluated over a 20-year time horizon in patients who continue to exacerbate despite receiving maximal inhaled therapies. The benefit of azithromycin was modeled as a reduction in exacerbation rates. Adverse events included cardiovascular death, hearing loss, gastrointestinal symptoms, and antimicrobial resistance. The incremental cost-effectiveness ratio (ICER) was calculated with costs in 2020 Canadian dollars (\$) and quality-adjusted life-years (QALYs) discounted at 1.5% per year. The analysis was stratified among patient subgroups based on exacerbation histories. **Results:** In patients with a positive exacerbation history (one or more events in the previous 12 mo), azithromycin was associated with \$49,732 costs, 7.65 QALYs, and 10.95 exacerbations per patient over 20 years. The corresponding values were \$48,436, 7.62, and 11.86 for the reference group, resulting in an ICER of \$43,200 per QALY gained. In patients defined as frequent exacerbators (two or more moderate or one or more severe events in the past 12 mo), the ICER was reduced to \$8,862 per QALY gained. In patients with no history of exacerbation, azithromycin had lower QALYs and higher costs than the reference group. **Conclusions:** Add-on azithromycin is cost effective in patients with a recent history of exacerbations at commonly accepted willingness-to-pay thresholds of \$50,000-\$100,000/QALY. Guidelines should consider recommending add-on azithromycin for patients who had at least one moderate or severe exacerbation in the past year, albeit more information about treatment efficacy would strengthen this recommendation.

Keywords: COPD; azithromycin; cost-effectiveness analysis; economic evaluation.

Comment in

- [The Price Is Right: Cost-Effectiveness of Long-Term Azithromycin for Chronic Obstructive Pulmonary Disease.](#)

Taylor B, Chiang S, Taylor S. Ann Am Thorac Soc. 2023 Dec;20(12):1707-1708. doi: 10.1513/AnnalsATS.202308-745ED. PMID: 38038601 No abstract available.

SUPPLEMENTARY INFO

Grants and funding [expand](#)

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Editorial

Respirology

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. 2023 Dec;28(12):1095-1097.

doi: 10.1111/resp.14597. Epub 2023 Sep 11.

[NLR in CBC: A holy grail for biomarker research in COPD?](#)

[Clarus Leung](#)^{1,2}, [Don D Sin](#)^{1,2}

Affiliations [expand](#)

- PMID: 37696582
- DOI: [10.1111/resp.14597](#)

No abstract available

Keywords: COPD; chronic obstructive pulmonary disease; complete blood count; neutrophil-to-lymphocyte ratio.

- [16 references](#)

SUPPLEMENTARY INFO

Publication types[expand](#)

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J Am Med Dir Assoc

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. 2023 Dec;24(12):1910-1917.e3.

doi: 10.1016/j.jamda.2023.08.010. Epub 2023 Sep 7.

[Preventing Avoidable Rehospitalizations through Standardizing Management of Chronic Conditions in Skilled Nursing Facilities](#)

[Ya Luan Hsiao](#)¹, [Eric B Bass](#)², [Albert W Wu](#)², [Denise Kelly](#)³, [Carol Sylvester](#)⁴, [Scott A Berkowitz](#)⁵, [Michele Bellantoni](#)⁶; [Johns Hopkins Community Health Partnership \(J-CHiP\) Team](#)⁴

Collaborators, Affiliations [expand](#)

- PMID: 37690461
- DOI: [10.1016/j.jamda.2023.08.010](https://doi.org/10.1016/j.jamda.2023.08.010)

Abstract

Objectives: This study evaluated the impact of standardized care protocols, as a part of a quality improvement initiative (Johns Hopkins Community Health Partnership, J-CHiP), on hospital readmission rates for patients with a diagnosis of congestive heart failure (CHF) and/or chronic obstructive pulmonary disease (COPD) after being discharged to skilled nursing facilities (SNFs).

Design: A retrospective study comparing 30-day hospital readmission rates the year before and 2 years following the implementation of the care protocol interventions.

Settings and participants: Patients discharged from Johns Hopkins Hospital or Johns Hopkins Bayview Medical Center to the participating SNFs diagnosed with CHF and/or COPD.

Methods: The standardized protocols included medical provider or nurse assessments on SNF admission, multidisciplinary care planning, and medication management to avoid unplanned readmissions to the hospital. Descriptive analyses were conducted to illustrate the 30-day readmission rates before and after protocol implementation.

Results: There were 1128 patients in the pre-J-CHiP cohort and 2297 patients in the J-CHiP cohort. About half of the patients with a recorded diagnosis of CHF without COPD had the standardized protocol initiated, whereas 47% of the patients with a recorded diagnosis of COPD without CHF had the standardized protocol initiated. Of patients with recorded diagnoses of COPD and CHF, 49% had both protocols initiated. A reduction in the readmission rate was observed for patients with COPD protocols, from 23.5% in 2011 to 12.1% in 2015. However, fluctuations in the readmission rates were observed for patients who initiated the CHF protocols.

Conclusions and implications: There were improvements in the readmission rates in this study, especially for patients who had initiated standardized care protocols in the SNFs. Our findings demonstrate great value in standardizing care management and strengthening collaboration with chronic care settings to facilitate a smooth transition of medically complex patients discharged from large health care systems. Future interventions could consider assessing nonclinical factors that may impact preventable hospital readmissions.

Keywords: Standardized care management; care coordination; community partnerships; healthcare quality improvement; multidisciplinary care; redesigned health care delivery.

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Conflict of interest statement

Disclosure The authors declare no conflicts of interest.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

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Review

Curr Opin Support Palliat Care

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. 2023 Dec 1;17(4):277-282.

doi: 10.1097/SPC.0000000000000671. Epub 2023 Aug 23.

Home ventilation for patients with end-stage chronic obstructive pulmonary disease

[Tim Raveling^{1,2}](#), [Heidi A Rantala^{3,4}](#), [Marieke L Duiverman^{1,2}](#)

Affiliations expand

- PMID: 37646583
- PMCID: [PMC10597445](#)
- DOI: [10.1097/SPC.0000000000000671](#)

Free PMC article

Abstract

Purpose of the review: The number of patients with end-stage chronic obstructive pulmonary disease (COPD) treated with chronic non-invasive ventilation (NIV) has greatly increased. In this review, the authors summarize the evidence for nocturnal NIV and NIV during exercise. The

authors discuss the multidisciplinary and advanced care of patients with end-stage COPD treated with NIV.

Recent findings: Nocturnal NIV improves gas exchange, health-related quality of life and survival in stable hypercapnic COPD patients. Improvements in care delivery have been achieved by relocating care from the hospital to home based; home initiation of chronic NIV is feasible, non-inferior regarding efficacy and cost-effective compared to in-hospital initiation. However, the effect of NIV on symptoms is variable, and applying optimal NIV for end-stage COPD is complex. While exercise-induced dyspnoea is a prominent complaint in end-stage COPD, nocturnal NIV will not change this. However, NIV applied solely during exercise might improve exercise tolerance and dyspnoea. While chronic NIV is often a long-standing treatment, patient expectations should be discussed early and be managed continuously during the treatment. Further, integration of advance care planning requires a multidisciplinary approach.

Summary: Although chronic NIV is an effective treatment in end-stage COPD with persistent hypercapnia, there are still important questions that need to be answered to improve care of these severely ill patients.

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Conflict of interest statement

There are no conflicts of interest.

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

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Diabetes Obes Metab

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. 2023 Dec;25(12):3599-3610.

Association between glycated haemoglobin and the risk of chronic obstructive pulmonary disease: A prospective cohort study in UK biobank

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Affiliations expand

- PMID: 37643990
- DOI: [10.1111/dom.15255](https://doi.org/10.1111/dom.15255)

Abstract

Aims: To investigate the association between glycated haemoglobin (HbA1c) levels and chronic obstructive pulmonary disease (COPD) incidents in the general population, and the association between HbA1c levels and mortality in patients with COPD.

Materials and methods: We investigated the association of HbA1c levels with COPD risk in the general population in the UK Biobank, using data from 420 065 participants. Survival analysis was conducted for 18 854 patients with COPD. We used restricted cubic spline analysis to assess the dose-response relationship between HbA1c levels and COPD risk and survival. Cox proportional hazards regression models were used to estimate hazard ratios (HRs) with 95% confidence intervals (CIs).

Results: During a median follow-up of 12.3 years, 11 556 COPD cases were recorded. HbA1c had a non-linear relationship with COPD risk (p for non-linearity $< .05$). Compared with the quintile 2 (32.2–<34.3 mmol/mol), those with HbA1c levels above 38.7 mmol/mol (quintile 5) had a 22% (HR, 1.22, 95% CI: 1.15–1.30) higher risk of COPD. Compared with the HbA1c decile 2 (30.5–<32.2 mmol/mol), the HRs (95% CI) of COPD risk were 1.16 (1.03–1.30) and 1.36 (1.24–1.50) in the lowest HbA1c decile (<30.5 mmol/mol) and highest decile (\geq 41.0 mmol/mol), respectively. The increased COPD risk associated with HbA1c was more pronounced in younger, current smokers, passive smokers, and participants with a higher Townsend deprivation index (all p for interaction $< .05$). Among patients with COPD, 4569 COPD cases died (488 because of COPD) during a median follow-up of 5.4 years. Regarding COPD survival, HbA1c had a non-linear relationship with all-cause death (p for non-linearity $< .05$). Those with HbA1c quintile 5 (\geq 38.7 mmol/mol) had a 23% (HR, 1.23, 95% CI: 1.10–1.37) higher risk of all-cause death compared with the quintile 2 (32.2–<34.3 mmol/mol). Compared with the HbA1c decile 4 (33.3–<34.3 mmol/mol), those in the lowest HbA1c decile (<30.5 mmol/mol) and highest HbA1c decile (\geq 41.0 mmol/mol) had 22% (HR, 1.22;

95% CI: 1.01-1.47) and 28% (HR, 1.28; 95% CI: 1.11-1.48) higher risk for overall death. However, no significant association was observed between HbA1c levels and the risk of COPD-specific death.

Conclusions: Our findings indicated that lower and higher HbA1c levels were associated with a higher risk of COPD. In COPD cases, lower and higher HbA1c levels were associated with a higher COPD all-cause death risk.

Keywords: chronic obstructive pulmonary disease; glycated haemoglobin; prospective cohort study.

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- [67 references](#)

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Publication types, MeSH terms, Substancesexpand

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J Pain Symptom Manage

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. 2023 Dec;66(6):611-620.e4.

doi: 10.1016/j.jpainsymman.2023.08.017. Epub 2023 Aug 22.

[Palliative Care Among Lung Cancer Patients With and Without COPD: A Population-Based Cohort Study](#)

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Affiliations expand

- PMID: 37619760

- DOI: [10.1016/j.jpainsymman.2023.08.017](https://doi.org/10.1016/j.jpainsymman.2023.08.017)

Abstract

Context: Lung cancer patients with chronic obstructive pulmonary disease (COPD) may have greater palliative care needs due to poor prognosis and symptom burden.

Objectives: We sought to compare the provision of timely palliative care and symptom burden by COPD status.

Methods: We performed a retrospective, population-based cohort study of individuals diagnosed with lung cancer in Ontario, Canada (2009-2019) using health administrative databases and cancer registries. The impact of COPD on the probability of receiving palliative care was determined accounting for dying as a competing event, overall and stratified by stage. The provision of palliative care for patients with severe symptoms (Edmonton Symptom Assessment Scale score ≥ 7), location of the first palliative care visit and symptom severity were compared by COPD status.

Results: A total of 74,993 patients were included in the study (48% of patients had available symptom data). At the time of lung cancer diagnosis, 50% of patients had COPD. Stage I-III patients with COPD were more likely to receive palliative care (adjusted Hazard Ratio (HR)s: 1.05-1.31) with no difference for stage IV (1.02, 95% CI: 1.00-1.04). Despite having severe symptoms, very few patients with early-stage disease received palliative care (Stage I: COPD-23% vs. no COPD-18%, SMD = 0.12). Most patients (84%) reported severe symptoms and COPD worsened symptom burden, especially among early-stage patients.

Conclusion: COPD impacts the receipt of palliative care and symptom burden for patients with early-stage lung cancer. Many patients with severe symptoms did not receive palliative care, suggesting unmet needs among this vulnerable population.

Keywords: COPD; Lung cancer; palliative care; symptoms.

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. 2023 Dec;20(1):274-283.

doi: 10.1080/15412555.2023.2242493.

Development of Multivariable Prediction Models for the Identification of Patients Admitted to Hospital with an Exacerbation of COPD and the Prediction of Risk of Readmission: A Retrospective Cohort Study using Electronic Medical Record Data

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Affiliations expand

- PMID: 37555513
- DOI: [10.1080/15412555.2023.2242493](https://doi.org/10.1080/15412555.2023.2242493)

Abstract

Background: Approximately 20% of patients who are discharged from hospital for an acute exacerbation of COPD (AECOPD) are readmitted within 30 days. To reduce this, it is important both to identify all individuals admitted with AECOPD and to predict those who are at higher risk for readmission.

Objectives: To develop two clinical prediction models using data available in electronic medical records: 1) identifying patients admitted with AECOPD and 2) predicting 30-day readmission in patients discharged after AECOPD.

Methods: Two datasets were created using all admissions to General Internal Medicine from 2012 to 2018 at two hospitals: one cohort to identify AECOPD and a second cohort to predict 30-day readmissions. We fit and internally validated models with four algorithms.

Results: Of the 64,609 admissions, 3,620 (5.6%) were diagnosed with an AECOPD. Of those discharged, 518 (15.4%) had a readmission to hospital within 30 days. For identification of patients with a diagnosis of an AECOPD, the top-performing models were LASSO and a four-variable regression model that consisted of specific medications ordered within the first 72 hours of admission. For 30-day readmission prediction, a two-variable regression model was the top performing model consisting of number of COPD admissions in the previous year and the number of non-COPD admissions in the previous year.

Conclusion: We generated clinical prediction models to identify AECOPDs during hospitalization and to predict 30-day readmissions after an acute exacerbation from a dataset derived from available EMR data. Further work is needed to improve and externally validate these models.

Keywords: COPD; acute exacerbations; machine learning; readmission.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grants and fundingexpand

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Review

COPD

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. 2023 Dec;20(1):284-291.

doi: 10.1080/15412555.2023.2242489.

[Statins and Mortality in COPD: A Methodological Review of Observational Studies](#)

Affiliations expand

- PMID: 37555454
- DOI: [10.1080/15412555.2023.2242489](https://doi.org/10.1080/15412555.2023.2242489)

Abstract

Randomized controlled trials and observational studies have reported conflicting results on the potential beneficial effects of statins on mortality in patients with chronic obstructive pulmonary disease (COPD). We performed a systematic search of the literature to review all observational studies reporting relative risks of death with statin use in COPD, focusing on potential sources of bias. We identified 15 observational studies, out of 2835, of which 12 were affected by time-related and other biases and the remaining 3 by confounding bias. All 15 studies were also subject to confounding bias due to lack of adjustment for important COPD-related factors. The risk of death associated with statin use was reduced across all 15 studies (pooled relative risk (PRR) 0.66; 95% CI: 0.59-0.74). The reduction was observed in 7 studies with immortal time bias (PRR 0.62; 95% CI: 0.53-0.72), two with collider-stratification bias (PRR 0.60; 95% CI: 0.45-0.80), one with time-window bias (RR 0.61; 95% CI: 0.38-0.98), one with immeasurable time bias (RR 0.50; 95% CI: 0.40-0.62), and one with exposure misclassification (RR 0.86; 95% CI: 0.72-1.03). The three studies that avoided these biases were, however, affected by confounding bias resulting in a PRR of 0.77 (95% CI: 0.61-0.98). In conclusion, the observational studies investigating statin use and mortality in COPD are affected by major biases, many of which can result in spurious protective effects. Well-designed observational studies that carefully emulate randomized trials are needed to resolve this uncertainty regarding the potential beneficial benefits of statins on mortality in patients with COPD.

Keywords: Confounding; database studies; immortal time bias; selection bias.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances expand

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COPD

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. 2023 Dec;20(1):9-17.

doi: 10.1080/15412555.2022.2136066.

Evaluation of Exacerbation and Symptom-Free Time in Patients with COPD

[Mirthe I de Vries^{1,2}](#), [Tanja W Effing^{3,4}](#), [Job van der Palen^{5,6}](#), [Jade Schrijver^{2,6}](#), [Paul van der Valk²](#), [Anke Lenferink^{1,2,7}](#)

Affiliations expand

- PMID: 37552476

- DOI: [10.1080/15412555.2022.2136066](https://doi.org/10.1080/15412555.2022.2136066)

Abstract

In clinical practice, clinicians mainly focus on Chronic Obstructive Pulmonary Disease (COPD) exacerbations and symptoms, while patients may prefer to evaluate periods free of COPD exacerbations and deteriorated symptoms. The latter would suit the positive health approach that centralizes people and their beliefs. We aimed to identify patient characteristics and health outcomes relating to: 1) COPD exacerbation-free days; 2) days with no more symptoms than usual; and 3) combined COPD exacerbation and comorbid flare-up-free days (i.e. chronic heart failure, anxiety, depression flare-ups) using negative binomial regression analyzes. Data were obtained from two self-management intervention trials including COPD patients with and without comorbidities. 313 patients (mean age 66.0 years, 63.6% male, 68.7% comorbidity) were included. Better baseline chronic respiratory questionnaire (CRQ) fatigue (incidence rate ratio (IRR) = 1.03 (95% CI 1.01-1.05), $p = 0.02$) and mastery scores (IRR = 1.03 (95% CI 1.00-1.06), $p = 0.04$) and fewer courses of antibiotics (IRR = 0.95 (95% CI 0.94-0.96), $p < 0.01$) were related to more COPD exacerbation-free days. Additionally, better baseline CRQ fatigue (IRR = 1.05 (95% CI 1.00-1.10), $p = 0.04$) and mastery scores (IRR = 1.06 (95% CI 1.00-1.12), $p = 0.04$), fewer courses of antibiotics (IRR = 0.94 (95% CI 0.91-0.96), $p < 0.01$), and improved CRQ dyspnea scores over 12 months of follow-up (IRR = 1.07 (95% CI 1.01-1.12), $p < 0.01$) were correlated to more days free of deteriorated symptoms. Less baseline dyspnea (modified Medical Research Council score) (IRR = 0.95 (95% CI 0.92-0.98), $p < 0.01$) and fewer courses of antibiotics (IRR = 0.94 (95% CI 0.93-0.95), $p < 0.01$) were associated with more combined COPD exacerbation and comorbid flare-up-free days. Healthcare professionals should be aware that less fatigue and better mastering of COPD relate to more exacerbation and symptom-free time in COPD patients.

Keywords: Chronic obstructive pulmonary disease; comorbidity; disease management; exacerbation-free time; positive health; symptom flare-up.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Randomized Controlled Trial

Med Sci Sports Exerc

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. 2023 Dec 1;55(12):2123-2131.

doi: 10.1249/MSS.0000000000003268. Epub 2023 Aug 2.

[The Impact of Exercise Training and Supplemental Oxygen on Peripheral Muscles in Chronic Obstructive Pulmonary Disease: A Randomized Controlled Trial](#)

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

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- PMID: 37535316

- PMID: [PMC10662626](#)
- DOI: [10.1249/MSS.0000000000003268](#)

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Abstract

Objective: Exercise training is a cornerstone of the treatment of chronic obstructive pulmonary disease, whereas the related interindividual heterogeneity in skeletal muscle dysfunction and adaptations are not yet fully understood. We set out to investigate the effects of exercise training and supplemental oxygen on functional and structural peripheral muscle adaptation.

Methods: In this prospective, randomized, controlled, double-blind study, 28 patients with nonhypoxemic chronic obstructive pulmonary disease (forced expiratory volume in 1 second, $45.92\% \pm 9.06\%$) performed 6 wk of combined endurance and strength training, three times a week while breathing either supplemental oxygen or medical air. The impact on exercise capacity, muscle strength, and quadriceps femoris muscle cross-sectional area (CSA) was assessed by maximal cardiopulmonary exercise testing, 10-repetition maximum strength test of knee extension, and magnetic resonance imaging, respectively.

Results: After exercise training, patients demonstrated a significant increase in functional capacity, aerobic capacity, exercise tolerance, quadriceps muscle strength, and bilateral CSA. Supplemental oxygen affected significantly the training impact on peak work rate when compared with medical air ($+0.20 \pm 0.03$ vs $+0.12 \pm 0.03$ W·kg⁻¹, $P = 0.047$); a significant increase in CSA ($+3.9 \pm 1.3$ cm², $P = 0.013$) was only observed in the training group using oxygen. Supplemental oxygen and exercise-induced peripheral desaturation were identified as significant opposing determinants of muscle gain during this exercise training intervention, which led to different adaptations of CSA between the respective subgroups.

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

Trial registration: ClinicalTrials.gov [NCT01150383](#).

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

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Semin Respir Crit Care Med

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. 2023 Dec;44(6):826-839.

doi: 10.1055/s-0043-1770121. Epub 2023 Jul 24.

Management of Pulmonary Hypertension Associated with Chronic Lung Disease

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Affiliations expand

- PMID: 37487524
- DOI: [10.1055/s-0043-1770121](https://doi.org/10.1055/s-0043-1770121)

Abstract

Pulmonary hypertension (PH) is a common complication of chronic lung diseases, particularly in chronic obstructive pulmonary disease (COPD) and interstitial lung diseases (ILD) and especially in advanced disease. It is associated with greater mortality and worse clinical course. Given the high prevalence of some respiratory disorders and because lung parenchymal abnormalities might be present in other PH groups, the appropriate diagnosis of PH associated with respiratory disease represents a clinical challenge. Patients with chronic lung disease presenting symptoms that exceed those expected by the pulmonary disease should be further evaluated by echocardiography. Confirmatory right heart catheterization is indicated in candidates to surgical treatments, suspected severe PH potentially amenable with targeted therapy, and, in general, in those conditions where the

result of the hemodynamic assessment will determine treatment options. The treatment of choice for these patients who are hypoxemic is long-term oxygen therapy and pulmonary rehabilitation to improve symptoms. Lung transplant is the only curative therapy and can be considered in appropriate cases. Conventional vasodilators or drugs approved for pulmonary arterial hypertension (PAH) are not recommended in patients with mild-to-moderate PH because they may impair gas exchange and their lack of efficacy shown in randomized controlled trials. Patients with severe PH (as defined by pulmonary vascular resistance >5 Wood units) should be referred to a center with expertise in PH and lung diseases and ideally included in randomized controlled trials. Targeted PAH therapy might be considered in this subset of patients, with careful monitoring of gas exchange. In patients with ILD, inhaled treprostinil has been shown to improve functional ability and to delay clinical worsening.

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Conflict of interest statement

None declared.

SUPPLEMENTARY INFO

MeSH termsexpand

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. 2023 Dec;20(1):210-215.

doi: 10.1080/15412555.2023.2215324.

[Sleep Hypoventilation is Common in Diurnal Normocapnic COPD Patients with Severe or Very Severe Obstruction](#)

and is Not Associated with Body Mass Index

[Safir Zewari](#)^{1,2}, [Bram van den Borst](#)², [Michel van den Heuvel](#)², [Frank van den Elshout](#)¹, [Manu Sastry](#)³, [Petra Vos](#)¹

Affiliations expand

- PMID: 37486242
- DOI: [10.1080/15412555.2023.2215324](https://doi.org/10.1080/15412555.2023.2215324)

Abstract

Sleep hypoventilation (SH) is common in COPD patients with diurnal hypercapnia, however there are little data on the presence of SH in COPD patients with diurnal normocapnia. In this study the prevalence of SH in stable normocapnic COPD patients with severe or very severe obstruction (GOLD stages III and IV) was evaluated across body mass index (BMI) classes and associations between SH and body composition measures were explored. A total of 56 diurnal normocapnic COPD patients, of whom 17 normal-weight (COPD_{NW}), 18 overweight (COPD_{OW}) and 21 obese (COPD_{OB}), underwent polysomnography to objectify SH and bioelectrical impedance analysis to assess body composition. The overall prevalence of SH was 66.1% and was not different across BMI classes. Logistic regression models indicated that SH was not associated with waist-to-hip ratio, body fat percentage and fat-free mass index. Our data indicate that SH is common in diurnal normocapnic COPD patients with severe or very severe obstruction and is not associated with BMI or body composition.

Keywords: COPD; obesity; sleep hypoventilation.

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. 2023 Dec;20(1):248-255.

doi: 10.1080/15412555.2023.2234992.

The Influence of Breathing Exercises on Regional Ventilation in Healthy and Patients with Chronic Obstructive Pulmonary Disease

[Lin Yang¹](#), [Ke Zhao²](#), [Zhiyun Gao¹](#), [Feng Fu³](#), [Hang Wang¹](#), [Chunchen Wang¹](#), [Jing Dai¹](#), [Yang Liu¹](#), [Yilong Qin¹](#), [Meng Dai³](#), [Xinsheng Cao¹](#), [Zhanqi Zhao⁴](#)

Affiliations expand

- PMID: 37477218
- DOI: [10.1080/15412555.2023.2234992](https://doi.org/10.1080/15412555.2023.2234992)

Abstract

We hypothesized that the respiratory exercises have uniform effects on ventilation in healthy subjects but the effects varied in patients with chronic obstructive pulmonary disease (COPD). In this study, a total of 30 healthy volunteers and 9 patients with COPD were included. Data were recorded continuously during (1) diaphragmatic breathing; (2) pursed lip breathing with full inhalation; (3) pursed lip combining diaphragmatic breathing. The sequence of the three breathing exercises was randomized using machine generated random permutation. Spatial and temporal ventilation distributions were evaluated with electrical impedance tomography. Results showed that, tidal volume was significantly larger during various breathing exercises compared to quiet tidal breathing, in both healthy and COPD ($p < 0.01$). However, for other EIT-based parameters, statistical significances were only observed in healthy volunteers, not in patients. Diaphragmatic breathing alone might not be able to decrease functional residual capacity in COPD and the effect varied largely from patient to patient (6:3, decrease vs. increase). Ventilation distribution moved toward ventral regions in healthy during breathing exercises ($p < 0.0001$). Although this trend was observed in the COPD, the differences were not significant. Ventilation became more homogeneous when diaphragmatic breathing technique was implemented ($p < 0.0001$). Again, the improvements were not significant in COPD. Regional ventilation delay was relatively high in COPD and comparable in various breathing periods. In conclusions, the impact of pursed lip and diaphragmatic breathing varied in different patients with COPD. Breathing exercise may need to be individualized to maximize the training efficacy with help of EIT.

Keywords: Respiratory exercises; chronic obstructive pulmonary disease; electrical impedance tomography; regional ventilation.

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Ann Am Thorac Soc

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. 2023 Dec;20(12):1709-1717.

doi: 10.1513/AnnalsATS.202304-288OC.

National Prevalence of Social Isolation and Loneliness in Adults with Chronic Obstructive Pulmonary Disease

[Angela O Suen](#)¹, [Anand S Iyer](#)², [Irena Cencer](#)^{3,4}, [Erica Farrand](#)¹, [Douglas B White](#)⁵, [Jonathan Singer](#)¹, [Rebecca Sudore](#)^{3,4}, [Ashwin Kotwal](#)^{3,4}

Affiliations [expand](#)

- PMID: 37463307
- DOI: [10.1513/AnnalsATS.202304-288OC](https://doi.org/10.1513/AnnalsATS.202304-288OC)

Abstract

Rationale: Social isolation and loneliness are gaining recognition for their role in health outcomes, yet they have not been defined in people with chronic obstructive pulmonary disease

(COPD). **Objective:** To determine the national prevalence of and characteristics associated with social isolation and loneliness in people with COPD. **Methods:** This is a cross-sectional study of community-dwelling adults aged ≥ 50 years in the nationally representative HRS (Health and Retirement Study) (2016-2018). Participants self-reported COPD and supplemental oxygen use and were categorized into three groups: 1) no COPD; 2) COPD; and 3) COPD on oxygen. Social isolation was defined using a nine-item scale indicating minimal household contacts, social network interaction, and community engagement. Loneliness was measured using the 3-Item UCLA Loneliness Scale. Multivariable logistic regression defined prevalence and associated characteristics for both. **Results:** Participants ($n = 10,384$) were on average 68 years old (standard deviation, ± 10.5), 54% female, 10% Black, 11% self-reported COPD, and 2% self-reported supplemental oxygen. Overall, 12% were socially isolated, 12% lonely, and 3% both socially isolated and lonely. People with COPD had a higher adjusted prevalence of social isolation (no COPD: 11%; COPD: 16%; COPD on oxygen: 20%; $P < 0.05$) and loneliness (no COPD: 11%; COPD: 18%; COPD on oxygen: 22%; $P < 0.001$). In those with COPD, characteristics associated with social isolation ($P < 0.05$) included sex (men: 22%; women: 13%), non-Hispanic White ethnicity (White: 19%; Black: 7%), low net worth ($< \$6,000$: 32%; $\$81,001$ - $\$239,000$: 10%), depression (depression: 24%; no depression: 14%), having difficulty with one or more activities of daily living (one or more difficulty: 22%; no difficulty: 14%), and current cigarette use (current: 24%; never: 13%). Characteristics associated with loneliness ($P < 0.05$) included younger age (50-64 yr: 22%; 75-84 yr: 12%), being single (single: 32%; married: 12%), depression (depression: 36%; no depression: 13%), having difficulty with one or more activities of daily living (one or more difficulty: 29%; no difficulty: 15%), diabetes (diabetes: 26%; no diabetes: 17%), and heart disease (heart disease 23%; no heart disease: 17%). **Conclusions:** Nearly one in six adults with COPD experience social isolation, and one in five experience loneliness, with almost twice the prevalence among those on supplemental oxygen compared with the general population. Demographic and clinical characteristics identify those at highest risk to guide clinical and policy interventions.

Keywords: respiratory insufficiency; social determinants of health; social environment; social support.

Comment in

- [All the Lonely People: Social Isolation and Loneliness in Chronic Obstructive Pulmonary Disease.](#)
Ferrante LE, Cohen AB. Ann Am Thorac Soc. 2023 Dec;20(12):1703-1704. doi: 10.1513/AnnalsATS.202309-833ED. PMID: 38038602 No abstract available.

SUPPLEMENTARY INFO

Grants and fundingexpand

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Review

COPD

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. 2023 Dec;20(1):197-209.

doi: 10.1080/15412555.2023.2187210.

Current Perspectives on Biological Therapy for COPD

[Ambedkar Kumar Yadav¹](#), [Wenhua Gu¹](#), [Tongyangzi Zhang¹](#), [Xianghuai Xu¹](#), [Li Yu^{1,2}](#)

Affiliations expand

- PMID: 37394963
- DOI: [10.1080/15412555.2023.2187210](https://doi.org/10.1080/15412555.2023.2187210)

Abstract

Chronic obstructive pulmonary disease (COPD) is a chronic, complex, and heterogeneous condition with significant mortality, morbidity, and socioeconomic burden. Given the heterogeneity, the current management of COPD, which mainly relies on bronchodilators and corticosteroids, cannot consider all COPD populations. Moreover, the present treatment modalities are directed at minimizing symptoms and reducing the risk of a future attack, but they exhibit few meaningful anti-inflammatory activities in preventing and reducing disease progression. Therefore, new anti-inflammatory molecules are needed to manage COPD better. Use of targeted biotherapy may obtain better results by increasing understanding of the underlying inflammatory process and identifying new biomarkers. In this review, we focus briefly on study of the underlying inflammatory process in the pathogenesis of COPD for better identification of novel target biomarkers, and we describe a novel class of anti-inflammatory biologics that are already under evaluation for their use in managing COPD.

Keywords: COPD; anti-inflammatory; biologics; management; new therapies.

SUPPLEMENTARY INFO

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Sleep Breath



. 2023 Dec;27(6):2407-2413.

doi: 10.1007/s11325-023-02875-4. Epub 2023 Jun 30.

Comorbidities are associated with self-reported sleep-disordered breathing and insomnia: a cross-sectional study from China

[Shengnan Li](#)¹, [Siyue Tan](#)¹, [Dong Liu](#)¹, [Ke Zhang](#)¹, [Yuyi Zhang](#)¹, [Bo Wang](#)², [Hui Zuo](#)^{3,4}

Affiliations [expand](#)

- PMID: 37389766
- DOI: [10.1007/s11325-023-02875-4](https://doi.org/10.1007/s11325-023-02875-4)

Abstract

Purpose: We aimed to examine the associations of comorbidities with self-reported sleep-disordered breathing (SDB) and insomnia among Chinese adults.

Methods: The study used data from a community-based cross-sectional survey performed in China in 2018–2020. Multivariable logistic regression models were used to analyze the associations of 12 comorbidities with SDB and insomnia.

Results: A total of 4329 Han Chinese adults aged ≥ 18 years were enrolled. Of these, 1970 (45.5%) were male, with a median age of 48 years (interquartile range: 34-59). Compared with the participants without any conditions, adjusted ORs for SDB and insomnia for those with ≥ 4 comorbidities were 2.33 (95% CI: 1.58, 3.43, P-trend < 0.001) and 3.89 (95% CI: 2.69, 5.64, P-trend < 0.001), respectively. Seven comorbidities (hypertension, hyperlipidemia, coronary heart disease (CHD), bone and joint disease, neck or lumbar disease, chronic digestive diseases, and chronic urological disease) were positively associated with both SDB and insomnia. Cancer and chronic obstructive pulmonary disease (COPD) were also independently associated with insomnia. Of all comorbidities, cancer was most strongly associated with insomnia (OR = 3.16; 95% CI: 1.78, 5.63; $P < 0.001$), and CHD was most strongly associated with SDB (OR = 1.77; 95% CI: 1.19, 2.64; $P < 0.001$).

Conclusions: The findings showed that adults with an increasing number of comorbidities had higher odds for SDB and insomnia, which were independent of sociodemographic and lifestyle factors.

Keywords: Chronic conditions; Comorbidities; Insomnia; Sleep-disordered breathing.

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Int J Circumpolar Health

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. 2023 Dec;82(1):2220476.

doi: 10.1080/22423982.2023.2220476.

High burden of symptoms reported among patients diagnosed with chronic obstructive pulmonary disease (COPD) in Greenland after introducing the COPD Assessment Test in clinical practice

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Affiliations expand

- PMID: 37267504
- PMCID: [PMC10240970](#)
- DOI: [10.1080/22423982.2023.2220476](#)

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Abstract

The aim was to test the internal consistency of the Greenlandic version of the COPD Assessment Test (CAT) questionnaire and to estimate the symptom burden in patients with chronic obstructive pulmonary disease (COPD) in Greenland using the CAT questionnaire. A Greenlandic version of the CAT questionnaire was developed including forward translation, reconciliation, backwards translation, and pilot test. Afterwards, a cross-sectional study of patients with COPD was conducted. The internal consistency assessed by the Cronbach α coefficient was 0.823 for the Greenlandic version of the questionnaire ($n = 103$). The CAT was negatively correlated to spirometry values and current smoking. In the cross-sectional study ($n = 250$), 81.1% of the patients experienced a high symptom burden (≥ 10). The main CAT score was 17 (range 0-38). The CAT was used in 9 out of 17 towns in Greenland. The Greenlandic version of the CAT questionnaire demonstrated a good internal consistency. We observed a high burden of symptoms associated with reduced lung function and active smoking status among patient diagnosed with COPD in Greenland. The questionnaire can be used in clinical practice for assessment of symptom burden in patients with COPD in Greenland and may help to increase focus on symptom control and quality of care.

Keywords: CAT questionnaire; COPD; COPD assessment test; Chronic obstructive pulmonary disease; symptom burden.

Conflict of interest statement

The authors wish to thank pulmonologist Sequssuna Olsen for discussion and revision of the Greenlandic version of the CAT questionnaire. Furthermore, we would like to thank the Language Secretariat of Greenland for proofreading the CAT questionnaire. At least, we would like to thank the healthcare providers from the lifestyle outpatient clinics in Greenland and from Steno Diabetes Center Greenland.

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

SUPPLEMENTARY INFO

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Meta-Analysis

COPD

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. 2023 Dec;20(1):167-174.

doi: 10.1080/15412555.2023.2200826.

[The Relationship between Physical Activity, Depression and Anxiety in People with COPD: A Systematic Review and Meta-analyses](#)

[Anne-Marie Selzler](#)¹, [Cindy Ellerton](#)¹, [Lauren Ellerton](#)¹, [Razanne Habash](#)¹, [Erica Nekolaichuk](#)², [Roger Goldstein](#)^{1,3,4,5}, [Dina Brooks](#)^{1,3,4,5,6}

Affiliations expand

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Abstract

Depression and anxiety are related to physical activity among people with chronic obstructive pulmonary disease (COPD), although the strength and direction of the reported relationships are inconsistent. This study systematically synthesized the relationships between physical activity and i) depression and ii) anxiety in people with COPD. Physical activity measurement type (objective, self-report) was examined as a moderator of these relationships. A systematic search of physical activity and COPD was conducted from inception to February 2022 across 8 databases. Studies were included if they provided correlation coefficients for the relationship between measures of physical activity and depression or anxiety in people with COPD and were published in English. Two reviewers independently screened, reviewed and extracted data, with discrepancies resolved by a third reviewer. Across 13 studies, a small relationship was found between physical activity and depression, weighted $r = -0.15$, 95%CI [-0.21, -0.10], which was not moderated by physical activity measurement type. Across 8 studies, a negligible relationship was found between physical activity and anxiety, weighted $r = -0.03$, 95%CI [-0.11, 0.04], although this was moderated by physical activity measurement type, such that self-reported physical activity had a small negative relationship with anxiety (weighted $r = -0.09$, 95% CI [-0.15, -0.03]) and objectively measured physical activity had a small positive relationship (weighted $r = 0.07$, 95% CI [-0.13, 0.26]). In COPD, the bivariate association between physical activity and anxiety and depression are small.

Keywords: anxiety; chronic obstructive pulmonary disease; depression; physical activity.

SUPPLEMENTARY INFO

Publication types, MeSH terms expand

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COPD



. 2023 Dec;20(1):162-166.

doi: 10.1080/15412555.2023.2165905.

Do Functional Tests Estimate Physical Activity in COPD?

[Natielly Soares Correia^{1,2}](#), [Joice Mara de Oliveira^{1,2}](#), [Lorena Paltanin Schneider^{1,2}](#), [Andrea Akemi Morita^{1,2}](#), [Fabio Pitta^{1,2}](#), [Karina Couto Furlanetto^{1,2}](#)

Affiliations expand

- PMID: 37166420
- DOI: [10.1080/15412555.2023.2165905](https://doi.org/10.1080/15412555.2023.2165905)

Abstract

The association between physical activity in daily life (PADL) and simple functional tests is not yet clearly understood in subjects with chronic obstructive pulmonary disease (COPD). Therefore, the aim of this study was to investigate the association of two functional tests (Sit-to-Stand test [STS] and the 4-Metre Gait Speed test [4MGS]) with PADL, as well as to identify whether these tests can discriminate those subjects who are physically inactive. In this cross-sectional study, 28 subjects with COPD performed the five repetitions Sit-to-Stand (STS5r), the 4MGS and used the DynaPort activity monitor for 7 days in order to assess PADL. Walking time, movement intensity while walking (MI) and Physical Activity Level index (PAL) were considered as PADL outcomes. STS5r and 4MGS, respectively, were significantly associated with walking time ($R^2 = 0.16$; $p = 0.024$ and $R^2 = 0.25$; $p = 0.006$) and PAL index ($R^2 = 0.17$; $p = 0.002$ and $R^2 = 0.30$; $p = 0.003$), whereas movement intensity was associated only with the 4MGS ($R^2 = 0.23$; $p = 0.009$). Additionally, both tests were able to discriminate physically inactive subjects (cutoffs: STS5r = 11.48s [AUC = 0.73]; 4MGS = 1.09m/s [AUC = 0.88]). In conclusion, STS5r and 4MGS can predict up to 30% of PADL in subjects with COPD. Both tests are related to PADL duration (e.g. time spent walking), while only the 4MGS reflects movement intensity. Both tests presented discriminative capacity to identify subjects with worse PADL pattern.

Keywords: Motor activity; activities of daily living; health evaluation; physical fitness; pulmonary disease chronic obstructive.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Randomized Controlled Trial

J Behav Med



. 2023 Dec;46(6):1010-1022.

doi: 10.1007/s10865-023-00411-z. Epub 2023 May 6.

Development of a targeted behavioral treatment for smoking cessation among individuals with Chronic Obstructive Pulmonary Disease

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Affiliations expand

- PMID: 37148395
- DOI: [10.1007/s10865-023-00411-z](https://doi.org/10.1007/s10865-023-00411-z)

Abstract

Objective: Smoking cessation for individuals with Chronic Obstructive Pulmonary Disease (COPD) is medically critical, but smoking for coping motives is a common barrier.

Method: In this evaluation of three treatment components (Mindfulness, Practice Quitting, and Countering Emotional Behaviors), we conducted two studies guided by the ORBIT model. Study 1 was a single-case design experiment (N = 18); Study 2 was a pilot feasibility study (N = 30). In both studies, participants were randomized to receive one of the three treatment modules. Study 1 examined implementation targets, changes in smoking for coping motives, and changes in smoking rate. Study 2 examined overall feasibility and participant-rated acceptability, and changes in smoking rate.

Results: Study 1: Treatment implementation targets were met by 3/5 Mindfulness participants, 2/4 Practice Quitting participants, and 0/6 Countering Emotional Behaviors participants. The Practice Quitting condition led to 100% of participants meeting the clinically significant threshold in smoking for coping motives. Incidence of quit attempts ranged from 0-50%, and smoking rate was reduced by 50% overall. Study 2: Recruitment and retention met feasibility targets, with 97% of participants completing all four treatment sessions. Participants reported high treatment satisfaction by qualitative responses and rating scales (M = 4.8/ 5.0). Incidence of quit attempts ranged from 25-58%, and smoking rate was reduced by 56% overall.

Conclusions: These two small-N studies provide complementary findings on internal validity and implementation of the novel intervention. While Study 1 provided initial support for plausibility of clinically significant change, Study 2 provided data on key feasibility parameters.

Implications: Smoking cessation for individuals with COPD is medically critical. We conducted an early-phase evaluation of a novel behavioral treatment focused on reducing smoking for coping motives. Results provided initial support for plausibility of clinically significant change and feasibility of the intervention.

Keywords: COPD; Tobacco; behavioral treatment; nicotine; smoking cessation.

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COPD

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. 2023 Dec;20(1):126-134.

doi: 10.1080/15412555.2023.2169120.

Incidence and Healthcare Burden of Pertussis among Older Adults with and without Pre-Existing Chronic Obstructive Pulmonary Disease or Asthma in South Korea

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Affiliations expand

- PMID: 37093711
- DOI: [10.1080/15412555.2023.2169120](https://doi.org/10.1080/15412555.2023.2169120)

Abstract

A retrospective cohort study was conducted to examine trends in the incidence and burden of pertussis among adults ≥ 50 years in South Korea, with/without pre-existing chronic obstructive pulmonary disease (COPD) or asthma. The nationwide Health Insurance Review and Assessment Service (HIRA) database was used to identify patients ≥ 50 years diagnosed with pertussis (2009-2018). Mean annual incidence of pertussis per 100 000 persons and overall mean incidence rate ratios (IRR) were calculated for patients with pre-existing COPD or asthma versus those with neither. Incremental healthcare costs (all-cause and pertussis-related) and healthcare utilisation (number of outpatient visits, emergency room visits, and number and length of hospitalisations) up to 12 months after, compared to 3 months before pertussis diagnosis, were also measured for each group (matched on sex, age, and Charlson Comorbidity Index). Of 1011 pertussis cases, 175 had asthma, 96 had COPD (not mutually exclusive), and 796 had neither. Overall mean pertussis incidence was 2.5, 3.4, and 0.5 for adults with pre-existing COPD, asthma, and those with neither. IRR (95% confidence interval) of pertussis for adults with pre-existing COPD and asthma was 4.9 (4.0-6.1) and 6.7 (5.7-7.9). Both COPD-pertussis and asthma-pertussis groups had higher mean incremental all-cause costs and length of hospitalisations than the general-pertussis group 3 months following pertussis diagnosis. In conclusion, individuals ≥ 50 years in South Korea with pre-existing COPD or asthma were at an increased risk of being diagnosed with pertussis and had higher healthcare resource utilisation than those without these conditions.

Keywords: Adult; COPD; South Korea; asthma; pertussis; vaccination; whooping cough.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Acad Radiol



. 2023 Dec;30(12):2894-2903.

doi: 10.1016/j.acra.2023.03.021. Epub 2023 Apr 14.

[CT-Based Radiomic Nomogram for the Prediction of Chronic Obstructive Pulmonary Disease in Patients with Lung cancer](#)

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Affiliations expand

- PMID: 37062629
- DOI: [10.1016/j.acra.2023.03.021](https://doi.org/10.1016/j.acra.2023.03.021)

Free article

Abstract

Rationale and objectives: To develop and validate a model for predicting chronic obstructive pulmonary disease (COPD) in patients with lung cancer based on computed tomography (CT) radiomic signatures and clinical and imaging features.

Materials and methods: We retrospectively enrolled 443 patients with lung cancer who underwent pulmonary function test as the primary cohort. They were randomly assigned to the training (n = 311) or validation (n = 132) set in a 7:3 ratio. Additionally, an independent external cohort of 54 patients was evaluated. The radiomic lung nodule signature was constructed using the least absolute shrinkage and selection operator algorithm, while key variables were selected using logistic regression to develop the clinical and combined models presented as a nomogram.

Results: COPD was significantly related to the radiomics signature in both cohorts. Moreover, the signature served as an independent predictor of COPD in the multivariate regression analysis. For the training, internal, and external cohorts, the area under the receiver operating characteristic curve (ROC, AUC) values of our radiomics signature for COPD prediction were 0.85, 0.85, and 0.76, respectively. Additionally, the AUC values of the radiomic nomogram for COPD prediction were 0.927, 0.879, and 0.762 for the three cohorts, respectively, which outperformed the other two models.

Conclusion: The present study presents a nomogram that incorporates radiomics signatures and clinical and radiological features, which could be used to predict the risk of COPD in patients with lung cancer with one-stop chest CT scanning.

Keywords: chronic obstructive pulmonary disease; computed tomography; lung cancer; radiomics.

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Conflict of interest statement

Declaration of Competing Interest None.

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. 2023 Dec;20(1):153-161.

doi: 10.1080/15412555.2023.2192789.

Prevalence, Trend, and Risk Factors for Early Chronic Obstructive Pulmonary Disease: An Analysis of the Nationwide Population-Based Survey from 2010 to 2019 in South Korea

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Affiliations expand

- PMID: 37036446
- DOI: [10.1080/15412555.2023.2192789](https://doi.org/10.1080/15412555.2023.2192789)

Abstract

This study aimed to evaluate the prevalence, trends, and risk factors of early chronic obstructive pulmonary disease (COPD) by using a nationally representative sample. The datasets of the Korea National Health and Nutrition Examination Survey 2010-2019 were used, where 80,860 individuals were identified; of these, 9,045 participants aged 40-49 years who underwent spirometry with no missing data were analyzed. Early COPD was defined as forced expiratory volume in 1 s /forced vital capacity ratio < the lower limit of normal (2.5th percentile) in individuals aged <50 years without a history of asthma, inhaler therapy, or persistent respiratory symptoms. The prevalence and trend of early COPD were estimated according to features such as smoking status and pack-years. Joinpoint regression analysis was used to analyze the significant annual change in the trend according to sex, smoking status, and pack-years. A complex sample multivariable-adjusted regression model was used to identify factors affecting early COPD. The estimated population size during 2010-2019 was 82,326,178. Early COPD was present in 4.5% of patients (6.5% of men and 2.3% of women). It was present in 7.7% of current smokers, followed by former and never smokers. Among smokers with ≥ 10 pack-years, early COPD was present in 8.2%, whereas it was present in 2.6% of smokers with < 10 pack-years. Joinpoint regression analyses found a recent decrease in the trend of prevalence in males who were former and current smokers. The multivariable-adjusted logistic regression model showed that being male, lower educational level, smoking status, and

pack-years were factors that affected the presence of early COPD. Continued surveillance of this pre-disease condition is required, and further research are warrant.

Keywords: Early COPD; KNHANES; prevalence; risk factor; trend.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Observational Study

COPD

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. 2023 Dec;20(1):144-152.

doi: 10.1080/15412555.2023.2174843.

[COPD Assessment Test as a Screening Tool for Anxiety and Depression in Stable COPD Patients: A Feasibility Study](#)

[Meishan Liu¹](#), [Yuna Li¹](#), [Danfeng Yin¹](#), [Ying Wang¹](#), [Tingting Fu¹](#), [Zhaomeng Zhu¹](#), [Chunming Zheng²](#), [Kewu Huang¹](#)

Affiliations expand

- PMID: 37036434

- DOI: [10.1080/15412555.2023.2174843](https://doi.org/10.1080/15412555.2023.2174843)

Abstract

Anxiety and depression are common comorbidities in chronic obstructive pulmonary disease (COPD) patients but are often under-diagnosed. We aimed to assess the suitability of the COPD Assessment Test (CAT) in screening anxiety and depression in patients with COPD. Stable COPD patients from a cross-sectional observational study were assessed by CAT. Anxiety and depression were identified using the Generalized Anxiety Disorder questionnaire (GAD-7) and Patient Health Questionnaire (PHQ-9), respectively. Logistic regression analysis and receiver operating characteristic curve analysis were used to identify factors associated with anxiety or depression and to calculate the predictive values. A total of 530 stable COPD patients were enrolled and of those, the proportions of anxiety and depression were 17.0% and 21.5%, respectively. The adjusted odds ratios of the CAT for the presence of anxiety and depression were 1.094 (95%CI: 1.057-1.131) and 1.143 (95%CI: 1.104-1.183), respectively. The CAT score had a significant predictive value for the presence of anxiety (AUC = 0.709) and depression (AUC = 0.791) with an optimum cutoff score of 15. However, the psychometric properties of CAT were undesirable, presenting high negative predictive value (NPV) but low positive predictive value (PPV). Among CAT items, analysis further showed that non-respiratory CAT components were superior to respiratory components in identifying both anxiety and depression. Our results indicated that CAT is more useful to exclude anxiety and depression rather than detect them.

Keywords: COPD assessment test; Chronic obstructive pulmonary disease; anxiety; depression.

- [Cited by 1 article](#)

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Meta-Analysis

Ann Med

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. 2023 Dec;55(1):746-759.

doi: 10.1080/07853890.2023.2172606.

Extracorporeal carbon dioxide removal for patients with acute respiratory failure: a systematic review and meta-analysis

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Affiliations expand

- PMID: 36856550
- PMCID: [PMC9980035](#)
- DOI: [10.1080/07853890.2023.2172606](#)

Free PMC article

Abstract

Background: Acute respiratory failure (ARF) is a common clinical critical syndrome with substantial mortality. Extracorporeal carbon dioxide removal (ECCO₂R) has been proposed for the treatment of ARF. However, whether ECCO₂R could provide a survival advantage for patients with ARF is still controversial.

Methods: Electronic databases (PubMed, Embase, Web of Science, and the Cochrane database) were searched from inception to 30 April 2022. Randomized controlled trials (RCTs) and observational studies that examined the following outcomes were included: mortality, length of hospital and ICU stay, intubation and tracheotomy rate, mechanical ventilation days, ventilator-free days (VFDs), respiratory parameters, and reported adverse events.

Results: Four RCTs and five observational studies including 1173 participants with ARF due to COPD or ARDS were included in this meta-analysis. Pooled analyses of related studies showed no significant difference in overall mortality between ECCO₂R and control group, neither in RCTs targeted ARDS or acute hypoxic respiratory failure patients (RR 1.05, 95% CI 0.83 to 1.32, $p = 0.70$, $I^2 = 0.0\%$), nor in studies targeted patients with ARF secondary to COPD (RR 0.80, 95% CI 0.58 to 1.11, $p = 0.19$, $I^2 = 0.0\%$). A shorter duration of ICU stay in the ECCO₂R group was only obtained in observational studies (WMD -4.25, $p < 0.01$), and ECCO₂R was associated with a longer length of hospital stay ($p = 0.02$). ECCO₂R was associated with lower intubation rate ($p <$

0.01) and tracheotomy rate ($p = 0.01$), and shorter mechanical ventilation days ($p < 0.01$) in comparison to control group in ARF patients with COPD. In addition, an improvement in pH ($p = 0.01$), PaO₂ ($p = 0.01$), respiratory rate ($p < 0.01$), and PaCO₂ ($p = 0.04$) was also observed in patients with COPD exacerbations by ECCO₂R therapy. However, the ECCO₂R-related complication rate was high in six of the included studies.

Conclusions: Our findings from both RCTs and observational studies did not confirm a significant beneficial effect of ECCO₂R therapy on mortality. A shorter length of ICU stay in the ECCO₂R group was only obtained in observational studies, and ECCO₂R was associated with a longer length of hospital stay. ECCO₂R was associated with lower intubation rate and tracheotomy rate, and shorter mechanical ventilation days in ARF patients with COPD. And an improvement in pH, PaO₂, respiratory rate and PaCO₂ was observed in the ECCO₂R group. However, outcomes largely relied on data from observational studies targeted patients with ARF secondary to COPD, thus further larger high-quality RCTs are desirable to strengthen the evidence on the efficacy and benefits of ECCO₂R for patients with ARF. Key messages ECCO₂R therapy did not confirm a significant beneficial effect on mortality. ECCO₂R was associated with lower intubation and tracheotomy rate, and shorter mechanical ventilation days in patients with ARF secondary to COPD. An improvement in pH, PaO₂, respiratory rate, and PaCO₂ was observed in ECCO₂R group in patients with COPD exacerbations. Evidence for the future application of ECCO₂R therapy for patients with ARF. The protocol of this meta-analysis was registered on PROSPERO (CRD42022295174).

Keywords: Extracorporeal carbon dioxide removal; acute respiratory failure; meta-analysis; mortality.

Conflict of interest statement

No potential conflict of interest was reported by the author(s).

- [Cited by 1 article](#)
- [42 references](#)
- [3 figures](#)

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. 2023 Dec;20(1):64-70.

doi: 10.1080/15412555.2022.2106840. Epub 2023 Jan 19.

Prognosis after Intensive Care for COPD Exacerbation in Relation to Long-Term Oxygen Therapy: A Nationwide Cohort Study

[Helena Nyström^{1,2}](#), [Magnus Ekström³](#), [Johan Berkius⁴](#), [Axel Ström⁵](#), [Sten Walther⁶](#), [Malin Inghammar²](#)

Affiliations expand

- PMID: 36656666
- DOI: [10.1080/15412555.2022.2106840](https://doi.org/10.1080/15412555.2022.2106840)

Free article

Abstract

Decisions to admit or refuse admission to intensive care for acute exacerbations of COPD (AECOPD) can be difficult, due to an uncertainty about prognosis. Few studies have evaluated outcomes after intensive care for AECOPD in patients with chronic respiratory failure requiring long-term oxygen therapy (LTOT). In this nationwide observational cohort study, we investigated survival after first-time admission for AECOPD in all patients aged ≥ 40 years admitted to Swedish intensive care units between January 2008 and December 2015, comparing patients with and without LTOT. Among the 4,648 patients enrolled in the study, 450 were on LTOT prior to inclusion. Respiratory support data was available for 2,631 patients; 73% of these were treated with noninvasive ventilation (NIV) only, 17% were treated with immediate invasive ventilation, and 10% were intubated after failed attempt with NIV. Compared to patients without LTOT, patients with LTOT had higher 30-day mortality (38% vs. 25%; $p < 0.001$) and one-year mortality (70% vs. 43%; $p < 0.001$). Multivariable logistic and Cox regression models adjusted for age, sex and SAPS3 score confirmed higher mortality in LTOT, odds ratio for 30-day mortality was 1.8 [95% confidence interval] 1.5-2.3 and hazard ratio for one-year mortality was 1.8 (1.6-2.0). In summary, although need for LTOT is a negative prognostic marker for survival after AECOPD

requiring intensive care, a majority of patients with LTOT survived the AECOPD and 30% were alive after one year.

Keywords: AECOPD; COPD exacerbation; ICU; LTOT; Long-term oxygen therapy; intensive care.

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Publication types, MeSH terms, Substancesexpand

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. 2023 Dec;20(1):55-63.

doi: 10.1080/15412555.2022.2164261.

[Time-Course of Changes in Multidimensional Fatigue and Functional Exercise Capacity and Their Associations during a Short Inpatient Pulmonary Rehabilitation Program](#)

[François Alexandre](#)¹, [Virginie Molinier](#)¹, [Louis Hognon](#)², [Laurène Charbonnel](#)³, [Amandine Calvat](#)⁴, [Adriana Castanyer](#)⁵, [Thomas Henry](#)³, [Aurélien Marcenac](#)³, [Morgane Jollive](#)⁴, [Antonin Vernet](#)⁵, [Nicolas Oliver](#)^{1,4}, [Nelly Heraud](#)¹

Affiliations expand

- PMID: 36655947

- DOI: [10.1080/15412555.2022.2164261](https://doi.org/10.1080/15412555.2022.2164261)

Abstract

This study aimed to assess the time-course of changes in multidimensional fatigue and functional exercise capacity and their associations during an inpatient pulmonary rehabilitation (PR) program. Seventy COPD patients from three centres were enrolled for a four-week PR program and were evaluated before (T0) and at the end of each week (T1, T2, T3, and T4). Weekly change in multidimensional fatigue was assessed by the multidimensional inventory questionnaire (MFI-20) and functional exercise capacity by the 6-minute walking distance (6MWD). Reaction time (RT) and heart rate variability (HRV) were also assessed as complementary markers of fatigue. HRV did not change during the study (all $p > 0.05$). MFI-20 score and RT decreased during the first part of the program ($p < 0.001$) and levelled off at T2 (all $p > 0.05$ compared with each preceding time). While 6MWD improved by almost 70% during the first part of the PR, it continued to increase, albeit at a greatly reduced pace, between T2 and T4 ($p < 0.05$). In parallel, a negative association was found between MFI-20 score and 6MWD at each evaluation time (r ranged from 0.43 to 0.71), with a significantly stronger T3 correlation compared with the other time periods (all $p < 0.05$). The strengthening of the association between fatigue and functional exercise capacity at T3, which occurred concomitantly with the slowdown of functional exercise capacity improvement, is consistent with a role for fatigue in the limitation of performance changes during PR. The limitation of fatigue during PR is thus an interesting aspect to improve the magnitude of performance changes.

Keywords: Respiratory tract diseases; chronic obstructive pulmonary disease; exercise tolerance; fatigue; rehabilitation outcome.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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. 2023 Dec;20(1):31-43.

A Systematic Review on the Association between Schizophrenia and Bipolar Disorder with Chronic Obstructive Pulmonary Disease

[María José Jaén-Moreno](#)^{1,2}, [Fernando Rico-Villademoros](#)³, [Cristina Ruiz-Rull](#)^{1,4}, [David Laguna-Muñoz](#)^{1,5}, [Gloria Isabel Del Pozo](#)^{1,5}, [Fernando Sarramea](#)^{1,2,5,6}

Affiliations expand

- PMID: 36655855
- DOI: [10.1080/15412555.2022.2154646](https://doi.org/10.1080/15412555.2022.2154646)

Abstract

A systematic review aimed to investigate the association between schizophrenia and bipolar disorder and chronic obstructive pulmonary disease (COPD), its prevalence and incidence, potential factors associated with its occurrence and its impact on mortality among these patients. We performed the literature search in PubMed, Scopus and PsycInfo from inception to February 2022 and identified 19 studies: ten cross-sectional, 5 that included cross-sectional and longitudinal analyses, and 4 retrospective cohort studies. The reported prevalence of COPD ranged from 2.6% to 52.7% in patients with schizophrenia and between 3.0% and 12.9% in patients with bipolar disorder. Two studies reported an annual incidence of COPD of 2.21 cases/100 person-years in patients with schizophrenia and 2.03 cases/100 person-years in patients with bipolar disorder. Among the risk factors evaluated in three studies, only advanced age was consistently associated with the presence/occurrence of COPD in patients with schizophrenia and bipolar disorder; the role of tobacco consumption was not investigated in those three studies. According to two studies, the likelihood of mortality from COPD showed an over 3-fold increase in patients with schizophrenia and a 2-fold increase in those with bipolar disorder compared to the overall population; COPD was also associated with increased inpatient mortality. Available data indicate that COPD in patients with schizophrenia and bipolar disorder is a major public health problem. National and international health organizations should strive to specifically address this issue by creating awareness about this health problem and developing specific programs for screening and early intervention aimed to reduce the burden of COPD in these populations.

Keywords: Chronic obstructive pulmonary disease; bipolar disorder; incidence; mortality; prevalence; schizophrenia; smoking.

- [Cited by 1 article](#)

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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COPD



. 2023 Dec;20(1):1-8.

doi: 10.1080/15412555.2022.2139671.

[Optimizing the Diagnostic Algorithm for Pulmonary Embolism in Acute COPD Exacerbation Using Fuzzy Rough Sets and Support Vector Machine](#)

[Rui Yu](#)¹, [Xianghua Kong](#)¹, [Youlun Li](#)²

Affiliations expand

- PMID: 36594682
- DOI: [10.1080/15412555.2022.2139671](https://doi.org/10.1080/15412555.2022.2139671)

Abstract

Aiming to optimize the diagnosis of pulmonary embolism (PE) in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD), we conducted a retrospective study enrolling 185 AECOPD patients, of whom 90 were diagnosed with PE based on computed tomography pulmonary angiography (CTPA). Ten characteristic indicators and 27 blood indicators were extracted for each patient. First, we quantified the importance of each indicator for diagnosing PE in AECOPD using fuzzy rough sets (FRS) and selected the more important indicators to construct a

support vector machine (SVM) diagnosis model called FRS-SVM. The performance of the proposed diagnosis model on the test sets was compared to that of the logistic regression model. The average accuracy and area under the curve (AUC) of the proposed model for the test sets in 10 independent trials were 94.67% and 0.944, respectively, compared to 80.41% and 0.809 for the logistic regression model. Thus, we validated the higher accuracy and stability of the FRS-SVM for PE diagnosis in patients with AECOPD. This model improved the prediction probability before CTPA and can be used in clinical practice to help doctors make decisions.

Keywords: Acute exacerbation of chronic obstructive pulmonary disease; fuzzy rough sets; pulmonary embolism; support vector machine.

SUPPLEMENTARY INFO

MeSH termsexpand

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Scand J Public Health

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. 2023 Dec;51(8):1189-1195.

doi: 10.1177/14034948221104351. Epub 2022 Jun 19.

Contribution of smoking change to 45-year trend in prevalence of chronic bronchitis in Finland

[Ville A Vartiainen](#)^{1,2,3}, [Pekka Jousilahti](#)¹, [Tiina Laatikainen](#)^{1,4,5}, [Erkki Vartiainen](#)¹

Affiliations expand

- PMID: 35722986

- PMID: [PMC10642213](#)
- DOI: [10.1177/14034948221104351](#)

Free PMC article

Abstract

Aims: Tobacco smoking has been identified as the most important risk factor of chronic bronchitis. The aim of this study was to assess the contribution of smoking to the trends in prevalence of chronic bronchitis among men and women in Finland.

Methods: For this purpose, we analysed questionnaires included in national FINRISK and FinHealth studies conducted between 1972 and 2017 in 5-year intervals. A total of 26,475 men and 28,684 women aged 30-59 years were included in the analysis. In addition to smoking, age and socioeconomic status were used as risk factors in the logistic regression model.

Results: Smoking in Finland has declined from 51% to 23% in men between 1972 and 2017. In women, it increased from 11% in 1972 to 23% in 2002, with a following decrease to 16% in 2017. The prevalence of chronic bronchitis has generally followed the trend of smoking. The population attributable risk was 60% in men and 49% in women. A decrease in chronic bronchitis was observed in male never-smokers.

Conclusions: Smoking is currently declining in Finland in both men and women. As result, the prevalence of chronic bronchitis is declining and it is approaching baseline independent of smoking. The decrease in never-smokers has yet to be explained.

Keywords: Tobacco smoking; chronic bronchitis; epidemiology.

Conflict of interest statement

Declaration of conflicting interestsThe author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

- [Cited by 1 article](#)
- [33 references](#)
- [1 figure](#)

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

Sage Journals
Open access full text



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

1

BMC Public Health

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. 2023 Dec 1;23(1):2392.

doi: 10.1186/s12889-023-16778-2.

Measuring generic health using the minimum european health module: does it work and is it better than self-rated health?

[Patrick Lazarević](#)¹

Affiliations expand

- PMID: 38041065
- DOI: [10.1186/s12889-023-16778-2](https://doi.org/10.1186/s12889-023-16778-2)

Abstract

Background: Health is a fundamental aspect of many scientific disciplines and its definition and measurement is the analytical core of many empirical studies. Comprehensive measures of health, however, are typically precluded in survey research due to financial and temporal restrictions. Self-rated health (SRH) as a single indicator of health, on the other hand, exhibits a lack of measurement invariance by age and is biased due to non-health influences. In the three-item Minimum European Health Module (MEHM), SRH is complemented with questions on chronic health conditions and activity

limitations, thus providing a compromise between single indicators and comprehensive measures.

Methods: Using data from the German Ageing Survey (2008 & 2014; n = 12,037), I investigated the feasibility to combine the MEHM into a generic health indicator and judged its utility in comparison to SRH as a benchmark. Additionally, I explored the option of an extended version of the MEHM by adding information on multimorbidity and the presence and intensity of chronic pain.

Results: The analyses showed that both versions of the MEHM had a good internal consistency and each represented a single latent variable that can be computed using generalized structural equation modeling. The utility of this approach showed great promise as it significantly reduced age-specific reporting behavior and some non-health biases present in SRH.

Conclusions: Using the MEHM to measure generic (physical) health is a promising approach with a wide array of applications. Further research could extend these analyses to additional age groups, other countries, and establish standardized weights for greater comparability.

Keywords: Generic health; Health measurement; Minimum european health module; Self-rated health.

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- [33 references](#)

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[Review](#)



. 2023 Dec 1;46(12):2092-2101.

doi: 10.2337/dci23-0035.

Diabetes and Multiple Long-term Conditions: A Review of Our Current Global Health Challenge

[Kamlesh Khunti](#)¹, [Yogini V Chudasama](#)¹, [Edward W Gregg](#)², [Monika Kamkuemah](#)³, [Shivani Misra](#)^{4,5}, [Jerry Suls](#)⁶, [Nikhil S Venkateshmurthy](#)^{7,8}, [Jonathan Valabhji](#)^{4,5}

Affiliations expand

- PMID: 38011523
- DOI: [10.2337/dci23-0035](https://doi.org/10.2337/dci23-0035)

Abstract

Use of effective treatments and management programs is leading to longer survival of people with diabetes. This, in combination with obesity, is thus contributing to a rise in people living with more than one condition, known as multiple long-term conditions (MLTC or multimorbidity). MLTC is defined as the presence of two or more long-term conditions, with possible combinations of physical, infectious, or mental health conditions, where no one condition is considered as the index. These include a range of conditions such as cardiovascular diseases, cancer, chronic kidney disease, arthritis, depression, dementia, and severe mental health illnesses. MLTC has major implications for the individual such as poor quality of life, worse health outcomes, fragmented care, polypharmacy, poor treatment adherence, mortality, and a significant impact on health care services. MLTC is a challenge, where interventions for prevention and management are lacking a robust evidence base. The key research directions for diabetes and MLTC from a global perspective include system delivery and care coordination, lifestyle interventions and therapeutic interventions.

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SUPPLEMENTARY INFO

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Multicenter Study

Lancet Glob Health

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. 2023 Dec;11(12):e1874-e1884.

doi: 10.1016/S2214-109X(23)00408-4.

Multimorbidity in patients with acute heart failure across world regions and country income levels (REPORT-HF): a prospective, multicentre, global cohort study

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Affiliations expand

- PMID: 37973338

- DOI: [10.1016/S2214-109X\(23\)00408-4](https://doi.org/10.1016/S2214-109X(23)00408-4)

Free article

Abstract

Background: Multimorbidity (two or more comorbidities) is common among patients with acute heart failure, but comprehensive global information on its prevalence and clinical consequences across different world regions and income levels is scarce. This study aimed to investigate the prevalence of multimorbidity and its effect on pharmacotherapy and prognosis in participants of the REPORT-HF study.

Methods: REPORT-HF was a prospective, multicentre, global cohort study that enrolled adults (aged ≥ 18 years) admitted to hospital with a primary diagnosis of acute heart failure from 358 hospitals in 44 countries on six continents. Patients who currently or recently participated in a clinical treatment trial were excluded. Follow-up data were collected at 1-year post-discharge. The primary outcome was 1-year post-discharge mortality. All patients in the REPORT-HF cohort with full data on comorbidities were eligible for the present study. We stratified patients according to the number of comorbidities, and countries by world region and country income level. We used one-way ANOVA, χ^2 test, or Mann-Whitney U test for comparisons between groups, as applicable, and Cox regression to analyse the association between multimorbidity and 1-year mortality.

Findings: Between July 23, 2014, and March 24, 2017, 18 553 patients were included in the REPORT-HF study. Of these, 18 528 patients had full data on comorbidities, of whom 11 360 (61%) were men and 7168 (39%) were women. Prevalence rates of multimorbidity were lowest in southeast Asia (72%) and highest in North America (92%). Fewer patients from lower-middle-income countries had multimorbidity than patients from high-income countries (73% vs 85%, $p < 0.0001$). With increasing comorbidity burden, patients received fewer guideline-directed heart failure medications, yet more drugs potentially causing or worsening heart failure. Having more comorbidities was associated with worse outcomes: 1-year mortality increased from 13% (no comorbidities) to 26% (five or more comorbidities). This finding was independent of common baseline risk factors, including age and sex. The population-attributable fraction of multimorbidity for mortality was higher in high-income countries than in upper-middle-income or lower-middle-income countries (for patients with five or more comorbidities: 61% vs 27% and 31%, respectively).

Interpretation: Multimorbidity is highly prevalent among patients with acute heart failure across world regions, especially in high-income countries, and is associated with higher mortality, less prescription of guideline-directed heart failure pharmacotherapy, and increased use of potentially harmful medications.

Funding: Novartis Pharma.

Translations: For the Arabic, French, German, Hindi, Mandarin, Russian and Spanish translations of the abstract see Supplementary Materials section.

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Conflict of interest statement

Declaration of interests JGFC reports grants and personal fees from Amgen, Bayer, Bristol Myers Squibb, and Torrent Pharmaceuticals; personal fees from AstraZeneca, Myokardia, Servier, and Abbott; grants, personal fees, and non-financial support from Medtronic, Novartis, and Vifor; and grants and non-financial support from Pharmacosmos and PharmaNord. UD reports research support from AstraZeneca, Pfizer, Boehringer Ingelheim, Vifor, Roche Diagnostics, and Boston Scientific; and speaker's honoraria and consultancies from AstraZeneca, Novartis, and Amgen. GE reports personal fees from AstraZeneca, Abbott, Boehringer Ingelheim, Novartis, and Vifor, all outside the submitted work; non-financial support from the University Hospital Würzburg, and the Comprehensive Heart Failure Center Würzburg; and grant support from German Ministry for Education and Research (BMBF). SVP reports support from Novartis for the present manuscript; consulting fees from Abbott and Bago; and personal fees from Abbott, Boehringer Ingelheim, and Bago. MG and AO were formerly Novartis employees. AS is employed by Novartis. SPC reports research grants from the National Institutes of Health, Agency for Research and Quality, American Heart Association, and the Patient-Centered Outcomes Research Institute; and consulting fees from Novartis, Medtronic, Aipha, Boehringer Ingelheim, Siemens, and Ortho Clinical. GF reports research grants from the EU; committee fees from Novartis related to REPORT-HF; and lecture fees or being a committee member in trials or registries sponsored by Servier, Boehringer Ingelheim, Medtronic, Vifor, Amgen, and Bayer. CSPL is supported by a Clinician Scientist Award from the National Medical Research Council of Singapore; has received research support from Bayer and Roche Diagnostics; has served as consultant or on the Advisory Board, Steering Committee, or Executive Committee for Actelion, Alleviant Medical, Allyn Pharma, Amgen, AnaCardio, Applied Therapeutics, AstraZeneca, Bayer, Boehringer Ingelheim, Boston Scientific, Cytokinetics, Darma, EchoNous, Eli Lilly, Impulse Dynamics, Ionis Pharmaceutical, Janssen Research & Development, Medscape WebMD Global, Merck, Novartis, Novo Nordisk, Prosciento, Radcliffe Group, Roche Diagnostics, Sanofi, Siemens Healthcare Diagnostics, and Us2.ai; and serves as co-founder and non-executive director of Us2.ai. JT has received consulting or speaker fees from Daiichi-Sankyo, Boehringer Ingelheim, Roche Diagnostics, and Us2.ai; and owns patent US-10702247-B2 unrelated to the present work. CEA reports grant support, personal fees, or non-financial support from Abbott, AstraZeneca, Boehringer Ingelheim, Medtronic, Novartis, Novo Nordisk, Radcliffe Group, and Vifor Pharma, all outside of the submitted work; and acknowledges non-financial support from the University Hospital Würzburg, and the Comprehensive Heart Failure Center Würzburg, and grant support from BMBF. All other authors declare no competing interests.

SUPPLEMENTARY INFO

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Acta Oncol

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. 2023 Dec;62(12):1653-1660.

doi: 10.1080/0284186X.2023.2270145. Epub 2023 Nov 25.

[Impact of multimorbidity and polypharmacy on mortality after cancer: a nationwide registry-based cohort study in Denmark 2005–2017](#)

[Mette K Thomsen](#)¹, [Katrine B Løppenthin](#)², [Pernille E Bidstrup](#)³, [Elisabeth W Andersen](#)³, [Susanne Dalton](#)³, [Lone N Petersen](#)², [Helle Pappot](#)², [Christiane E Mortensen](#)², [Mikkel B Christensen](#)^{4,5}, [Anne Frølich](#)^{6,7}, [Ulrik Lassen](#)², [Christoffer Johansen](#)^{1,2}

Affiliations expand

- PMID: 37874076
- DOI: [10.1080/0284186X.2023.2270145](https://doi.org/10.1080/0284186X.2023.2270145)

Abstract

Background: Concurrent chronic diseases and treatment hereof in patients with cancer may increase mortality. In this population-based study we examined the individual and combined impact of multimorbidity and polypharmacy on mortality, across 20 cancers and with 13-years follow-up in Denmark.

Materials and methods: This nationwide study included all Danish residents with a first primary cancer diagnosed between 1 January 2005 and 31 December 2015, and followed until the end of 2017. We defined multimorbidity as having one or more of 20 chronic conditions in addition to cancer, registered in the five years preceding diagnosis, and polypharmacy as five or more redeemed medications 2-12 months prior to cancer diagnosis. Cox regression analyses were used to estimate the effects of multimorbidity and polypharmacy, as well as the combined effect on mortality.

Results: A total of 261,745 cancer patients were included. We found that patients diagnosed with breast, prostate, colon, rectal, oropharynx, bladder, uterine and cervical cancer, malignant melanoma, Non-Hodgkin lymphoma, and leukemia had higher mortality when the cancer diagnosis was accompanied by multimorbidity and polypharmacy, while in patients with cancer of the lung, esophagus, stomach, liver, pancreas, kidney, ovarian and brain & central nervous system, these factors had less impact on mortality.

Conclusion: We found that multimorbidity and polypharmacy was associated with higher mortality in patients diagnosed with cancer types that typically have a favorable prognosis compared with patients without multimorbidity and polypharmacy. Multimorbidity and polypharmacy had less impact on mortality in cancers that typically have a poor prognosis.

Keywords: Mortality; multimorbidity; polypharmacy; prognosis.

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MeSH termsexpand

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Neurobiol Aging

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. 2023 Dec:132:145-153.

doi: 10.1016/j.neurobiolaging.2023.09.003. Epub 2023 Sep 11.

Biological age and brain age in midlife: relationship to multimorbidity and mental health

[Fengqing Zhang](#)¹, [Hansoo Chang](#)², [Stacey M Schaefer](#)³, [Jiangtao Gou](#)⁴

Affiliations expand

- PMID: 37804610
- DOI: [10.1016/j.neurobiolaging.2023.09.003](https://doi.org/10.1016/j.neurobiolaging.2023.09.003)

Abstract

Biological age and brain age estimated using biological and neuroimaging measures have recently emerged as surrogate aging biomarkers shown to be predictive of diverse health outcomes. As aging underlies the development of many chronic conditions, surrogate aging biomarkers capture health at the whole person level, having the potential to improve our understanding of multimorbidity. Our study investigates whether elevated biological age and brain age are associated with an increased risk of multimorbidity using a large dataset from the Midlife in the United States Refresher study. Ensemble learning is utilized to combine multiple machine learning models to estimate biological age using a comprehensive set of biological markers. Brain age is obtained using Gaussian processes regression and neuroimaging data. Our study is the first to examine the relationship between accelerated brain age and multimorbidity. Furthermore, it is the first attempt to explore how biological age and brain age are related to multimorbidity in mental health. Our findings hold the potential to advance the understanding of disease accumulation and their relationship with aging.

Keywords: Biological age; Brain age; Machine learning; Mental health multimorbidity; Multimorbidity.

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Arch Gerontol Geriatr

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. 2023 Dec;115:105134.

doi: 10.1016/j.archger.2023.105134. Epub 2023 Jul 20.

Multimorbidity patterns in older persons and their association with self-reported quality of life and limitations in activities of daily living

[Jennifer E Lutomski](#)¹, [Trynke Hoekstra](#)², [Marjan van den Akker](#)³, [Jeanet Blom](#)⁴, [Amaia Calderón-Larrañaga](#)⁵, [Alessandra Marengoni](#)⁶, [Alexandra Prados-Torres](#)⁷, [Marcel Olde-Rikkert](#)⁸, [Rene Melis](#)⁸, [TOPICS-MDS Consortium](#)

Affiliations expand

- PMID: 37516060
- DOI: [10.1016/j.archger.2023.105134](https://doi.org/10.1016/j.archger.2023.105134)

Free article

Abstract

Background: As populations age, multimorbidity (the presence of two or more chronic morbidities) is increasingly more common. These evolving demographics demand further research into the identification of morbidity patterns in different settings as well as the longitudinal effects of these patterns.

Methods: Prospectively collected data on 12,755 older persons aged 65+ years were derived from The Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS, www.topics-mds.eu). Latent class analyses were performed to identify unobserved relationship patterns between morbidities in older persons. Using linear mixed models, the average difference in health-related quality of life (EQ-5D) and general quality of life scores (Cantril's Self Anchoring Ladder) as well as limitations in Activities of Daily Living and Instrumental Activities of Daily Living (ADL/IADL) were examined over a 12-month period.

Results: Five multimorbidity patterns were identified: sensory (n = 3882), cardio-metabolic (n = 2627), mental health (n = 920), osteo-articular (n = 4486), and system decline (n = 840). Relative to older persons in the sensory group, multimorbidity patterns did not have a strong effect on health-related quality of life, general quality of life or ADL/IADLs over a one-year period.

Conclusions: The observed multimorbidity patterns are similar to others based on different methodologies and study populations. When examining the effect of such patterns on quality of life, the EQ-5D and Cantril's Ladder may be insufficient outcome measures. Further investigations into the prognostic value of morbidity patterns would be of benefit.

Keywords: ADLs; EQ-5D; Latent class analysis; Multimorbidity; Quality of life.

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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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Geroscience

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. 2023 Dec;45(6):3257-3265.

doi: 10.1007/s11357-023-00880-9. Epub 2023 Jul 27.

Systemic inflammation and biological aging in the Health and Retirement Study

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

Affiliations expand

- PMID: 37501048
- PMCID: [PMC10643484](#)
- DOI: [10.1007/s11357-023-00880-9](#)

Free PMC article

Abstract

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

positively associated with DNA methylation age acceleration for 10 of the 13 epigenetic clocks, after adjustment for sociodemographics and chronic disease risk factors. The latent variable for systemic inflammation was associated with 4-year mortality independent of DNA methylation age acceleration and was a better predictor of 4-year mortality than any of the epigenetic clocks examined, as well as mortality risk factors, including obesity and multimorbidity. Inflammaging and DNA methylation age acceleration may represent different biological processes contributing to mortality risk. Leveraging multiple measured inflammation markers to capture inflammaging is important for biology of aging research.

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

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Conflict of interest statement

The authors declare no competing interests.

- [Cited by 1 article](#)
- [34 references](#)
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BMJ Open

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. 2023 Nov 30;13(11):e076903.

doi: 10.1136/bmjopen-2023-076903.

Current definitions of advanced multimorbidity: a protocol for a scoping review

[Sarah P Bowers](#)¹, [Polly Black](#)², [Lewis McCheyne](#)³, [Darcy Wilson](#)⁴, [Sarah E E Mills](#)^{2,3}, [Utkarsh Agrawal](#)⁵, [Linda Williams](#)⁶, [Frances Quirk](#)^{2,3}, [Jo Bowden](#)^{2,3}

Affiliations expand

- PMID: 38035744
- PMCID: [PMC10689385](#)
- DOI: [10.1136/bmjopen-2023-076903](#)

Free PMC article

Abstract

Introduction: People living with and dying from multimorbidity are increasing in number, and ensuring quality care for this population is one of the major challenges facing healthcare providers. People with multimorbidity often have a high burden of palliative and end-of-life care needs, though they do not always access specialist palliative care services. A key reason for this is that they are often not identified as being in the last stages of their life by current healthcare providers and systems. This scoping review aims to identify and present the available evidence on how people with multimorbidity are currently included in research, policy and clinical practice.

Methods and analysis: Scoping review methodology, based on Arksey and O'Malley's framework, will be undertaken and presented using the Preferred Reporting Items for Systematic Review and Meta-Analyses extension for Scoping Reviews. Search terms have been generated using the key themes of 'multimorbidity', 'end of life' and 'palliative care'. Peer-reviewed research will be obtained through systematic searching of Medline, EMBASE, CINAHL, Scopus and PsycINFO. Grey literature will be searched in a systematic manner. Literature containing a definition for adults with multimorbidity in a terminal phase of their illness experience will be included. After screening studies for eligibility, included studies will be described in terms of setting and characteristics as well as using inductive content analysis to highlight the commonalities in definitions.

Ethics and dissemination: Ethical approval is not required for this scoping review. The findings of the scoping review will be used internally as part of SPB's PhD thesis at the University of St Andrews through the Multimorbidity Doctoral Training Programme for Health Professionals, which is supported by the Wellcome Trust (223499/Z/21/Z) and published in an open access, peer-reviewed journal for wider dissemination.

Keywords: Adult palliative care; Decision Making; INTERNAL MEDICINE; Life Change Events; PALLIATIVE CARE; Patient-Centered Care.

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Conflict of interest statement

Competing interests: None declared.

- [44 references](#)

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PLoS One

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. 2023 Nov 30;18(11):e0294935.

doi: 10.1371/journal.pone.0294935. eCollection 2023.

[Functional limitation in the older Brazilian adults: Association with multimorbidity and socioeconomic conditions](#)

Affiliations expand

- PMID: 38032910
- PMCID: [PMC10688755](#)
- DOI: [10.1371/journal.pone.0294935](#)

Abstract

The aim of this study was to assess the association between multimorbidity and the presence of functional limitation in basic (BADL) and instrumental activities of daily living (IADL) among Brazilian older adults and to verify whether this association is moderated by socioeconomic conditions. Cross-sectional study with data from the Brazilian National Health Survey (PNS) (2019) for the Brazilian population aged 60 years and over. The dependent variables were functional limitation, based on self-reported difficulty in performing one or more activities of daily living, including six BADL (feeding, bathing, using the toilet, dressing, crossing a room on the same floor and getting out of bed) and four IADL (shopping, managing money, taking medication and using transportation). The independent variables were multimorbidity (presence of two or more self-reported chronic diseases) and socioeconomic measures (per capita household income, asset score, and education level). The association between multimorbidity and outcomes was assessed using adjusted logistic regression models. The moderating effect of socioeconomic conditions on the association between multimorbidity and functional limitations was assessed by including an interaction term. The final sample consisted of 22,725 individuals. The prevalence of functional limitation was 8.5% (95%CI: 7.9-9.2) and 18.6% (95%CI: 17.8-19.5) in BADL and IADL, respectively. Multimorbidity was associated with BADL [OR: 2.30 (95%CI: 1.93-2.74)] and IADL [OR: 2.26 (95%CI: 1.98-2.57)]. The odds of functional limitation were higher among individuals with lower levels of education and income, but there was no interaction between multimorbidity and socioeconomic position measures. Multimorbidity was associated with functional limitation (BADL and IADL) and socioeconomic conditions, and this association was constant across socioeconomic position levels.

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Conflict of interest statement

The authors have declared that no competing interests exist.

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- [2 figures](#)

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. 2023 Nov 29;18(11):e0294666.

doi: 10.1371/journal.pone.0294666. eCollection 2023.

[Clustering long-term health conditions among 67728 people with multimorbidity using electronic health records in Scotland](#)

[Adeniyi Francis Fagbamigbe](#)^{1,2,3,4}, [Utkarsh Agrawal](#)⁵, [Amaya Azcoaga-Lorenzo](#)^{1,6}, [Briana MacKerron](#)¹, [Eda Bilici Özyiğit](#)⁷, [Daniel C Alexander](#)⁷, [Ashley Akbari](#)⁸, [Rhiannon K Owen](#)⁸, [Jane Lyons](#)⁸, [Ronan A Lyons](#)⁸, [Spiros Denaxas](#)^{9,10}, [Paul Kirk](#)¹¹, [Ana Corina Miller](#)¹², [Gill Harper](#)¹³, [Carol Dezateux](#)¹³, [Anthony Brookes](#)¹⁴, [Sylvia Richardson](#)¹¹, [Krishnarajah Nirantharakumar](#)¹⁵, [Bruce Guthrie](#)¹⁶, [Lloyd Hughes](#)¹, [Umesh T Kadam](#)¹⁷, [Kamlesh Khunti](#)¹⁸, [Keith R Abrams](#)¹⁹, [Colin McCowan](#)¹

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- PMID: 38019832
- PMCID: [PMC10686427](#)
- DOI: [10.1371/journal.pone.0294666](#)

Free PMC article

Abstract

There is still limited understanding of how chronic conditions co-occur in patients with multimorbidity and what are the consequences for patients and the health care system. Most reported clusters of conditions have not considered the demographic characteristics of these patients during the clustering process. The study used data for all registered patients that were resident in Fife or Tayside, Scotland and aged 25 years or more on 1st January 2000 and who were followed up until 31st December 2018. We used linked demographic information, and secondary care electronic health records from 1st January 2000. Individuals with at least two of the 31 Elixhauser Comorbidity Index conditions were identified as having multimorbidity. Market basket analysis was used to cluster the conditions for the whole population and then repeatedly stratified by age, sex and deprivation. 318,235 individuals were included in the analysis, with 67,728 (21.3%) having multimorbidity. We identified five distinct clusters of conditions in the population with multimorbidity: alcohol misuse, cancer, obesity, renal failure, and heart failure. Clusters of long-term conditions differed by age, sex and socioeconomic deprivation, with some clusters not present for specific strata and others including additional conditions. These findings highlight the importance of considering demographic factors during both clustering analysis and intervention planning for individuals with multiple long-term conditions. By taking these factors into account, the healthcare system may be better equipped to develop tailored interventions that address the needs of complex patients.

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Conflict of interest statement

The authors have declared that no competing interests exist.

- [33 references](#)
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J Allergy Clin Immunol Pract

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. 2023 Nov 28:S2213-2198(23)01305-3.

doi: 10.1016/j.jaip.2023.11.036. Online ahead of print.

[Associations of Breathing Pattern Disorder and Nijmegen Score with Clinical Outcomes in Difficult-to-treat Asthma](#)

[Anna Freeman](#)¹, [Steevo Abraham](#)², [Latha Kadalayil](#)², [Judit Varkonyi-Sepp](#) [CPsychol](#)³, [Ben Ainsworth](#)⁴, [J J Hudson-Colby](#)⁵, [Clair Barber](#)⁶, [Paddy Dennison](#)⁷, [Adnan Azim](#)⁶, [Heena Mistry](#)⁶, [Peter Howarth](#)⁶, [Ratko Djukanovic](#)⁶, [Hongmei Zhang](#)⁸, [S Hasan Arshad](#)⁹, [Hans Michael Haitchi](#)¹⁰, [Ramesh J Kurukulaaratchy](#)¹¹

Affiliations [expand](#)

- PMID: 38036249

- DOI: [10.1016/j.jaip.2023.11.036](https://doi.org/10.1016/j.jaip.2023.11.036)

Abstract

Background: Breathing pattern disorder (BPD) reflects altered biomechanical patterns of breathing that drive breathing difficulty and commonly accompanies difficult-to-treat asthma. Diagnosis of BPD has no gold standard, but Nijmegen Questionnaire (NQ) >23 is commonly used.

Objectives: We sought to advance clinical characterisation of BPD and better understand clinical utility of NQ in difficult asthma, in patients from the Wessex AsThma CoHort of difficult asthma (WATCH) study.

Methods: Association between demographic and clinical factors in difficult asthma and BPD, ascertained by clinical diagnosis (yes/no, n=476), by NQ scores (≤ 23 : normal (no suggestion of BPD) and > 23 : abnormal (suggested BPD), n=372, as well as the continuous raw NQ scores) were assessed in univariate models to identify significant risk factors associated with the three BPD outcomes. For the clinician-diagnosed and NQ-based BPD, associations of continuous factors were assessed using independent samples t-test or Mann-Whitney U test as appropriate for the data distribution or by Spearman correlation test. Dichotomous associations were evaluated using chi-squared tests. Multivariable logistic (dichotomous outcomes) and linear regression models (continuous outcomes) were developed to identify predictive factors associated with clinician-diagnosed and NQ-based BPD, dichotomous and continuous. Patients with data on NQ scores were grouped into NQ quartiles (low, moderate, high, and very high). The patterns of association of the quartiles with four health-related questionnaire outcomes were assessed using linear regression analyses.

Results: Multivariable regression identified that clinically diagnosed BPD was associated with female sex (OR 1.85; 95% CI 1.07, 3.20), comorbidities (rhinitis (OR 2.46; 95% CI 1.45, 4.17), GORD (OR 2.77; 95% CI 1.58, 4.84), ILO (OR 4.37; 95% CI 2.01, 9.50) and any psychological co-morbidity (OR 1.86; 95% CI 1.13, 3.07)) and healthcare usage (exacerbations (OR 1.07; 95% CI 1.003, 1.14) and previous ICU admissions (OR 2.03; 95% CI 1.18, 3.47)). Abnormal NQ-based BPD diagnosis was associated with history of eczema (OR 1.83; 95% CI 1.07, 3.14), GORD (OR 1.94; 95% CI 1.15, 3.27) or any psychological comorbidity (OR 4.29; 95% CI 2.64, 6.95) at multivariable regression. Differences between clinical and NQ-based BPD traits were also found with 42% discordance in BPD-state between these definitions. Multivariable linear regression analysis with NQ as a continuous outcome showed positive association with worse asthma outcomes (admission to ICU, $p=0.037$), different phenotypic traits (female sex $p=0.001$, ever smoker, $p=0.025$) and greater multimorbidity (GORD, $p=0.002$, sleep apnoea, $p=0.040$, any psychological comorbidity, $p<0.0001$).

Conclusion: BPD is associated with worse health outcomes and negative health impacts in difficult asthma within a multimorbidity disease model. It therefore merits better

recognition and prompt treatment. Clinical diagnosis and NQ offer different perspectives on BPD, so this goal may be best addressed by considering clinical features alongside magnitude of NQ.

Keywords: Breathing-pattern-disorder (BPD); Nijmegen questionnaire (NQ); difficult asthma; multimorbidity; treatable trait.

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J Aging Health

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. 2023 Nov 28:8982643231215476.

doi: 10.1177/08982643231215476. Online ahead of print.

[An Exploration of Methods to Resolve Inconsistent Self-Reporting of Chronic Conditions and Impact on Multimorbidity in the Canadian Longitudinal Study on Aging](#)

[Alessandra T Andreacchi](#)¹, [Alberto Brini](#)², [Edwin Van den Heuvel](#)², [Graciela Muniz-Terrera](#)³, [Alexandra Mayhew](#)^{1,4,5}, [Philip St John](#)⁶, [Lucy E Stirland](#)^{7,8}, [Lauren E Griffith](#)^{1,4,5}

Affiliations expand

- PMID: 38016065

- DOI: [10.1177/08982643231215476](https://doi.org/10.1177/08982643231215476)

Abstract

Objectives: To quantify inconsistent self-reporting of chronic conditions between the baseline (2011-2015) and first follow-up surveys (2015-2018) in the Canadian Longitudinal Study on Aging (CLSA), and to explore methods to resolve inconsistent responses and impact on multimorbidity.

Methods: Community-dwelling adults aged 45-85 years in the baseline and first follow-up surveys were included ($n = 45,184$). At each survey, participants self-reported whether they ever had a physician diagnosis of 35 chronic conditions. Identifiable inconsistent responses were enumerated.

Results: 32-40% of participants had at least one inconsistent response across all conditions. Illness-related information (e.g., taking medication) resolved most inconsistent responses (>93%) while computer-assisted software asking participants to confirm their inconsistent disease status resolved $\leq 53\%$. Using these adjudication methods, multimorbidity prevalence at follow-up increased by $\leq 1.6\%$ compared to the prevalence without resolving inconsistent responses.

Discussion: Inconsistent self-reporting of chronic conditions is common but may not substantially affect multimorbidity prevalence. Future research should validate methods to resolve inconsistencies.

Keywords: CLSA; Canadian longitudinal study on aging; chronic disease; morbidity.

Conflict of interest statement

Declaration of Conflicting Interests The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

FULL TEXT LINKS

Sage Journals 

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

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. 2023 Dec 1.

doi: 10.1111/all.15964. Online ahead of print.

Telemedicine with special focus on allergic diseases and asthma–Status 2022: An EAACI position paper

[Sylvia Smolinska](#)¹, [Florin-Dan Popescu](#)², [Elena Izquierdo](#)³, [Darío Antolín-Amérigo](#)⁴, [Oliver J Price](#)⁵, [Alberto Alvarez-Perea](#)^{6,7}, [Ibon Eguíluz Gracia](#)⁸, [Nikolaos G Papadopoulos](#)⁹, [Oliver Pfaar](#)¹⁰, [Filippo Fassio](#)¹¹, [Karin Hoffmann-Sommergruber](#)¹², [Stephanie Dramburg](#)¹³, [Ioana Agache](#)¹⁴, [Marek Jutel](#)^{1,15}, [Helen A Brough](#)^{16,17}, [João A Fonseca](#)¹⁸, [Elizabeth Angier](#)¹⁹, [Cristina Boccabella](#)²⁰, [Matteo Bonini](#)^{21,22,23}, [Audrey Dunn Galvin](#)²⁴, [Peter G Gibson](#)²⁵, [Radosław Gawlik](#)²⁶, [Farah Hannachi](#)²⁷, [Ömer Kalayci](#)²⁸, [Ludger Klimek](#)²⁹, [Rebecca Knibb](#)³⁰, [Paolo Matricardi](#)¹³, [Tomás Chivato](#)³¹

Affiliations expand

- PMID: 38041429

- DOI: [10.1111/all.15964](https://doi.org/10.1111/all.15964)

Abstract

Efficacious, effective and efficient communication between healthcare professionals (HCP) and patients is essential to achieve a successful therapeutic alliance. Telemedicine (TM) has been used for decades but during the COVID-19 pandemic its use has become widespread. This position paper aims to describe the terminology and most important forms of TM among HCP and patients and review the existing studies on the uses of TM for asthma and allergy. Besides, the advantages and risks of TM are discussed, concluding that TM application reduces costs and time for both, HCP and patients, but cannot completely replace face-to-face visits for physical examinations and certain tests that are critical in asthma and allergy. From an ethical point of view, it is important to identify those involved in the TM process, ensure confidentiality and use communication channels that fully guarantee the security of the information. Unmet needs and directions for the future regarding implementation, data protection, privacy regulations, methodology and efficacy are described.

Keywords: e-health; m-health; telecare; telehealth; telemedicine.

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Review

Allergy

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. 2023 Dec 1.

doi: 10.1111/all.15963. Online ahead of print.

[Telehealth interventions for transition to self-management in adolescents with allergic conditions: A systematic review](#)

[Meg O' Sullivan](#)^{1,2}, [Margaret Curtin](#)¹, [Rachel Flynn](#)¹, [Caoimhe Cronin](#)¹, [James O' Mahony](#)¹, [Juan Trujillo](#)^{1,2}

Affiliations [expand](#)

- PMID: 38041398
- DOI: [10.1111/all.15963](https://doi.org/10.1111/all.15963)

Abstract

Telehealth is an emerging approach that uses technology to provide healthcare remotely. Recent publications have outlined the importance of supporting the transition to self-management of adolescents with allergic conditions. However, no synthesis of the evidence base on the use and impact of telehealth interventions for this purpose has been conducted to date. This review achieves these aims, in addition to exploring the language use surrounding these interventions, and their implementation. Four databases were searched systematically. References were independently screened by two reviewers. Methodological quality was assessed using the Mixed Methods Appraisal Tool. A narrative synthesis was undertaken. Eighteen articles were included, reporting on 15 telehealth interventions. A total of 86% targeted adolescents with asthma. Mobile applications were the most common telehealth modality used, followed by video-conferencing, web-based, virtual reality and artificial intelligence. Five intervention content categories were identified; educational, monitoring, behavioural, psychosocial and healthcare navigational. Peer and/or healthcare professional interaction, gamification and tailoring may increase engagement. The studies showed positive effects of the interventions or no difference from active controls, in self-management outcomes such as knowledge, health outcomes such as quality-of-life, and economic outcomes such as healthcare utilization. The most common implementation outcomes reported were acceptability, appropriateness, feasibility and fidelity.

Keywords: adolescent; mobile applications; self-management; telemedicine; transition to adult care.

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BMJ Open



. 2023 Dec 1;13(12):e076884.

doi: 10.1136/bmjopen-2023-076884.

Relationship Between Birth Weight and Asthma Diagnosis: A Cross-Sectional Survey Study Based on the National Survey of Children's Health in the U.S

[Meng Ni](#)^{#123}, [Baihe Li](#)^{#123}, [Qianqian Zhang](#)¹²³, [Jiuru Zhao](#)¹²³, [Wei Li](#)¹²³, [Sudong Qi](#)¹²³, [Qianwen Shen](#)¹²³, [Dongting Yao](#)¹²³, [Ze Chen](#)¹²³, [Tao Wang](#)¹²³, [Xiya Ding](#)¹²³, [Zhenying Lin](#)¹²³, [Chunyu Cheng](#)¹²³, [Zhiwei Liu](#)⁴²³, [Hao Chen](#)⁵

Affiliations expand

- PMID: 38040432
- DOI: [10.1136/bmjopen-2023-076884](https://doi.org/10.1136/bmjopen-2023-076884)

Abstract

Objective: To assess the association between birth weight and childhood asthma risk using data from the 2019-2020 National Survey of Children's Health database.

Design: Cross-sectional study.

Setting: The USA.

Patients: A representative cohort of American children.

Exposure: The exposure of this study was birth weight regardless of gestational age. Birth weight was divided into three groups: <1500 g, 1500-2500 g and >2500 g.

Main outcome measures: Primary outcomes were parent-reported diagnosis of asthma.

Method: The Rao-Scott χ^2 test was used to compare the groups. The main analyses examined the association between birth weight and parent-report asthma in children using univariable and multivariable logistic models adjusting for preterm birth, age, sex, race, family poverty, health insurance, smoking, maternal age. Subgroup analysis was performed based on interaction test.

Results: A total of 60 172 children aged 3-17 years were enrolled in this study; of these, 5202 (~8.6%) had asthma. Children with asthma were more likely to be born preterm, with low birth weight (LBW) or very LBW (VLBW). The incidence of asthma was the highest in VLBW children at 20.9% and showed a downward trend with an increase in birth weight class, with rates of 10.7% and 8.1% in the LBW and normal birthweight groups, respectively. Children with VLBW (OR 1.97; 95% CI 1.29 to 3.01) had higher odds of developing asthma in the adjusted analysis model. However, VLBW was only shown to be a risk factor for asthma among Hispanics, black/African-Americans and children between the ages of 6 and 12 years, demonstrating racial and age disparities.

Conclusions: VLBW increases the risk of childhood asthma; however, racial and age disparities are evident.

Keywords: Asthma; EPIDEMIOLOGIC STUDIES; Fetal medicine.

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Conflict of interest statement

Competing interests: None declared.

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Curr Environ Health Rep

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. 2023 Dec 1.

doi: 10.1007/s40572-023-00420-9. Online ahead of print.

Health Impacts of Wildfire Smoke on Children and Adolescents: A Systematic Review and Meta-analysis

[Yiwen Zhang](#)¹, [Ye Tingting](#)¹, [Wenzhong Huang](#)¹, [Pei Yu](#)¹, [Gongbo Chen](#)¹, [Rongbin Xu](#)¹, [Jiangning Song](#)², [Yuming Guo](#)¹, [Shanshan Li](#)³

Affiliations expand

- PMID: 38038861
- DOI: [10.1007/s40572-023-00420-9](https://doi.org/10.1007/s40572-023-00420-9)

Abstract

Purpose of review: Wildfire smoke is associated with human health, becoming an increasing public health concern. However, a comprehensive synthesis of the current evidence on the health impacts of ambient wildfire smoke on children and adolescents, an exceptionally vulnerable population, is lacking. We conduct a systematic review of peer-reviewed epidemiological studies on the association between wildfire smoke and health of children and adolescents.

Recent findings: We searched for studies available in MEDLINE, EMBASE, and Scopus from database inception up to October 11, 2022. Of 4926 studies initially identified, 59 studies from 14 countries were ultimately eligible. Over 33.3% of the studies were conducted in the USA, and two focused on multi-countries. The exposure assessment of wildfire smoke was heterogenous, with wildfire-specific particulate matters with diameters $\leq 2.5 \mu\text{m}$ (PM_{2.5}, 22.0%) and all-source (22.0%) PM_{2.5} during wildfire period most frequently used. Over half of studies (50.6%) focused on respiratory-related morbidities/mortalities. Wildfire smoke exposure was consistently associated with enhanced risks of adverse health outcomes in

children/adolescents. Meta-analysis results presented a pooled relative risk (RR) of 1.04 (95% confidence interval [CI], 0.96-1.12) for all-cause respiratory morbidity, 1.11 (95% CI: 0.93-1.32) for asthma, 0.93 (95% CI, 0.85-1.03) for bronchitis, and 1.13 (95% CI, 1.05-1.23) for upper respiratory infection, whilst - 21.71 g for birth weight (95% CI, - 32.92 to - 10.50) per 10 µg/m³ increment in wildfire-specific PM_{2.5}/all-source PM_{2.5} during wildfire event. The majority of studies found that wildfire smoke was associated with multiple adverse health outcomes among children and adolescents, with respiratory morbidities of significant concern. In-utero exposure to wildfire smoke may increase the risk of adverse birth outcomes and have long-term impacts on height. Higher maternal baseline exposure to wildfire smoke and poor family-level baseline birthweight respectively elevated risks in preterm birth and low birth weight associated with wildfire smoke. More studies in low- and middle-income countries and focusing on extremely young children are needed. Despite technological progress, wildfire smoke exposure measurements remain uncertain, demanding improved methodologies to have more precise assessment of wildfire smoke levels and thus quantify the corresponding health impacts and guide public mitigation actions.

Keywords: Air pollution; Children/adolescent health; Meta-analysis; Systematic reviews; Wildfire smoke.

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Pediatrics

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. 2023 Dec 1;152(Suppl 3):S53-S54.

doi: 10.1542/peds.2023-064344NC.

[Azithromycin for Poorly Controlled Asthma in Children: A Randomized Controlled Trial](#)

[Kristina Roth](#)¹, [Lindsey Moore](#)¹

Affiliations expand

- PMID: 38038591
- DOI: [10.1542/peds.2023-064344NC](https://doi.org/10.1542/peds.2023-064344NC)

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. 2023 Dec 1;152(Suppl 3):S49-S50.

doi: 10.1542/peds.2023-064344M.

[Determinants of Lung Function Across Childhood in the Severe Asthma Research Program \(SARP\) 3](#)

[Tevon Hood](#)¹, [Pooja Varshney](#)¹

Affiliations expand

- PMID: 38038586
- DOI: [10.1542/peds.2023-064344M](https://doi.org/10.1542/peds.2023-064344M)

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. 2023 Dec 1;152(Suppl 3):S46-S47.

doi: [10.1542/peds.2023-064344LD](https://doi.org/10.1542/peds.2023-064344LD).

[Community Interventions for Childhood Asthma ED Visits and Hospitalizations: A Systematic Review](#)

[Susan Laubach](#)¹

Affiliations expand

- PMID: 38038585
- DOI: [10.1542/peds.2023-064344LD](https://doi.org/10.1542/peds.2023-064344LD)

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. 2023 Dec 1;152(Suppl 3):S45-S46.

doi: 10.1542/peds.2023-064344LB.

[Prepregnancy Body Mass Index and Risk of Childhood Asthma](#)

[Stephania Lairet](#)¹, [Vivian Hernandez-Trujillo](#)¹

Affiliations expand

- PMID: 38038583
- DOI: [10.1542/peds.2023-064344LB](https://doi.org/10.1542/peds.2023-064344LB)

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. 2023 Dec 1;152(Suppl 3):S55-S56.

doi: 10.1542/peds.2023-064344NF.

Comparative Efficacy of Mepolizumab, Benralizumab, and Dupilumab in Eosinophilic Asthma: A Bayesian Network Meta-analysis

[Mitchell R Lester](#)¹

Affiliations expand

- PMID: 38038579
- DOI: [10.1542/peds.2023-064344NF](https://doi.org/10.1542/peds.2023-064344NF)

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. 2023 Dec 1;152(Suppl 3):S44-S45.

doi: 10.1542/peds.2023-064344L.

Early-life Respiratory Tract Infections and the Risk of School-age Lower Lung Function and Asthma: a Meta-analysis of 150 000 European Children

[Lily Nguyen](#)¹, [Lindsey Moore](#)¹

Affiliations expand

- PMID: 38038571
- DOI: [10.1542/peds.2023-064344L](https://doi.org/10.1542/peds.2023-064344L)

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. 2023 Dec 1;152(Suppl 3):S55.

doi: 10.1542/peds.2023-064344NE.

Efficacy of Tezepelumab in Patients With Evidence of Severe Allergic Asthma: Results From the Phase 3 NAVIGATOR Study

[Meaghan J Bank](#)¹, [Luke A Wall](#)¹

Affiliations expand

- PMID: 38038569
- DOI: [10.1542/peds.2023-064344NE](https://doi.org/10.1542/peds.2023-064344NE)

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. 2023 Dec 1;152(Suppl 3):S47-S48.

doi: [10.1542/peds.2023-064344LE](https://doi.org/10.1542/peds.2023-064344LE).

Childhood Asthma Incidence, Early and Persistent Wheeze, and Neighborhood

Socioeconomic Factors in the ECHO/CREW Consortium

[Ashley Sang Eun Lee](#)¹, [Julie Wang](#)¹

Affiliations expand

- PMID: 38038543
- DOI: [10.1542/peds.2023-064344LE](https://doi.org/10.1542/peds.2023-064344LE)

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. 2023 Dec 1;152(Suppl 3):S48.

doi: [10.1542/peds.2023-064344LF](https://doi.org/10.1542/peds.2023-064344LF).

Understanding Racial Disparities in Childhood Asthma Using Individual- and Neighborhood-level Risk Factors

[Tevon Hood](#)¹, [Pooja Varshney](#)¹

Affiliations expand

- PMID: 38038542

- DOI: [10.1542/peds.2023-064344LF](https://doi.org/10.1542/peds.2023-064344LF)

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. 2023 Dec 1;152(Suppl 3):S52.

doi: [10.1542/peds.2023-064344N](https://doi.org/10.1542/peds.2023-064344N).

[Albuterol–Budesonide Fixed–Dose Combination Rescue Inhaler for Asthma](#)

[Samantha K Knox](#)¹, [Todd A Mahr](#)¹

Affiliations expand

- PMID: 38038518

- DOI: [10.1542/peds.2023-064344N](https://doi.org/10.1542/peds.2023-064344N)

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. 2023 Dec 1;152(Suppl 3):S52-S53.

doi: 10.1542/peds.2023-064344NA.

[As-Needed Use of Short-Acting \$\beta\$ 2-Agonists Alone Versus As-Needed Use of Short-acting \$\beta\$ 2-Agonists Plus Inhaled Corticosteroids in Pediatric Patients With Mild Intermittent \(Step 1\) Asthma: A Cost-Effectiveness Analysis](#)

[Brit Trogen](#)¹, [Scott Sicherer](#)¹

Affiliations expand

- PMID: 38038517
- DOI: [10.1542/peds.2023-064344NA](https://doi.org/10.1542/peds.2023-064344NA)

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. 2023 Dec 1;152(Suppl 3):S23-S24.

doi: 10.1542/peds.2023-064344HC.

[Mendelian Randomization Analysis Reveals a Complex Genetic Interplay Among Atopic Dermatitis, Asthma and Gastroesophageal Reflux Disease](#)

[Samantha K Knox](#)¹, [Todd A Mahr](#)¹

Affiliations expand

- PMID: 38038511
- DOI: [10.1542/peds.2023-064344HC](https://doi.org/10.1542/peds.2023-064344HC)

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. 2023 Dec 1;152(Suppl 3):S48-S49.

doi: 10.1542/peds.2023-064344LG.

Childhood Asthma and Household Exposures to Nitrogen Dioxide and Fine Particles: A Triple Crossover Randomized Intervention Trial

[Devyn L Rohlfs](#)¹, [Andrew Abreo](#)¹

Affiliations expand

- PMID: 38038507
- DOI: [10.1542/peds.2023-064344LG](https://doi.org/10.1542/peds.2023-064344LG)

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. 2023 Dec 1;152(Suppl 3):S49.

doi: 10.1542/peds.2023-064344LH.

Asthma and Anxiety Development in Australian Children and Adolescents

[Smridhi Mahajan](#)¹, [Christopher Parrish](#)¹

Affiliations expand

- PMID: 38038506
- DOI: [10.1542/peds.2023-064344LH](https://doi.org/10.1542/peds.2023-064344LH)

No abstract available

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Allergy

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. 2023 Dec 1.

doi: 10.1111/all.15965. Online ahead of print.

Correspondence to 'association between chronic rhinosinusitis and new

onset asthma implications for prevention'

[Iressa Cheng](#)¹, [Chin-Yuan Yü](#)^{2,3}, [Liang-Chun Shih](#)⁴, [Jiu Yao Wang](#)^{5,6}, [Su-Boon Yong](#)^{5,6,7}

Affiliations expand

- PMID: 38037748
- DOI: [10.1111/all.15965](https://doi.org/10.1111/all.15965)

No abstract available

Keywords: chronic rhinosinusitis; new onset asthma.

- [6 references](#)

SUPPLEMENTARY INFO

Publication types, Grants and fundingexpand

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Br J Gen Pract

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. 2023 Nov 30;73(737):565-568.

doi: 10.3399/bjgp23X735813. Print 2023 Dec.

Fractional exhaled nitric oxide (FeNO): the future of asthma care?

[Kay Wang](#)¹, [Carol Stonham](#)², [Christine Rutherford](#)³, [Ian D Pavord](#)⁴

Affiliations expand

- PMID: 38035806
- DOI: [10.3399/bjgp23X735813](https://doi.org/10.3399/bjgp23X735813)

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Lancet Respir Med

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. 2023 Dec;11(12):1044-1045.

doi: 10.1016/S2213-2600(23)00369-7.

T2-low asthma in school-aged children: unacknowledged and understudied

[Pooja E Mishra](#)¹, [Erik Melén](#)², [Gerard H Koppelman](#)³, [Juan C Celedón](#)⁴

Affiliations expand

- PMID: 38030372

- DOI: [10.1016/S2213-2600\(23\)00369-7](https://doi.org/10.1016/S2213-2600(23)00369-7)

No abstract available

Conflict of interest statement

PEM declares no conflicts of interest. EM is supported by grants from the Swedish Research Council, Swedish Heart-Lung Foundation and Region Stockholm (ALF). EM has received advisory board or lecture fees from Airsonett, ALK, AstraZeneca, Chiesi, Novartis, and Sanofi outside of the study. GHK is supported by a ZON-MW VICI grant, and reports receiving research grants from Netherlands Lung Foundation, Ubbo Emmius Foundation, Health Holland, EU, GSK, Vertex, and TEVA the Netherlands outside of the submitted work. GHK received advisory board or lecture fees from Astra Zeneca, PURE-IMS, Sanofi, and Boehringer-Ingelheim. JCC is supported by grants HL152475, HL168539 and HL150431 from the US National Institutes of Health. JCC has received research materials (inhaled corticosteroids) from Merck to provide medications free of cost to participants in an NIH-funded study.

SUPPLEMENTARY INFO

MeSH termsexpand

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Lancet Respir Med

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. 2023 Dec;11(12):1041-1043.

doi: 10.1016/S2213-2600(23)00436-8.

Chronic obstructive pulmonary disease: hiding in plain sight, a Statement from the COPD Foundation Medical and Scientific Advisory Committee

[Surya P Bhatt](#)¹, [Richard Casaburi](#)², [Alvar Agusti](#)³, [Bartolome R Celli](#)⁴, [Bruce E Miller](#)⁵, [Nirupama Putcha](#)⁶, [Jean Rommes](#)⁷, [Mark T Dransfield](#)⁸; [Medical and Scientific Advisory Committee of the COPD Foundation](#)

Affiliations expand

- PMID: 38030371
- DOI: [10.1016/S2213-2600\(23\)00436-8](https://doi.org/10.1016/S2213-2600(23)00436-8)

No abstract available

Conflict of interest statement

SPB reports grants from the National Institutes of Health; research support from Nuaira and Sanofi/Regeneron; consulting or advisory board fees from Sanofi/Regeneron, GSK, and Boehringer Ingelheim; honorarium from Integrity Continuing Education for continued medical education. AA declares grants from GSK, AstraZeneca, Chiesi, Sanofi, and Menarini; and consulting or advisory board fees from GSK, AstraZeneca, Chiesi, Menarini, Cipla, Zambon, Sanofi, and Regeneron. BRC reports consulting or advisory board fees or honoraria from GSK, AstraZeneca, Menarini, Sanofi, Axios, and Chiesi; and fees for participation in data safety monitoring boards from AstraZeneca, Sanofi, and Vertex. BEM serves as a contractor and consultant for the COPD Foundation. NP reports grants from the National Institutes of Health; and fees for participation on data safety monitoring boards for CSL Behring, GSK, and Pharmacosmos. NP reports grants from the National Institutes of Health, the American Lung Association, and the Department of Defense; royalties from Up To Date; serves on the Board of Directors of the COPD Foundation (unpaid); and consulting fees from AstraZeneca, Genentech, GSK, Novartis, Pulmonx, and Teva. All other authors declare no competing interests.

SUPPLEMENTARY INFO

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23

Lancet Reg Health Eur

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. 2023 Nov 6:35:100759.

doi: 10.1016/j.lanepe.2023.100759. eCollection 2023 Dec.

[Impact of the metabolic syndrome on cardiopulmonary morbidity and mortality in individuals with lung function impairment: a prospective cohort study of the Danish general population](#)

[Jacob Louis Marott](#)^{1 2}, [Truls Sylvan Ingebrigtsen](#)¹, [Yunus Çolak](#)^{1 2 3}, [Hannu Kankaanranta](#)^{4 5 6}, [Per Sigvald Bakke](#)⁷, [Jørgen Vestbo](#)^{8 9}, [Børge Grønne Nordestgaard](#)^{1 2 10 11}, [Peter Lange](#)^{1 3 12}

Affiliations [expand](#)

- PMID: 38023334
- PMCID: [PMC10652137](#)
- DOI: [10.1016/j.lanepe.2023.100759](#)

Free PMC article

Abstract

Background: Whether the metabolic syndrome plays a role for the prognosis of individuals with lung function impairment (preserved ratio impaired spirometry (PRISm) or airflow limitation) is unclear. We hypothesised that the metabolic syndrome in individuals with lung function impairment is associated with increased cardiopulmonary morbidity and mortality.

Methods: The Copenhagen General Population Study was initiated in 2003 based on a random sample of white men and women aged 20-100 years drawn from the Danish general population. The risk of ischemic heart disease/heart failure, respiratory disease, and all-cause mortality was analysed with Cox models adjusted for age, sex, current smoking, and asthma during 15 years of follow-up.

Findings: Among 106,845 adults, 86,159 had normal lung function, 6126 had PRISm, and 14,560 had airflow limitation. We observed 10,448 hospital admissions for ischemic heart disease/heart failure, 21,140 for respiratory disease, and 11,125 deaths. Individuals with versus individuals without the metabolic syndrome generally had higher 5-year absolute risk of all outcomes, including within those with normal lung function, mild-moderate-severe PRISm, and very mild-mild-moderate-severe airflow limitation alike. Compared to individuals without the metabolic syndrome and with normal lung function, those with both the metabolic syndrome and severe PRISm had hazard ratios of 3.74 (95% CI: 2.53-5.55; $p < 0.0001$) for ischemic heart disease/heart failure, 5.02 (3.85-6.55; $p < 0.0001$) for respiratory disease, and 5.32 (3.76-7.54; $p < 0.0001$) for all-cause mortality. Corresponding hazard ratios in those with both the metabolic syndrome and severe airflow limitation were 2.89 (2.34-3.58; $p < 0.0001$) for ischemic heart disease/heart failure, 5.98 (5.28-6.78; $p < 0.0001$) for respiratory disease, and 4.16 (3.50-4.95; $p < 0.0001$) for all-cause mortality, respectively. The metabolic syndrome explained 13% and 27% of the influence of PRISm or airflow limitation on ischemic heart disease/heart failure and all-cause mortality.

Interpretation: The metabolic syndrome conferred increased risk of cardiopulmonary morbidity and mortality at all levels of lung function impairment.

Funding: Danish Lung Foundation, Danish Heart Foundation, Capital Region of Copenhagen, and Boehringer Ingelheim. JV is supported by the NIHR Manchester BRC.

Keywords: Airflow limitation; Cardiopulmonary morbidity; Mortality; PRISm; Preserved ratio impaired spirometry.

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Conflict of interest statement

J.L.M. received an unrestricted grant from The Danish Lung Foundation in relation to the present work. T.S.I. received an advisory board fee from AstraZeneca. Y.Ç. received

speaking fees from Sanofi Genzyme, AstraZeneca, GlaxoSmithKline, and Boehringer Ingelheim. H.K. reports funding from The Swedish Science Council, The Swedish Heart and Lung Foundation, The Swedish Asthma and Allergy Foundation, The Tampere Tuberculosis Foundation, The Swedish ALF-funding, and The Finnish Anti-Tuberculosis Association Foundation outside the submitted work; being a committee member of the research council of the Swedish Heart and Lung Foundation; consulting fees from GlaxoSmithKline, AstraZeneca, MSD, Novartis, Orion Pharma, and Sanofi Genzyme; and speaking fees from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, and Orion Pharma. P.S.B. received lecture fees from AstraZeneca and Boehringer Ingelheim and advisory board fees from GlaxoSmithKline and AstraZeneca. J.V. received consulting fees from ALK, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, and Teva, as well as speaking fees from AstraZeneca, Boehringer Ingelheim, Chiesi, and GlaxoSmithKline and advisory board fees from AstraZeneca. P.L. received an unrestricted grant in relation to the present work from Boehringer Ingelheim; advisory board fees from AstraZeneca, GlaxoSmithKline, Boehringer Ingelheim, and Sanofi; and speaking fees from AstraZeneca, Boehringer Ingelheim, and GlaxoSmithKline. B.G.N. declares no potential conflicts of interest.

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

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[Review](#)

J Comp Eff Res

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. 2023 Dec;12(12):e230136.

doi: 10.57264/cer-2023-0136. Epub 2023 Nov 24.

Rational use of inhaled corticosteroids for the treatment of COPD: a plain language summary

[Amnon Ariel](#)¹, [Peter J Barnes](#)², [Tiago Maricoto](#)^{3,4,5}, [Miguel Román-Rodríguez](#)⁶, [Andy Powell](#)⁷, [Jennifer K Quint](#)²

Affiliations expand

- PMID: 38009437
- DOI: [10.57264/cer-2023-0136](https://doi.org/10.57264/cer-2023-0136)

Free article

Abstract

What is this summary about?: Inhaled corticosteroids (ICS) are a type of medication delivered via an inhaler device that are commonly used in the treatment of asthma. ICS can also be used to treat chronic obstructive pulmonary disease (COPD), a progressive respiratory condition in which the lungs become worse over time. However, unlike in asthma, ICS are only effective in a small proportion of people with COPD. ICS can cause significant side effects in people with COPD, including pneumonia. Because of this, guidelines written by COPD experts recommend that ICS should largely be prescribed to people with COPD whose symptoms flare up frequently and become difficult to manage (episodes known as exacerbations). Despite this guidance, records collected from routine clinical practice suggest that many healthcare professionals prescribe ICS to people with COPD who do not have frequent exacerbations, putting them at unnecessary risk of side effects. The over-prescription of ICS in COPD may partly be due to the recent introduction of single-inhaler combination therapies, which combine ICS with other medicines (bronchodilators). This 'one inhaler for all' approach is a concerning trend as it goes against global COPD treatment guidelines, which recommend ICS use in only a small proportion of people. This is a plain language summary of a review article originally published in the journal *NPJ Primary Care Respiratory Medicine*. In this review, we investigate the benefits and risks of ICS use in COPD. Using data from both randomized controlled trials (RCTs) and observational studies, we explain which people benefit from ICS use, and why health regulatory bodies have concluded that ICS do not help people with COPD to live longer. Lastly, we provide practical guidance for doctors and people with COPD regarding when ICS should be prescribed and when they should be withdrawn.

Keywords: ICS; LAMA/LABA; chronic obstructive pulmonary disease COPD; inhaled corticosteroids; lay summary; long-acting bronchodilators; observational study; plain language summary; randomized controlled trial; real-world evidence; treatment guidelines.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Review

Pharmacol Ther

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. 2023 Dec;252:108551.

doi: 10.1016/j.pharmthera.2023.108551. Epub 2023 Oct 30.

Biologics for severe asthma and beyond

[Carlo Mummeler](#)¹, [Katrin Milger](#)²

Affiliations expand

- PMID: 37907197
- DOI: [10.1016/j.pharmthera.2023.108551](https://doi.org/10.1016/j.pharmthera.2023.108551)

Abstract

Advances in pathophysiological understanding and the elucidation of a type 2 inflammatory signature with interleukins 4, 5 and 13 at its center have led to the development of targeted antibody therapies that are now approved for the treatment of severe asthma. In suitable patients, these medications reduce asthma exacerbations and the necessity for oral corticosteroids, improve asthma control, quality of life and lung function. A proportion of patients with severe asthma may even achieve remission under ongoing biologic therapy. Type-2 inflammatory comorbidities are frequent in patients with severe asthma, sharing overlapping pathophysiology and may similarly respond to biologic treatment. Here, we give an overview of the six biologic therapies currently approved for severe asthma and review randomized clinical trials and real-life studies in asthma and other type-2 inflammatory diseases. We also discuss selection of biologics according to licensing criteria, asthma phenotype and biomarkers, monitoring of treatment response and proceedings in case of insufficient outcome under therapy.

Keywords: Antibody; Asthma; Atopic dermatitis; Biologics; CRSwNP; Severe asthma; T2.

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Conflict of interest statement

Declaration of Competing Interest CM: Travel support from Sanofi outside the current work. KM reports speaker and/or advisory fees from AstraZeneca, Chiesi, GSK, Novartis, Sanofi outside the current work.

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Publication typesexpand

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26

Br J Gen Pract

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. 2023 Nov 30;73(737):e876-e884.

Early detection of chronic obstructive pulmonary disease in primary care: a randomised controlled trial

[Anthony Chapron](#)¹, [Emilie Andres](#)², [Laure Fiquet](#)², [Fabienne Pelé](#)³, [Emmanuel Allory](#)², [Estelle Le Pabic](#)³, [Aurélié Veislinger](#)², [Lisa Le Guillou](#)⁴, [Stéphanie Guillot](#)⁴, [Bruno Laviolle](#)⁵, [Stéphane Jouneau](#)⁶

Affiliations expand

- PMID: 37903640
- PMCID: [PMC10633669](#)
- DOI: [10.3399/BJGP.2022.0565](#)

Free PMC article

Abstract

Background: Worldwide, chronic obstructive pulmonary disease (COPD) remains largely underdiagnosed.

Aim: To assess whether the use of Global Initiative for Chronic Obstructive Lung Disease (GOLD) questions and COPD coordination, either alone or combined, would detect new COPD cases in primary care.

Design and setting: GPs in Brittany, France, systematically enrolled patients aged 40–80 years over a 4-month period in this French multicentre cluster randomised controlled study.

Method: GPs were randomly allocated to one of four groups: control (standard of care), GOLD questions (adapted from symptoms and risk factors identified by GOLD), COPD coordination, and GOLD questions with COPD coordination. New cases of COPD were those confirmed by spirometry: post-bronchodilator forced expiratory volume in 1 second over forced vital capacity of <0.7.

Results: In total, 11 430 consultations were conducted by 47 GPs, who enrolled 3162 patients who did not have prior diagnosed asthma or COPD. Among these, 802 (25%) were

enrolled in the control, 820 (26%) in the GOLD questions, 802 (25%) in the COPD coordination, and 738 (23%) in the GOLD questions with COPD coordination groups. In the control group, COPD was not evoked, and no spirometry was prescribed. All new cases of COPD diagnosed ($n = 24$, 0.8%) were in the intervention groups, representing 6.8% of patients who performed spirometry. Statistically significantly more new cases of COPD were detected with COPD coordination ($P = 0.01$).

Conclusion: Interventions that can be easily implemented, such as the GOLD questions and COPD coordination, can identify new cases of COPD. Studies are needed to identify the most appropriate case-finding strategies for GPs to detect COPD in primary care for each country.

Keywords: GOLD questions; chronic obstructive pulmonary disease; early detection; general practice; primary care.

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Conflict of interest statement

The authors have declared no competing interests.

- [Cited by 1 article](#)
- [32 references](#)
- [3 figures](#)

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[Review](#)

Curr Opin Allergy Clin Immunol

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. 2023 Dec 1;23(6):514-519.

doi: 10.1097/ACI.0000000000000945. Epub 2023 Oct 17.

Safety of allergen immunotherapy in children

[Kristin A Schmidlin](#)¹, [David I Bernstein](#)

Affiliations expand

- PMID: 37846900
- DOI: [10.1097/ACI.0000000000000945](https://doi.org/10.1097/ACI.0000000000000945)

Abstract

Purpose of review: The current review discusses allergen immunotherapy (AIT) safety in children.

Recent findings: AIT is a well tolerated and effective treatment for pediatric allergic conditions. While mostly well tolerated, severe reactions and near fatal reactions may occur with subcutaneous immunotherapy (SCIT) once in every 160 000 visits. Sublingual immunotherapy (SLIT) is associated more with local side effects, but severe systemic reactions, including anaphylaxis, have been rarely reported. Providing informed consent, recognizing risk factors for severe systemic reactions, such as severe or uncontrolled asthma, and mitigating the risk of severe reactions are important components to improving the safety of AIT.

Summary: Overall, AIT is well tolerated in children, and data suggest that the incidence of systemic reactions in children receiving SCIT is no less than mixed populations of adult and pediatric patients. SLIT carries less risk for systemic reactions, and local oral site-application reactions are usually mild and resolve within 15 days of treatment.

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Int Arch Occup Environ Health

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. 2023 Dec;96(10):1325-1332.

doi: 10.1007/s00420-023-02011-5. Epub 2023 Oct 11.

Association between household cleaning product exposure in infancy and development of recurrent wheeze and asthma

[Isis F Baroni](#)¹, [Geneva D Mehta](#)², [Ashley F Sullivan](#)¹, [Carlos A Camargo Jr](#)¹, [Orianne Dumas](#)³

Affiliations expand

- PMID: 37819536
- DOI: [10.1007/s00420-023-02011-5](https://doi.org/10.1007/s00420-023-02011-5)

Abstract

Objective: Household chemicals may act as irritants in the lungs; however, their association with recurrent wheeze and asthma in children remains controversial. We aimed to investigate if household cleaning product exposure in infancy is associated with recurrent wheezing and asthma development in children.

Methods: We analyzed data from two cohorts: MARC-35 consisting of 815 children with history of severe bronchiolitis in infancy, and MARC-43 consisting of 525 healthy children

in infancy. Frequency of use of cleaning product at the child's home during infancy was collected via telephone interview with parents. Outcomes were recurrent wheezing by age 3 years and asthma diagnosis at age 6 years.

Results: In MARC-35, there was no association between cleaning product exposure in infancy and recurrent wheeze (adjusted HR = 1.01 [95% CI 0.66-1.54] for 4-7 days/week exposure frequency), nor asthma (adjusted OR = 0.91 [95% CI 0.51-1.63]). In MARC-43, there was also no association between cleaning product exposure in infancy and recurrent wheeze (adjusted HR = 0.69 [95% CI 0.29-1.67] for 4-7 days/week exposure frequency).

Conclusion: We found no association between household cleaning product exposure in infancy and later development of recurrent wheeze or asthma, even among children who are at high risk for asthma due to history of severe bronchiolitis.

Keywords: Asthma; Bronchiolitis; Child; Disinfectants; Lung.

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MeSH terms, Grants and fundingexpand

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Pediatr Pulmonol

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. 2023 Dec;58(12):3406-3415.

doi: 10.1002/ppul.26647. Epub 2023 Oct 11.

Budesonide/formoterol maintenance and reliever therapy in childhood asthma: Real-world effectiveness and economic assessment

[Yuncui Yu](#)^{1,2}, [Wang Cao](#)^{1,2}, [Yue Xiao](#)³, [Ang Li](#)⁴, [Huijie Huang](#)⁴, [Kejun Liu](#)³, [Lihua Hu](#)², [Xiaoling Hou](#)⁴, [Li Xiang](#)⁴, [Xiaoling Wang](#)^{1,2}

Affiliations expand

- PMID: 37818789
- DOI: [10.1002/ppul.26647](https://doi.org/10.1002/ppul.26647)

Abstract

Introduction: The study aims to compare the real-world effectiveness and economy of the budesonide/formoterol reliever and maintenance therapy (SMART) with fixed-dose inhaled corticosteroids (ICS)/long-acting β -agonist (LABA) or ICS alone plus as-needed, short-acting β_2 agonists (SABA) in pediatric patients.

Methods: The outpatient data warehouse of a hospital in China was used. A total of 103 patients under 18 years old in the SMART group and 63 patients in the control group were included from January 1, 2020 to December 31, 2021. The effectiveness was assessed using asthma attacks and lung function at baseline, 6 months and 12 months follow-up. Cost-effectiveness analysis was performed with a three-state Markov model from the healthcare system perspective. One-way sensitivity analyses and probabilistic sensitivity analyses were performed to check the robustness of the results.

Results: The SMART regimen was more effective than other strategies in reducing the risk of mild and severe attacks in the real-life management of childhood asthma. Patients in both groups showed significant improvement in lung function at 6 and 12 months in contrast to baseline. Compared with other strategies, the forced expiratory volume in 1 s (FEV_1) level in the SMART group was markedly improved at 6 months. The total cost of outpatient service using the SMART regimen was lower than that of other strategies, while the drug costs were similar in different groups. Incremental cost-effectiveness analysis results showed that using the SMART regimen reduced the total cost by approximately CNY 10,516.11 per year with a 0.12 quality-adjusted life year (QALYs) increase. Sensitive analyses supported that the SMART regimen was the dominant choice at the willingness-to-pay threshold of CNY 85,698, per capita GDP in China.

Conclusions: Collectively, our findings indicate that the real-world effectiveness and economy of the SMART regimen are superior to the traditional strategies in pediatric asthma patients.

Keywords: SMART; asthma; budesonide/formoterol; economic assessment; real-world data.

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- [25 references](#)

SUPPLEMENTARY INFO

MeSH terms, Substances, Grants and funding[expand](#)

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Econ Hum Biol

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. 2023 Dec:51:101311.

doi: 10.1016/j.ehb.2023.101311. Epub 2023 Oct 6.

[Exposure to wildfires and health outcomes of vulnerable people: Evidence from US data](#)

[Jiyuan Zheng](#)¹

Affiliations [expand](#)

- PMID: 37816268

- DOI: [10.1016/j.ehb.2023.101311](https://doi.org/10.1016/j.ehb.2023.101311)

Abstract

This paper investigates the causal effect of wildfire exposure on birth outcomes and older people's health outcomes in United States (US). The study focuses on three sub-questions for each health outcome: (1) the causal effect of each of the five largest wildfires on individual health, (2) the causal impact of multiple large wildfires on individual health outcomes, and (3) the causal influence of wildfires larger than different sizes within different distances of counties on health outcomes at the county level. The analysis exploits data from National Vital Statistics System, Behavioural Risk Factor Surveillance System and FIRESTAT. In terms of birth outcomes, the findings show that the largest wildfire slightly increased the risk of other circulatory or respiratory anomalies. Multiple large wildfires moderately raised the risk of prematurity and led to a small decline in the probability of getting omphalocele and cleft lip. The county-level analysis suggests an increased risk of macrosomia following maternal exposure to wildfires. As for the elderly aged 65 + , the results indicate that exposure to multiple massive wildfires led to frequent occurrence of asthma symptoms, while the largest wildfire led to sleeping difficulty caused by asthma symptoms. The number of days older people experienced psychological problems was increased following exposure to multiple large wildfires.

Keywords: Birth outcomes; Causal inference; Health outcomes; Older people; Wildfire exposure.

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Allergy

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. 2023 Dec;78(12):3154-3165.

doi: 10.1111/all.15909. Epub 2023 Oct 4.

Blood CD62L^{low} inflammatory eosinophils are related to the severity of asthma and reduced by mepolizumab

[Alessandra Vultaggio](#)¹, [Matteo Accinno](#)¹, [Emanuele Vivarelli](#)², [Valentina Mecheri](#)¹, [Giandomenico Maggiore](#)³, [Lorenzo Cosmi](#)¹, [Paola Parronchi](#)¹, [Olivero Rossi](#)⁴, [Enrico Maggi](#)⁵, [Oreste Gallo](#)³, [Andrea Matucci](#)⁴

Affiliations expand

- PMID: 37792721
- DOI: [10.1111/all.15909](https://doi.org/10.1111/all.15909)

Abstract

Background: Eosinophils have been divided into different subpopulations with distinct phenotypes based on CD62L expression. No data are available regarding the correlation between eosinophils subphenotypes and clinical severity of asthma, as well as the effect of anti-IL-5 therapy on these cells. The study investigates the correlation between blood CD62L^{low} inflammatory eosinophils (iEos) and clinical severity of severe eosinophilic asthma (SEA) and evaluates the impact of mepolizumab on iEos.

Methods: 112 patients were screened and were divided in two groups: biological-naïve (n = 51) and biological-treated patients (n = 61). The Biological-naïve patients were analyzed before treatment (Group A) and 19 out of 51 patients, were longitudinally analyzed before and after treatment with mepolizumab 100 mg s.c/4 weeks (Group B); 32 patients were excluded because they were being treated with other biological therapies. Blood eosinophils were analyzed by FACS and correlated with clinical scores. In vitro effect of IL-5 and mepolizumab on CD62L expression was assessed.

Results: A significant correlation between blood CD62L^{low} cells and clinical scores of asthma and nasal polyps, as well as the number of asthma exacerbations in the last year was shown in untreated patients. In longitudinally studied patients we observed a marked reduction of CD62L^{low} cells paralleled by an increase in the proportion of CD62L^{bright} cells,

associated with clinical improvement of asthma control. In vitro, CD62L expression on eosinophils is modulated by IL-5 and anti-IL-5.

Conclusion: A positive correlation between CD62L^{low} iEos and the baseline clinical features of SEA with CRSwNP was shown. Furthermore mepolizumab restores the healthy balance among eosinophils sub-phenotypes in SEA patients.

Keywords: CD62L; IL-5; eosinophils; inflammatory eosinophils; mepolizumab; nasal polyps; severe asthma.

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Prehosp Disaster Med

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. 2023 Dec;38(6):807-812.

doi: 10.1017/S1049023X23006398. Epub 2023 Sep 29.

[Medical Assistance in the De-Occupied Ukrainian Territory](#)

[Oleg V Mazurenko](#)¹, [Georgiy G Roshchin](#)¹, [Ivan Yo Slychko](#)¹

Affiliations expand

- PMID: 37770387

- DOI: [10.1017/S1049023X23006398](https://doi.org/10.1017/S1049023X23006398)

Abstract

Introduction: The Russian invasion of Ukraine in 2022 has affected more people and destroyed a local public health facility. When some territories in Ukraine were de-occupied, national and international mobile clinics (MCs) were involved for medical assistance to local inhabitants. Knowledge about population health, medical, and humanitarian needs after they have been de-occupied has to improve planning for health system response.

Objective: The aim of this study was to summarize the MC experience at the first month after the area was de-occupied, as well as to show out-patient visits and to identify a need for medicines and medical equipment in the MC.

Methods: The information related to the missions was obtained by direct observation and estimation on empirical data gathering in the field during a twelve-day mission in April-May 2022. All patients were divided by age, sex, and diseases according to the International Classification of Diseases-10 (ICD-10). During the twelve-day MC mission, medical assistance was provided for 478 out-patients. Descriptive statistical methods were undertaken using Microsoft Office 2019, Excel with data analysis.

Interventions: All out-patients were evaluated clinically. Personal medical cards were completed for each patient. Glucose testing as well as tests for coronavirus disease 2019/COVID-19 had been done, if it was necessary. All sick persons were treated for their disease.

Results: The priority needs for emergency and primary medical care, medicines, and hygienic and sanitation supplies after the area was de-occupied were fixed. The most frequent reasons for visiting the MC were: hypertension (27.6%), musculoskeletal-related (arthritis) diseases (26.9%), heart and peripheral vascular diseases (12.1%), upper gastrointestinal disorder (5.4%), upper respiratory infection (5.0%), and diabetes Type-2 (3.7%). Other diagnoses such as lower respiratory tract infection, diagnoses of the digestive system (hemorrhoids and perianal venous thrombosis), chronic obstructive pulmonary disease/COPD or asthma, eye diseases, gynecology-related condition, menstrual condition, and urinary tract disorder were distributed almost equally (0.21%-2.51%) among the patient population.

Conclusions: In the de-occupied territories, a health responder could be ready for medical assistance to patients with noncommunicable diseases (NCDs) as well as to support a person with psychological reactions who asked for sedatives and sleep-inducing medicines. These data clearly demonstrate that MCs must be equipped by blood pressure (BP) monitor, stethoscope, pulse oximeter, and diabetes testing kit glucose with essential medicines. This study improves health response planning for local civilian populations in de-occupied territory.

Keywords: Russian-Ukraine war; de-occupied territory; health; mobile clinic; rural population.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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Editorial

Respirology

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. 2023 Dec;28(12):1091-1092.

doi: 10.1111/resp.14606. Epub 2023 Sep 21.

[Which biologic? New findings from a real-world study](#)

[Gabriel Lavoie](#)¹, [Ian D Pavord](#)¹

Affiliations expand

- PMID: 37735863
- DOI: [10.1111/resp.14606](https://doi.org/10.1111/resp.14606)

Free article

No abstract available

Keywords: asthma; benralizumab; biologic; eosinophilic asthma; mepolizumab; real world; severe asthma.

- [15 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Observational Study

Ann Rheum Dis

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. 2023 Dec;82(12):1587-1593.

doi: 10.1136/ard-2023-224756. Epub 2023 Sep 21.

[Dupilumab for relapsing or refractory sinonasal and/or asthma manifestations in eosinophilic granulomatosis with polyangiitis: a European retrospective study](#)

[Berengere Molina](#)¹, [Roberto Padoan](#)², [Maria Letizia Urban](#)³, [Pavel Novikov](#)⁴, [Marco Caminati](#)⁵, [Camille Taillé](#)⁶, [Antoine Néel](#)⁷, [Laurence Bouillet](#)^{8,9}, [Paolo Fraticelli](#)¹⁰, [Nicolas Schleinitz](#)¹¹, [Christine Christides](#)¹², [Laura Moi](#)¹³, [Bertrand Godeau](#)¹⁴, [Ann Knight](#)¹⁵, [Jan Walter](#)

[Schroeder](#)¹⁶, [Sylvain Marchand-Adam](#)¹⁷, [Helder Gil](#)¹⁸, [Vincent Cottin](#)¹⁹, [Cécile-Audrey Durel](#)²⁰, [Elena Gelain](#)²¹, [Boris Lerais](#)²², [Marc Ruivard](#)²³, [Matthieu Groh](#)²⁴, [Maxime Samson](#)^{25 26}, [Luca Moroni](#)²⁷, [Jens Thiel](#)^{28 29}, [Anna Kernder](#)³⁰, [Jan Willem Cohen Tervaert](#)^{31 32}, [Giulia Costanzo](#)³³, [Marco Folci](#)³⁴, [Sonia Rizzello](#)³⁵, [Pascal Cohen](#)³⁶, [Giacomo Emmi](#)^{3 37}, [Benjamin Terrier](#)³⁸

Affiliations expand

- PMID: 37734881
- DOI: [10.1136/ard-2023-224756](https://doi.org/10.1136/ard-2023-224756)

Abstract

Background: Eosinophilic granulomatosis with polyangiitis (EGPA) is often associated with glucocorticoid-dependent asthma and/or ear, nose and throat (ENT) manifestations. When immunosuppressants and/or mepolizumab are ineffective, dupilumab could be an option. We describe the safety and efficacy of off-label use of dupilumab in relapsing and/or refractory EGPA.

Patients and methods: We conducted an observational multicentre study of EGPA patients treated with dupilumab. Complete response was defined by Birmingham Vasculitis Activity Score (BVAS)=0 and prednisone dose ≤ 4 mg/day, and partial response by BVAS=0 and prednisone dose > 4 mg/day. Eosinophilia was defined as an eosinophil count $> 500/\text{mm}^3$.

Results: Fifty-one patients were included. The primary indication for dupilumab was disabling ENT symptoms in 92%. After a median follow-up of 13.1 months, 18 patients (35%) reported adverse events (AEs), including two serious AEs. Eosinophilia was reported in 34 patients (67%), with a peak of $2195/\text{mm}^3$ (IQR 1268-4501) occurring at 13 weeks (IQR 4-36) and was associated with relapse in 41%. Twenty-one patients (41%) achieved a complete response and 12 (24%) a partial response. Sixteen (31%) patients experienced an EGPA relapse while on dupilumab, which was associated with blood eosinophilia in 14/16 (88%) patients. The median eosinophil count at the start of dupilumab was significantly lower in relapsers than in non-relapsers, as was the median time between stopping anti-IL-5/IL-5R and switching to dupilumab.

Conclusion: These results suggest that dupilumab may be effective in treating patients with EGPA-related ENT manifestations. However, EGPA flares occurred in one-third of patients and were preceded by eosinophilia in 88%, suggesting that caution is required.

Keywords: Autoimmune Diseases; Biological Therapy; Immune System Diseases; Systemic vasculitis; Therapeutics.

Conflict of interest statement

Competing interests: None declared.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Randomized Controlled Trial

Pediatr Pulmonol

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. 2023 Dec;58(12):3487-3497.

doi: 10.1002/ppul.26679. Epub 2023 Sep 20.

A multicenter randomized, double-blind, placebo-controlled, parallel-group study to evaluate the effects of a 1-year regimen of orally inhaled fluticasone furoate 50 µg once daily on

growth velocity in prepubertal, pediatric participants with well-controlled asthma

[Philippe Bareille](#)¹, [Varsha Imber](#)², [Jodie Crawford](#)², [Bernadetta Majorek-Olechowska](#)³, [Zeina Karam-Absi](#)⁴, [Sally Stone](#)², [Ruby Birk](#)²

Affiliations expand

- PMID: 37728224
- DOI: [10.1002/ppul.26679](https://doi.org/10.1002/ppul.26679)

Abstract

Introduction: Growth impairment is a known adverse event (AE) of corticosteroids in children. This study aimed to assess the effect of once-daily (QD) inhaled fluticasone furoate (FF) versus placebo on growth velocity over 1 year in prepubertal children with well-controlled asthma.

Materials and methods: This randomized, double-blind, parallel-group, placebo-controlled, multicenter study ([NCT02889809](#)) included prepubertal children, aged 5 to <9 years (boys), and 5 to <8 years (girls), with ≥ 6 months' asthma history. Children received inhaled placebo QD plus background open-label montelukast QD for a 16-week run-in period and were then randomized 1:1 to receive inhaled FF 50 μg QD or placebo QD (whilst continuing background open-label montelukast) for a 52-week treatment period. The primary endpoint was the difference in growth velocity (cm/year) over the treatment period. Other growth endpoints were measured, as were incidence of AEs and asthma exacerbation. Growth analyses included all intent-to-treat (ITT) participants with ≥ 3 post-randomization, on-treatment clinic visit height assessments (GROWTH population).

Results: Of 644 children in the run-in period, 477 (mean age 6.2 years, 63% male) entered the 52-week treatment period (ITT population: FF N = 238, placebo N = 239; GROWTH population: N = 457 [FF N = 231; placebo N = 226]). The least-squares mean difference in growth velocity for FF versus placebo was -0.160 cm/year (95% confidence interval: -0.462, 0.142). There were no new safety signals.

Conclusions: Over 1 year, FF 50 μg QD had a minimal effect on growth velocity versus placebo, with no new safety signals.

Keywords: height; inhaled corticosteroids; pediatric asthma.

- [29 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grants and funding [expand](#)

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[Review](#)

Immunotherapy

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. 2023 Dec;15(17):1435-1447.

doi: 10.2217/imt-2023-0079. Epub 2023 Sep 19.

Tezepelumab: an anti-thymic stromal lymphopoietin monoclonal antibody for the treatment of asthma

[Masaharu Shinkai](#)¹, [Tadataka Yabuta](#)²

Affiliations [expand](#)

- PMID: 37724378
- DOI: [10.2217/imt-2023-0079](https://doi.org/10.2217/imt-2023-0079)

Abstract

Asthma is a common chronic respiratory disease in which epithelial cytokines and airway inflammation play critical pathophysiological roles. Thymic stromal lymphopoietin (TSLP), an epithelial cytokine, is central in the initiation and persistence of airway inflammation in asthma. Tezepelumab is a human immunoglobulin G2 λ (IgG2 λ) monoclonal antibody developed for treating moderate-to-severe asthma by specifically binding to TSLP and preventing its binding to the TSLP receptor on inflammatory cells. In this narrative review, we describe the results of clinical trials that evaluated the pharmacokinetics, pharmacodynamics, efficacy and safety of tezepelumab in patients with moderate-to-severe asthma. We also introduce the ongoing clinical trials in patients with asthma as well as future trials investigating the use of tezepelumab for other indications.

Keywords: Th2 cell; asthma; clinical trial; epithelial cytokine; inflammation; innate lymphocyte; lung health; tezepelumab; thymic stromal lymphopoietin.

Plain language summary

Asthma is a long-term disease that causes inflammation in the cells of the lung. One of the cytokines (proteins) involved in asthma is called thymic stromal lymphopoietin (TSLP). This cytokine is produced by the airway epithelium, a layer of cells covering the respiratory tract in the lungs, where it activates inflammatory cells. Tezepelumab is a new drug that blocks the activity of TSLP in the lungs and helps reduce asthma symptoms, such as coughing and breathlessness. In this article, we describe the clinical trials that investigated how well tezepelumab works, as well as its safety, in people with moderate or severe asthma. We also describe the trials of tezepelumab that are now underway in people with asthma, allergies or other inflammatory diseases.

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Environ Res

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. 2023 Dec 1;238(Pt 1):117154.

doi: 10.1016/j.envres.2023.117154. Epub 2023 Sep 15.

Emergency department visits associated with wildfire smoke events in California, 2016–2019

[Annie I Chen](#)¹, [Keita Ebisu](#)¹, [Tarik Benmarhnia](#)², [Rupa Basu](#)³

Affiliations expand

- PMID: 37716386
- DOI: [10.1016/j.envres.2023.117154](https://doi.org/10.1016/j.envres.2023.117154)

Free article

Abstract

Wildfire smoke has been associated with adverse respiratory outcomes, but the impacts of wildfire on other health outcomes and sensitive subpopulations are not fully understood. We examined associations between smoke events and emergency department visits (EDVs) for respiratory, cardiovascular, diabetes, and mental health outcomes in California during the wildfire season June–December 2016–2019. Daily, zip code tabulation area-level wildfire-specific fine particulate matter (PM_{2.5}) concentrations were aggregated to air basins. A "smoke event" was defined as an air basin-day with a wildfire-specific PM_{2.5} concentration at or above the 98th percentile across all air basin-days (threshold = 13.5 µg/m³). We conducted a two-stage time-series analysis using quasi-Poisson regression considering lag effects and random effects meta-analysis. We also conducted analyses stratified by race/ethnicity, age, and sex to assess potential effect modification. Smoke events were associated with an increased risk of EDVs for all respiratory diseases at lag 1 [14.4%, 95% confidence interval (CI): (6.8, 22.5)], asthma at lag 0 [57.1% (44.5, 70.8)],

and chronic lower respiratory disease at lag 0 [12.7% (6.2, 19.6)]. We also found positive associations with EDVs for all cardiovascular diseases at lag 10. Mixed results were observed for mental health outcomes. Stratified results revealed potential disparities by race/ethnicity. Short-term exposure to smoke events was associated with increased respiratory and schizophrenia EDVs. Cardiovascular impacts may be delayed compared to respiratory outcomes.

Keywords: Emergency department visits; Fine particulate matter; Health impacts; PM(2.5); Wildfire smoke.

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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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Ann Am Thorac Soc

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. 2023 Dec;20(12):1825-1828.

doi: 10.1513/AnnalsATS.202304-321RL.

Effect of Biologic Therapy on Total Body Composition in Severe Asthma

[Edith Visser](#)^{1,2}, [Lianne Ten Have](#)¹, [Anneke Ten Brinke](#)¹, [Kim de Jong](#)¹

Affiliations expand

- PMID: 37703386
- DOI: [10.1513/AnnalsATS.202304-321RL](https://doi.org/10.1513/AnnalsATS.202304-321RL)

No abstract available

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Pediatr Pulmonol

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. 2023 Dec;58(12):3458-3465.

doi: 10.1002/ppul.26676. Epub 2023 Sep 13.

Screening for sleep disordered breathing among children hospitalized for asthma exacerbation

[Neepa Gurbani](#)^{1,2}, [Christine L Schuler](#)^{1,2,3}, [Daniel Ignatiuk](#)^{1,2}, [Jennifer Albrecht](#)⁴, [Yuping Guo](#)¹, [Amanda Waits](#)³, [Carolyn M Kerckmar](#)^{1,2}

Affiliations expand

- PMID: 37701984
- DOI: [10.1002/ppul.26676](https://doi.org/10.1002/ppul.26676)

Abstract

Background: Sleep disordered breathing (SDB) may exacerbate asthma and is a treatable comorbidity.

Objective: To design and implement a screening process for SDB in patients hospitalized for asthma exacerbation using quality improvement (QI) methods. We sought to improve screening for SDB from zero to 60% from July 2019 to December 2020.

Design/methods: A multidisciplinary team used QI methods to screen for SDB using the Michigan pediatric sleep questionnaire (PSQ) in patients 2-18 years hospitalized for asthma exacerbation. Key interventions included: pairing the PSQ screen with another element of routine care (the asthma risk factor screen), educating staff and physicians, engaging respiratory therapists to complete the PSQ and document scores, and modifying the electronic medical record (asthma order set and flowsheet for PSQ score documentation). A run chart tracked progress and descriptive statistics were generated.

Results: There were 2067 patients admitted for asthma exacerbation during this project. The PSQ was completed for 1531 patients (74%) overall. Of screened patients, 360 (24%) had a positive PSQ; the mean age was 8.6 years. Approximately 14 months after the project began, ~90% of children admitted for asthma were being screened; subsequently, >80% of patients were being screened until May 2022. Screening with the PSQ occurred approximately 90% of the time when routine asthma risk screens were completed.

Conclusion: A screening process for SDB was successfully implemented and appeared feasible and sustainable. The high proportion of positive screens reinforces the importance of evaluating for SDB in the high-risk population of children requiring hospitalization for asthma exacerbation.

Keywords: child; snoring; wheezing.

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- [24 references](#)

SUPPLEMENTARY INFO

MeSH terms, Grants and fundingexpand

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Randomized Controlled Trial

Thorax

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. 2023 Dec;78(12):1168-1174.

doi: 10.1136/thorax-2022-219725. Epub 2023 Sep 11.

Atopic and non-atopic effects of fish oil supplementation during pregnancy

[Hans Bisgaard¹](#), [Marianne Mikkelsen¹](#), [Morten Arendt Rasmussen^{1,2}](#), [Astrid Sevelsted¹](#), [Ann-Marie Malby Schoos^{1,3,4}](#), [Nicklas Brustad¹](#), [Anders U Eliassen¹](#), [Jonathan Thorsen¹](#), [Bo Chawes^{1,4}](#), [Gözde Gürdeniz¹](#), [Andreanne Morin⁵](#), [Ken Stark⁶](#), [Jakob Stokholm^{1,3}](#), [Carole Ober⁵](#), [Casper Emil Tingskov Pedersen¹](#), [Klaus Bønnelykke^{7,4}](#)

Affiliations expand

- PMID: 37696621
- DOI: [10.1136/thorax-2022-219725](https://doi.org/10.1136/thorax-2022-219725)

Abstract

Background: We recently conducted a double-blinded randomised controlled trial showing that fish-oil supplementation during pregnancy reduced the risk of persistent wheeze or asthma in the child by 30%. Here, we explore the mechanisms of the intervention.

Methods: 736 pregnant women were given either placebo or n-3 long-chain polyunsaturated fatty acids (LCPUFAs) in the third trimester in a randomised controlled trial. Deep clinical follow-up of the 695 children in the trial was done at 12 visits until age 6 years, including assessment of genotype at the fatty acid desaturase (FADS) locus, plasma fatty acids, airway DNA methylation, gene expression, microbiome and metabolomics.

Results: Supplementation with n-3 LCPUFA reduced the overall risk of non-atopic asthma by 73% at age 6 (relative risk (RR) 0.27 (95% CI 0.06 to 0.85), $p=0.042$). In contrast, there was no overall effect on asthma with atopic traits (RR 1.42 (95% CI 0.63 to 3.38), $p=0.40$), but this was significantly modified by maternal FADS genotype and LCPUFA blood levels (interaction $p<0.05$), and supplementation did reduce the risk of atopic asthma in the subgroup of mothers with FADS risk variants and/or low blood levels of n-3 LCPUFA before the intervention (RR 0.31 (95% CI 0.11 to 0.75), $p=0.016$). Furthermore, n-3 LCPUFA significantly reduced the number of infections (croup, gastroenteritis, tonsillitis, otitis media and pneumonia) by 16% (incidence rate ratio 0.84 (95% CI 0.74 to 0.96), $p=0.009$).

Conclusions: n-3 LCPUFA supplementation in pregnancy showed protective effects on non-atopic asthma and infections. Protective effects on atopic asthma depended on maternal FADS genotype and n-3 LCPUFA levels. This indicates that the fatty acid pathway is involved in multiple mechanisms affecting the risk of asthma subtypes and infections.

Trial registration number: [NCT00798226](https://www.clinicaltrials.gov/ct2/show/study?term=NCT00798226).

Keywords: asthma; respiratory infection.

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Conflict of interest statement

Competing interests: None declared.

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Publication types, MeSH terms, Substances, Associated dataexpand

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Pediatr Pulmonol

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. 2023 Dec;58(12):3428-3436.

doi: 10.1002/ppul.26667. Epub 2023 Sep 6.

Association of rhinovirus and potentially pathogenic bacterial detections in the first 3 months of life with subsequent wheezing in childhood

[Mari D Takashima](#)¹, [Keith Grimwood](#)^{1,2}, [Peter D Sly](#)^{3,4}, [Stephen B Lambert](#)^{5,6}, [Robert S Ware](#)¹

Affiliations expand

- PMID: 37671813
- DOI: [10.1002/ppul.26667](https://doi.org/10.1002/ppul.26667)

Abstract

Objective: Airway interactions between viruses, especially rhinoviruses, and potentially pathogenic bacteria (PPB; *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*) in early infancy may increase the risk of subsequent wheezing and asthma. We evaluated the association between rhinovirus and PPB in the first 3 months of life and wheezing episodes before age 2 years and asthma at age 5-7 years.

Methods: An Australian community-based birth cohort of healthy children involved parents collecting nasal swabs weekly and completing symptom diaries daily until age 2 years. In a follow-up subset, asthma diagnosis was assessed annually until age 7 years.

Swabs were analyzed by real-time polymerase chain reaction assays. Children were included if they returned symptom diaries beyond age 3 months (wheeze) or were reviewed at age 5-7 years (asthma).

Results: 1440 swabs were returned by 146 children in the first 3 months of life. Wheeze and asthma outcomes were recorded for 146 and 84 children, respectively. Each additional week of rhinovirus detection increased the incidence of wheezing before age 2 years by 1.16 times (95% confidence interval [CI]: 0.99-1.35). There were no significant associations between bacteria and wheeze. Each additional week with H. influenzae increased the odds of asthma at age 5-7 years by 135% (odds ratio: 2.35, 95% CI: 0.99-5.58). No significant interaction was observed between rhinovirus and PPB for wheezing or asthma.

Conclusion: Early life rhinovirus infection was associated with wheezing before age 2 years and H. influenzae with asthma by age 5-7 years. Microbes may play an etiologic role in wheezing and asthma, warranting further study.

Keywords: Rhinovirus; asthma; children; respiratory bacteria; wheeze.

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- [43 references](#)

SUPPLEMENTARY INFO

MeSH terms, Grants and funding[expand](#)

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42

Ann Rheum Dis

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. 2023 Dec;82(12):1580-1586.

doi: 10.1136/ard-2023-224624. Epub 2023 Aug 7.

Benralizumab for eosinophilic granulomatosis with polyangiitis

[Adrien Cottu](#)¹, [Matthieu Groh](#)², [Charlene Desaintjean](#)³, [Sylvain Marchand-Adam](#)⁴, [Loïc Guillevin](#)¹, [Xavier Puechal](#)¹, [Stacy Beaumesnil](#)⁵, [Estibaliz Lazaro](#)⁵, [Maxime Samson](#)⁶, [Camille Taille](#)⁷, [Cécile-Audrey Durel](#)⁸, [Elizabeth Diot](#)⁹, [Sarah Nicolas](#)⁹, [Laurent Guilleminault](#)^{10 11}, [Mikael Ebbo](#)¹², [Pascal Cathebras](#)¹³, [Clairelyne Dupin](#)¹⁴, [Halil Yildiz](#)¹⁵, [Nabil Belfeki](#)¹⁶, [Grégory Pugnet](#)¹⁷, [Pierre Chauvin](#)¹⁸, [Stephane Jouneau](#)¹⁹, [Francois Lifermann](#)²⁰, [Jean-Philippe Martellosio](#)²¹, [Vincent Cottin](#)³, [Benjamin Terrier](#)^{22 23}, [French Vasculitis Study Group](#)

Affiliations expand

- PMID: 37550002
- DOI: [10.1136/ard-2023-224624](https://doi.org/10.1136/ard-2023-224624)

Abstract

Background: Benralizumab is effective in the treatment of eosinophilic asthma and is being investigated for the treatment of other eosinophil-associated diseases. Reports on the use of benralizumab for the treatment of eosinophilic granulomatosis with polyangiitis (EGPA) are limited to case reports and small case series.

Methods: We conducted a multicentre, retrospective study including EGPA patients treated with off-label benralizumab. The primary endpoint was the rate of complete response defined as no disease activity (Birmingham Vasculitis Activity Score=0) and a prednisone dose ≤ 4 mg/day. Partial response was defined as no disease activity and a prednisone dose ≥ 4 mg/day.

Results: Sixty-eight patients were included, including 31 (46%) who had previously received mepolizumab. The use of benralizumab was warranted by uncontrolled asthma in 54 (81%), persistent ear, nose and throat (ENT) manifestations in 27 (40%) and persistent glucocorticoids (GCs) use in 48 (74%) patients. Median (IQR) follow-up after starting benralizumab was 23 (9-34) months. Thirty-three patients (49%) achieved a complete response, 24 (36%) achieved a partial response and 10 (15%) did not respond. Among the 57 patients who initially responded, 10 (18%) eventually required further line treatments. GCs were discontinued in 23 patients (38%). Prior mepolizumab use was associated with a higher rate of primary failure (26.7% vs 5.4%, $p=0.034$) and less frequent GCs discontinuation (14.8% vs 55.9%, $p=0.001$). Vasculitis flares occurred in 7 patients (11%) and were associated with histological evidence of vasculitis and/or antineutrophil cytoplasmic antibodies positivity at benralizumab initiation ($p=0.004$).

Conclusions: Benralizumab appears to be an effective treatment for refractory asthma or ENT manifestations in EGPA and allows GC-sparing. However, its efficacy was lower after prior failure of mepolizumab.

Keywords: Biological Therapy; Glucocorticoids; Systemic vasculitis; Treatment.

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Conflict of interest statement

Competing interests: The authors declare no financial support. MG reports personal fees from GlaxoSmithKline and AstraZeneca outside the submitted work. CT reports personal fees from AstraZeneca, Sanofi, GlaxoSmithKline, Chiesi and Novartis outside the submitted work. CDupin reports personal fees from AstraZeneca and GlaxoSmithKline outside the submitted work. HY reports personal fees from GlaxoSmithKline outside the submitted work. Other authors has nothing to disclose.

- [Cited by 1 article](#)

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS



[Proceed to details](#)

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Thorax

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. 2023 Dec;78(12):1175-1180.

doi: 10.1136/thorax-2022-219757. Epub 2023 Jul 31.

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

[Constantinos Kallis¹](#), [Ekaterina Maslova²](#), [Ann D Morgan¹](#), [Ian Sinha^{3,4}](#), [Graham Roberts^{5,6,7}](#), [Ralf J P van der Valk²](#), [Jennifer K Quint¹](#), [Trung N Tran⁸](#)

Affiliations expand

- PMID: 37524391
- DOI: [10.1136/thorax-2022-219757](https://doi.org/10.1136/thorax-2022-219757)

Free article

Abstract

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

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

Results: Annual asthma incidence rates decreased by 51% from 1403.4 (95% CI 1383.7 to 1423.2) in 2008 to 688.0 (95% CI 676.3 to 699.9) per 10⁵ person-years (PYs) in 2018, with the most pronounced decrease observed in 1–5-year olds (decreasing by 65%, from 2556.9 (95% CI 2509.8 to 2604.7) to 892.3 (95% CI 866.9 to 918.3) per 10⁵ PYs). The corresponding decreases for the 6–11- and 12–17-year-olds were 36% (1139.9 (95% CI 1110.6 to 1169.7) to 739.9 (95% CI 720.5 to 759.8)) and 20% (572.3 (95% CI 550.4 to 594.9) to 459.5 (95% CI 442.9 to 476.4)) per 10⁵ PYs, respectively. The incidence of preschool wheeze decreased over time and was slightly more pronounced in the 1–3 year-olds than in the 4-year-olds. Prevalence of asthma and preschool wheeze also decreased over time, from 18.0% overall

in 2008 to 10.2% in 2018 for asthma. Exacerbation rates increased over time from 1.33 (95% CI 1.31 to 1.35) per 10 PYs in 2008 to 1.81 (95% CI 1.78 to 1.83) per 10 PYs in 2018.

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

Keywords: Asthma Epidemiology; Paediatric asthma.

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Conflict of interest statement

Competing interests: EM is an employee of AstraZeneca and owns stock in AstraZeneca. IS received consultancy from AstraZeneca to their institutions for this work. GR received consultancy from AstraZeneca to their institutions for this work. RJPvdV is an employee of AstraZeneca and owns stock in AstraZeneca and GlaxoSmithKline. JKQ reports grants from AUK-BLF and The Health Foundation; grants and personal fees from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline and Bayer; and grants from Chiesi, outside the submitted work. JKQ's research group received funding from AstraZeneca for this work. TNT is an employee of AstraZeneca and owns stock in AstraZeneca. CK and ADM have nothing to declare.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS



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COPD

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. 2023 Dec;20(1):233-247.

doi: 10.1080/15412555.2023.2229906.

Sex-Specific Genetic Determinants of Asthma-COPD Phenotype and COPD in Middle-Aged and Older Canadian Adults: An Analysis of CLSA Data

[Ugochukwu Odimba](#)¹, [Ambikaipakan Senthilselvan](#)², [Jamie Farrell](#)^{1,3}, [Zhiwei Gao](#)¹

Affiliations expand

- PMID: 37466093
- DOI: [10.1080/15412555.2023.2229906](https://doi.org/10.1080/15412555.2023.2229906)

Abstract

The etiology of sex differences in the risk of asthma-COPD phenotype and COPD is still not completely understood. Genetic and environmental risk factors are commonly believed to play an important role. This study aims to identify sex-specific genetic markers associated with asthma-COPD phenotype and COPD using the Canadian Longitudinal Study on Aging (CLSA) Baseline Comprehensive and Genomic data. There were a total of 1,415 COPD cases. Out of them, 504 asthma-COPD phenotype cases were identified. 20,524 participants without a diagnosis of asthma and COPD served as controls. We performed genome-wide SNP-by-sex interaction analysis. SNPs with an interaction p-value $< 10^{-5}$ were included in a sex-stratified multivariable logistic regression for asthma-COPD phenotype and COPD outcomes. 18 and 28 SNPs had a significant interaction term p-value $< 10^{-5}$ with sex in the regression analyses of asthma-COPD phenotype and COPD outcomes, respectively. Sex-stratified multivariable analysis of asthma-COPD phenotype showed that 7 SNPs in/near SMYD3, FHIT, ZNF608, RIMBP2, ZNF133, BPIFB1, and S100B loci were significant in males. Sex-stratified multivariable analysis of COPD showed that 8 SNPs in/near MAGI1, COX18, OSTC, ELOVL5, C7orf72 FGF14, and NKAIN4 were significant in males, and 4 SNPs in/near genes CAMTA1, SATB2, PDE10A, and LINC00908 were significant in females. An SNP in the ZPBP gene was associated with COPD in both males and females. Identification of sex-specific loci associated with asthma-COPD phenotype and COPD may offer valuable evidence toward a better understanding of the sex-specific differences in the pathophysiology of the diseases.

Keywords: Asthma-COPD phenotype; CLSA; chronic obstructive pulmonary disease; polymorphisms; sex.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grants and fundingexpand

FULL TEXT LINKS



[Proceed to details](#)

Cite

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45

Case Reports

J Asthma

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. 2023 Dec;60(12):2243-2247.

doi: 10.1080/02770903.2023.2233606. Epub 2023 Jul 14.

[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

Affiliations expand

- PMID: 37427873
- DOI: [10.1080/02770903.2023.2233606](https://doi.org/10.1080/02770903.2023.2233606)

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.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS



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Cite

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J Asthma

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. 2023 Dec;60(12):2224-2232.

doi: 10.1080/02770903.2023.2231078. Epub 2023 Jul 10.

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](https://doi.org/10.1080/02770903.2023.2231078)

Abstract

Objective: Adult-onset asthma is a recognized but heterogeneous phenotype and has been described to associate with poor asthma control. Knowledge about associations between clinical characteristics including comorbidities and control of adult-onset asthma is limited, especially in older populations. We aimed to study how clinical biomarkers and comorbidities 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 ($ACT \leq 19$) was significantly associated with a blood neutrophil count $\geq 5/\mu l$, BMI ≥ 30 , and several comorbidities. In multivariable regression analysis, uncontrolled asthma was associated with neutrophils $\geq 5/\mu l$ (OR 2.35; 95% CI 1.11-4.99). In age-stratified analysis, BMI ≥ 30 (OR 3.04; 1.24-7.50), eosinophils

$\geq 0.3/\mu\text{l}$ (OR 3.17; 1.20-8.37), neutrophils $\geq 5/\mu\text{l}$ (OR 4.39; 1.53-12.62) and allergic rhinitis (OR 5.10; 1.59-16.30) were associated with uncontrolled asthma among the middle-aged. Among the older adults, uncontrolled asthma was only associated with comorbidities: chronic rhinitis (OR 4.08; 1.62-10.31), ischemic heart disease (OR 3.59; 1.17-10.98), malignancy (OR 3.10; 1.10-8.73), and depression/anxiety (OR 16.31; 1.82-146.05).

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

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

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS



[Proceed to details](#)

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COPD

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. 2023 Dec;20(1):224-232.

doi: 10.1080/15412555.2023.2228903.

Development of a Diagnostic Nomogram to Predict CAP in Hospitalized Patients with AECOPD

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Affiliations expand

- PMID: 37403800
- DOI: [10.1080/15412555.2023.2228903](https://doi.org/10.1080/15412555.2023.2228903)

Abstract

The purpose of this study was to establish a nomogram for predicting community-acquired pneumonia (CAP) in hospitalized patients with acute exacerbations of chronic obstructive pulmonary disease (AECOPD). The retrospective cohort study included 1249 hospitalized patients with AECOPD between January 2012 and December 2019. The patients were divided into pneumonia-complicating AECOPD (pAECOPD) and non-pneumonic AECOPD (npAECOPD) groups. The least absolute shrinkage and selection operator (LASSO) regression and multivariate logistic regression were utilized to identify prognostic factors. A prognostic nomogram model was established, and the bootstrap method was used for internal validation. Discrimination and calibration of the nomogram model were evaluated by receiver operating characteristic (ROC) curve, calibration curve, and decision curve analysis (DCA). Logistic and LASSO regression analysis showed that C-reactive protein (CRP) > 10 mg/L, albumin (Alb) <40 g/L, alanine transferase (ALT) >50 U/L, fever, bronchiectasis, asthma, previous hospitalization for pAECOPD in the past year (Pre-H for pAECOPD), and age-adjusted Charlson score (aCCI) ≥ 6 were independent predictors of pAECOPD. The area under the ROC curve (AUC) of the nomogram model was 0.712 (95% CI: 0.682-0.741). The corrected AUC of internal validation was 0.700. The model had well-fitted calibration curves and good clinical usability DCA curve. A nomogram model was developed to assist clinicians in predicting the risk of pAECOPD. **China Clinical Trials Registry:** ChiCTR2000039959.

Keywords: Chronic obstructive pulmonary disease; community-acquired pneumonia; exacerbations; logistic regression; predictive model.

SUPPLEMENTARY INFO

MeSH terms, Associated dataexpand

FULL TEXT LINKS



[Proceed to details](#)

Cite

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Review

J Asthma

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. 2023 Dec;60(12):2104-2110.

doi: 10.1080/02770903.2023.2228911. Epub 2023 Jul 2.

An update on asthma diagnosis

[Charis Armeftis](#)¹, [Christina Gratziou](#)², [Nikolaos Siafakas](#)³, [Paraskevi Katsaounou](#)², [Zoi Dorothea Pana](#)⁴, [Petros Bakakos](#)²

Affiliations expand

- PMID: 37358228
- DOI: [10.1080/02770903.2023.2228911](https://doi.org/10.1080/02770903.2023.2228911)

Abstract

Objective: Asthma imposes a significant health and socioeconomic burden with an average prevalence impacting 5-10% of the global population. The aim of this narrative review is to update the current literature on topics related to asthma diagnosis.

Data sources: Original research articles were identified from PubMed using the search terms "asthma diagnosis" and "asthma misdiagnosis".

Study selections: Recently published articles ($n = 51$) detailing the diagnosis, misdiagnosis of asthma, and the updated recommendations of the European and international asthma guidelines.

Results: Emerging evidence revealed that asthma might represent a rather heterogenous clinical entity with varying underlying molecular mechanisms. Attempts have been made to unravel these traits to better provide accurate diagnosis and a more efficient patient-based management approach. The lack of a gold standard test for asthma diagnosis has contributed to its over- and underdiagnosis. This is problematic, given that overdiagnosis

might lead to delay of both diagnosis and prompt treatment of other diseases, while underdiagnosis might substantially impact quality of life due to progression of asthma by increased rate of exacerbations and airway remodeling. In addition to poor asthma control and potential patient harm, asthma misdiagnosis is also associated with excessive costs. As a result, current international guidelines emphasize the need for a standardized approach to diagnosis, including objective measurements prior to treatment.

Conclusion: Future research is warranted to define the optimal diagnostic and treatable traits approach especially for patients with severe asthma, as they may benefit from the advent of newly targeted asthma management.

Keywords: Lancet Commission; Misdiagnosis; endotype; guidelines; overdiagnosis; phenotype; treatable trait; underdiagnosis.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS



[Proceed to details](#)

Cite

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J Asthma

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. 2023 Dec;60(12):2121-2129.

doi: 10.1080/02770903.2023.2220795. Epub 2023 Jun 20.

Based on what parameters is safe to discontinue inhaled corticosteroids in children with asthma?

[Iva Mihatov Štefanović](#)^{1,2}, [Renata Vrsalović](#)¹

Affiliations expand

- PMID: 37262011
- DOI: [10.1080/02770903.2023.2220795](https://doi.org/10.1080/02770903.2023.2220795)

Abstract

Objective: Remission of childhood asthma has not been widely studied. Patients in clinical remission continue to have some degree of bronchial hyperresponsiveness (BHR). The aim of this study was to investigate whether clinical parameters and lung function test are good parameters for discontinuation of inhaled corticosteroids (ICS) in asthmatic children, including patients with persistent BHR, as measured by the methacholine challenge test (MCT).

Methods: One year after discontinuation of inhaled corticosteroids (ICS), MCT was performed in a group of 40 asthmatic children to confirm or exclude BHR. In all patients, ICS treatment was discontinued based on the same parameters: symptoms, spirometry, daily PEF, and negative bronchodilator test. After achieving complete asthma control for at least 6 to 12 months, ICS treatment was stepped down and discontinued. Clinical course and spirometry were followed up after ICS discontinuation.

Results: Positive MCT was found in 50% of the patients. There was no statistically significant difference between the positive and negative MCT groups in age at initiation and discontinuation of ICS therapy, duration of ICS therapy, duration of stepping down period, FEV1, and PEF at the time of withdrawal of ICS and one year later. ICS treatment had to be restarted in two patients from the positive MCT group, due to recurrence of asthma symptoms.

Conclusion: Clinical parameters, normal spirometry, daily PEF values, and a negative bronchodilator test are good parameters for discontinuing ICS treatment in asthmatic children, even in patients with persistent BHR. Children should continue to be monitored, as symptoms may recur.

Keywords: Airway hyperresponsiveness; bronchial provocation test; childhood asthma; control, guidelines, inhaled corticosteroids.

SUPPLEMENTARY INFO

MeSH terms, Substances expand

FULL TEXT LINKS

[Proceed to details](#)

Cite

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Thorax

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. 2023 Dec;78(12):1223-1232.

doi: 10.1136/thorax-2022-219634. Epub 2023 May 19.

[Risk factors for poorer respiratory outcomes in adolescents and young adults born preterm](#)

[Elizabeth F Smith](#)^{1,2}, [Naomi R Hemy](#)¹, [Graham L Hall](#)^{1,2}, [Andrew C Wilson](#)^{1,2,3}, [Conor P Murray](#)⁴, [Shannon J Simpson](#)^{5,2}

Affiliations expand

- PMID: 37208189
- DOI: [10.1136/thorax-2022-219634](https://doi.org/10.1136/thorax-2022-219634)

Free article

Abstract

Rationale: The respiratory outcomes for adult survivors of preterm birth in the postsurfactant era are wide-ranging with prognostic factors, especially those encountered after the neonatal period, poorly understood.

Objectives: To obtain comprehensive 'peak' lung health data from survivors of very preterm birth and identify neonatal and life-course risk factors for poorer respiratory outcomes in adulthood.

Methods: 127 participants born ≤ 32 weeks gestation (64%, n=81 with bronchopulmonary dysplasia (BPD), initially recruited according to a 2 with-BPD:1 without-BPD strategy), and 41 term-born controls completed a lung health assessment at 16-23 years, including lung function, imaging and symptom review. Risk factors assessed against poor lung health included neonatal treatments, respiratory hospitalisation in childhood, atopy and tobacco smoke exposure.

Measurements and main results: Young adults born prematurely had greater airflow obstruction, gas trapping and ventilation inhomogeneity, in addition to abnormalities in gas transfer and respiratory mechanics, compared with term. Beyond lung function, we observed greater structural abnormalities, respiratory symptoms and inhaled medication use. A previous respiratory admission was associated with airway obstruction; mean forced expiratory volume in 1 s/forced vital capacity z-score was -0.561 lower after neonatal confounders were accounted for (95% CI -0.998 to -0.125; $p=0.012$). Similarly, respiratory symptom burden was increased in the preterm group with a respiratory admission, as was peribronchial thickening (6% vs 23%, $p=0.010$) and bronchodilator responsiveness (17% vs 35%, $p=0.025$). Atopy, maternal asthma and tobacco smoke exposure did not influence lung function or structure at 16-23 years in our preterm cohort.

Conclusions: Even after accounting for the neonatal course, a respiratory admission during childhood remained significantly associated with reduced peak lung function in the preterm-born cohort, with the largest difference seen in those with BPD. A respiratory admission during childhood should, therefore, be considered a risk factor for long-term respiratory morbidity in those born preterm, especially for individuals with BPD.

Keywords: Imaging/CT MRI etc; Lung Physiology; Paediatric Lung Disease.

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Conflict of interest statement

Competing interests: None declared.

SUPPLEMENTARY INFO

MeSH terms, Substances expand

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COPD

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. 2023 Dec;20(1):101-108.

doi: 10.1080/15412555.2022.2162377. Epub 2023 Jan 19.

Association between Galectin-13 Expression and Eosinophilic Airway Inflammation in Chronic Obstructive Pulmonary Disease

[Lingling Yi](#)^{1,2}, [Yuchen Feng](#)^{1,2}, [Dian Chen](#)^{1,2}, [Yanling Jin](#)³, [Shuchen Zhang](#)⁴

Affiliations expand

- PMID: 36656660
- DOI: [10.1080/15412555.2022.2162377](https://doi.org/10.1080/15412555.2022.2162377)

Abstract

Chronic obstructive pulmonary disease (COPD) and asthma are chronic inflammatory diseases of the airways. Galectin-13 has recently been forwarded as a biomarker for airway eosinophilic inflammation in asthma. However, the association between galectin-13 and COPD remains unknown. To examine the changes in galectin-13 expression in acute exacerbations of COPD (AECOPD) and the stable phase of COPD and unveil the association between galectin-13 expression and eosinophilic inflammation in COPD, we measured plasma galectin-13 expression in different phases of COPD patients ($n = 60$, 44 AECOPD patients, and 16 stable COPD patients) and healthy controls ($n = 15$). Plasma levels of galectin-13 in 60 COPD patients were further analyzed and compared to systemic inflammation, airway eosinophilic inflammation, and lung function. The plasma galectin-13 level was markedly increased in subjects with AECOPD compared to stable COPD patients and healthy controls. Plasma galectin-13 levels in COPD subjects were positively correlated with serum CRP ($r_s = 0.46$, $p = 0.0003$), peripheral blood eosinophilia count ($r_s = 0.57$, $p < 0.0001$), and FeNO ($r_s = 0.46$, $p = 0.0002$). In addition, the level of galectin-13 was

negatively correlated with FEV₁ ($r_s = -0.43$, $p = 0.0001$), FEV₁ pred (%) ($r_s = -0.544$, $p < 0.0001$), as well as FEV₁/FVC ($r_s = -0.46$, $p < 0.0001$). Multiple linear regression analysis suggested that plasma galectin-13 levels were affected by FEV₁ pred (%), peripheral blood eosinophilia count, and FeNO. We concluded that galectin-13 levels were increased in COPD patients, and elevated galectin-13 expressions related to airway eosinophilic inflammation. Galectin-13 may facilitate the identification of COPD endotypes and may become a potential therapeutic target.

Keywords: CRP; chronic obstructive pulmonary disease; eosinophilic inflammation; galectin-13.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS



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Cite

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Review

Phys Sportsmed

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. 2023 Dec;51(6):549-557.

doi: 10.1080/00913847.2022.2148137. Epub 2022 Nov 27.

[Exercise-induced bronchoconstriction in elite athletes: a narrative review](#)

[Tianchang He](#)¹, [Tienan Song](#)¹

Affiliations expand

- PMID: 36373406

- DOI: [10.1080/00913847.2022.2148137](https://doi.org/10.1080/00913847.2022.2148137)

Abstract

Exercise-induced bronchoconstriction (EIB) is the most common chronic disease among elite athletes and when left untreated, can impact both respiratory health and sports performance. In recent years, there has been an increase in the awareness and detection of EIB in elite athletes. This narrative review aims to evaluate the risk, prevention, diagnosis, medication, and anti-doping policies of EIB in elite athletes, and to provide more references for athletes with EIB. The results showed that athletes of endurance, winter, and water sports generally have a higher prevalence of EIB than athletes of other sports. Adaptive warm-up before formal exercise and using heat exchange masks at low temperatures are effective ways for athletes to prevent EIB. For physicians, the exercise challenge test and eucapnic voluntary hyperpnea are the recommended diagnostic methods for EIB in athletes. The treatment of athletes with EIB is medication-based, such as inhaled corticosteroids and beta-2 agonists, but current anti-doping policies should be considered when used.

Keywords: EIB; anti-doping policy; diagnosis; elite athletes; medication; prevention; risk.

- [Cited by 1 article](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms [expand](#)

FULL TEXT LINKS



[Proceed to details](#)

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Int Arch Allergy Immunol

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. 2023 Nov 30:1-7.

doi: 10.1159/000534902. Online ahead of print.

Effectiveness of Mepolizumab in Patients with Severe Eosinophilic Asthma with/without Nasal Polyposis: A Real-Life Study

[Francisco Javier Bravo-Gutiérrez¹](#), [Juan Carlos Miralles-López²](#), [José Valverde-Molina³](#), [María Loreto Alemany Francés⁴](#), [Rubén Andújar-Espinosa⁵](#), [Manuel Castilla-Martínez⁶](#), [María Jesús Avilés-Inglés⁷](#), [Ana Mora-González⁸](#), [Manuel José Pajarón-Fernández⁹](#), [Sheila Cabrejos-Perotti¹⁰](#), [José Meseguer-Arce¹¹](#), [Isabel Flores Martín¹²](#), [Virginia Pérez-Fernández¹³](#), [RE-ASGRAMUR Group](#)

Affiliations expand

- PMID: 38035559
- DOI: [10.1159/000534902](https://doi.org/10.1159/000534902)

Abstract

Introduction: Asthma is one of the most common chronic diseases and affects around 334 million people worldwide. The estimated prevalence of severe asthma is 3-10% of the asthmatic population. Mepolizumab has demonstrated efficacy in reducing exacerbations, oral corticosteroid use, and improving quality of life, asthma control, and lung function in patients with severe eosinophilic asthma (SEA). Our study aimed to check the response to mepolizumab in a series of severe asthma patients regarding exacerbations, oral corticosteroid use, asthma control, quality of life, and lung function and to compare the response between patients with and without nasal polyps.

Method: This is a retrospective, multicenter study of RE-ASGRAMUR (Register of Severe Asthma of the Region of Murcia) performed in eight hospitals of the Region of Murcia (Spain) under routine clinical practice conditions. We included patients diagnosed with SEA who completed at least 1 year of treatment with mepolizumab. We analyzed clinical characteristics, drug tolerance, and effectiveness: exacerbations, ACT, miniAQLQ, forced expiratory volume in 1 s (FEV1), and use of oral corticosteroids. We also compared the results between patients with and without nasal polyps.

Results: The median of exacerbations before treatment was 3 and decreased to 0 after treatment (mean decrease of 77.4%). The median diary oral prednisone intake was 15 mg before treatment and 5 mg after treatment (mean 56% reduction). We have obtained a significant improvement in other variables: ED visits and hospitalizations, asthma control (ACT), quality of life (miniAQLQ), and lung function (FEV1). Thirty-four out of 70 patients (48.57%) fulfilled the criteria of super-responder, and 17 out of 70 (24.29%) had a complete response. More patients in the group with nasal polyps fulfilled the criteria of super-responder and complete response to mepolizumab.

Conclusions: Mepolizumab is a safe and effective treatment for SEA patients, improving exacerbations, oral corticosteroid intake, asthma control, quality of life, and lung function. In patients with associated nasal polyposis, there is a statistically significant higher proportion of super-responders and complete responders.

Keywords: Effectiveness; Mepolizumab; Nasal polyps; Severe eosinophilic asthma; Super-responders.

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Publication typesexpand

FULL TEXT LINKS



[Proceed to details](#)

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[Review](#)

Adv Drug Deliv Rev

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. 2023 Nov 29:115146.

doi: 10.1016/j.addr.2023.115146. Online ahead of print.

Long-acting inhaled medicines: Present and future

[Chengqian Zhang](#)¹, [Davide D'Angelo](#)², [Francesca Buttini](#)³, [Mingshi Yang](#)⁴

Affiliations expand

- PMID: 38040120
- DOI: [10.1016/j.addr.2023.115146](https://doi.org/10.1016/j.addr.2023.115146)

Abstract

Inhaled medicines continue to be an essential part of treatment for respiratory diseases such as asthma, chronic obstructive pulmonary disease, and cystic fibrosis. In addition, inhalation technology, which is an active area of research and innovation to deliver medications via the lung to the bloodstream, offers potential advantages such as rapid onset of action, enhanced bioavailability, and reduced side effects for local treatments. Certain inhaled macromolecules and particles can also end up in different organs via lymphatic transport from the respiratory epithelium. While the majority of research on inhaled medicines is focused on the delivery technology, particle engineering, combination therapies, innovations in inhaler devices, and digital health technologies, researchers are also exploring new pharmaceutical technologies and strategies to prolong the duration of action of inhaled drugs. This is because, in contrast to most inhaled medicines that exert a rapid onset and short duration of action, long-acting inhaled medicines (LAIM) improve not only improve patient compliance by reducing the dosing frequency, but also the effectiveness and convenience of inhaled therapies to better manage patients' conditions. This paper reviews the advances in LAIM, the pharmaceutical technologies and strategies for developing LAIM, and emerging new inhaled modalities that possess a long-acting nature and potential in the treatment and prevention of various diseases. The challenges in the development of the future LAIM are also discussed where active research and innovations are taking place.

Keywords: Inhaled medicines; Long-acting effects; New inhaled modalities; Pulmonary drug delivery.

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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 typesexpand

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J Allergy Clin Immunol Pract

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. 2023 Nov 29:S2213-2198(23)01306-5.

doi: 10.1016/j.jaip.2023.11.037. Online ahead of print.

Effectiveness of a Maintenance and Reliever Digihaler System in Asthma: 24-week Randomized Study (CONNECT2)

[Giselle S Mosnaim](#)¹, [Flavia C L Hoyte](#)², [Guilherme Safioti](#)³, [Randall Brown](#)⁴, [Tanisha Hill](#)⁵, [Thomas Li](#)⁶, [Katja Sagalovich](#)⁷, [Michael DePietro](#)⁸, [Michael E Wechsler](#)⁹

Affiliations expand

- PMID: 38040117
- DOI: [10.1016/j.jaip.2023.11.037](https://doi.org/10.1016/j.jaip.2023.11.037)

Abstract

Background: Digital health tools have been shown to help address challenges in asthma control, including inhaler technique, treatment adherence and short-acting beta₂-agonist overuse. The maintenance and reliever Digihaler System (DS) comprises two Digihaler inhalers (fluticasone propionate/salmeterol and albuterol) with an associated patient App and web-based Dashboard. Clinicians can review patients' inhaler use and Digihaler inhalation parameter data to support clinical decision-making.

Objective: CONNECT2 evaluated asthma control in participants using the DS versus standard-of-care (SoC) maintenance and reliever inhalers.

Methods: Participants (≥13 years) with uncontrolled asthma (Asthma Control Test [ACT] score <19) were randomized 4:3 (open-label) to the DS (n = 210) or SoC (n = 181) for 24 weeks. The primary endpoint was the proportion of patients achieving well-controlled asthma (i.e., an ACT score ≥20 or increase from baseline of ≥3 units at Week 24).

Results: There was an 88.7% probability that participants using the DS would have greater odds of achieving improvement in asthma control compared with SoC after 24 weeks. Mean odds ratio (95% credible interval) for DS versus SoC was 1.35 (0.846-2.038), indicating a 35% higher odds of improved asthma control with the DS. The DS group had more clinician-participant interactions versus SoC, mainly addressing poor inhaler technique. DS participants' maintenance treatment adherence was good (Month 1: 79.2%; Month 6: 68.6%); reliever use decreased by 38.2% versus baseline. App and Dashboard usability were rated 'good'.

Conclusion: The positive results in asthma control in this study after 24 weeks demonstrate the effectiveness of the DS in asthma management.

Keywords: Adherence; SABA usage; asthma; asthma control; digital inhaler system; effectiveness; randomized.

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. 2023 Nov 29;62(5):2302009.

doi: 10.1183/13993003.02009-2023. Print 2023 Nov.

An attack of asthma is not an attack of the heart: clarifying causal links between asthma and incident coronary heart disease

[Caitlin Morgan](#)^{1,2}, [Daniel Higbee](#)^{3,2}

Affiliations expand

- PMID: 38035696
- DOI: [10.1183/13993003.02009-2023](https://doi.org/10.1183/13993003.02009-2023)

No abstract available

Conflict of interest statement

Conflict of interest: The authors have no potential conflicts of interest to disclose.

Comment on

- [Asthma and incident coronary heart disease: an observational and Mendelian randomisation study.](#)
Valencia-Hernández CA, Del Greco M F, Sundaram V, Portas L, Minelli C, Bloom CI. Eur Respir J. 2023 Nov 29;62(5):2301788. doi: 10.1183/13993003.01788-2023. Print 2023 Nov. PMID: 37945032

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Review

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. 2023 Nov 29;12(4):22799036231205870.

doi: 10.1177/22799036231205870. eCollection 2023 Oct.

[The impact of the air pollution on health in New York City](#)

[Eugene S Mananga](#)^{1,2,3}, [Erika Lopez](#)², [Aissata Diop](#)², [Paulin Jt Dongomale](#)⁴, [Fambougouri Diane](#)²

Affiliations expand

- PMID: 38034845
- PMCID: [PMC10687960](#)
- DOI: [10.1177/22799036231205870](#)

Abstract

New York City is attempting to find a solution to an issue that many states and cities face: how to minimize air pollution so that it has fewer negative impacts on human health. Despite having the highest population in the United States (US), New York City typically has reasonably clean air. As the City and State of New York have worked to reduce emissions from local and regional sources, the air quality in New York City has improved during the past few decades. Despite these advancements, air pollution still poses a severe hazard to the health of everyone living in New York's environment. Various diseases including respiratory, circulatory, neurological, gastrointestinal, and urinary illnesses, which can be fatal, are intimately associated with air pollution. This review article will concentrate on how air pollution affects respiratory diseases such as asthma in children. In addition to analyzing the severe effects of air pollution on the vulnerable population, this review article will highlight the health repercussions of air pollution on New York City and its residents. furthermore, we argue for potential ideas and discoveries while also putting up a policy option to lower air pollution.

Keywords: Health impacts; New York City; air pollution; asthma case; respiratory diseases; vulnerable population.

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Conflict of interest statement

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Allergy

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. 2023 Nov 29.

doi: 10.1111/all.15958. Online ahead of print.

Longitudinal asthma phenotypes by multi-trajectory analysis

[Duong Duc Pham](#)¹, [Chaelin Hong](#)², [Ji-Hyang Lee](#)¹, [Hyouk-Soo Kwon](#)¹, [Woo-Jung Song](#)¹, [You Sook Cho](#)¹, [Ji Seon Oh](#)², [Tae-Bum Kim](#)¹

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- PMID: 38031506
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- [5 references](#)

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. 2023 Nov 29.

doi: 10.4046/trd.2023.0103. Online ahead of print.

Tailored Biologics Selection in Severe Asthma

[Sang Hyuk Kim](#)¹, [Youlim Kim](#)²

Affiliations expand

- PMID: 38018037
- DOI: [10.4046/trd.2023.0103](https://doi.org/10.4046/trd.2023.0103)

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Abstract

The management of severe asthma presents a significant challenge in asthma treatment. Over the past few decades, remarkable progress has been made in developing new treatments for asthma, primarily in the form of biological agents. These advances have been made possible through a deeper understanding of the underlying pathogenesis of asthma. Most biological agents focus on targeting specific inflammatory pathways known as type 2 inflammation. However, recent developments have introduced a new agent targeting upstream alarmin signaling pathways. This opens up new possibilities, and it is anticipated that additional therapeutic agents targeting various pathways will be developed in the future. Despite this recent progress, the mainstay of asthma treatment has long been inhalers. As a result, the guidelines for the appropriate use of biological agents are not yet firmly established. In this review, we aim to emphasize the current state of biological therapy for severe asthma and provide insights into its future prospects.

Keywords: Asthma; Biological Products; Lung Disease, Obstructive.

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Eur Respir J



. 2023 Nov 29;62(5):2301788.

doi: 10.1183/13993003.01788-2023. Print 2023 Nov.

Asthma and incident coronary heart disease: an observational and Mendelian randomisation study

[Carlos A Valencia-Hernández](#)¹, [Fabiola Del Greco M](#)², [Varun Sundaram](#)³, [Laura Portas](#)^{1,4}, [Cosetta Minelli](#)¹, [Chloe I Bloom](#)⁵

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- PMID: 37945032
- DOI: [10.1183/13993003.01788-2023](https://doi.org/10.1183/13993003.01788-2023)

Free article

Abstract

Background: Observational studies suggest asthma is a risk factor for coronary heart disease (CHD) and sex modifies the risk, but they may suffer from methodological limitations. To overcome these, we applied a "triangulation approach", where different methodologies, with different potential biases, were leveraged to enhance confidence in findings.

Methods: First, we conducted an observational study using UK medical records to match asthma patients 1:1, by age, sex and general practitioner (GP) practice, to the general population. We measured the association between asthma and incident CHD (myocardial infarction: hospitalisation/death) by applying minimal sufficient adjustment: model 1, smoking, body mass index, oral corticosteroids, atopy and deprivation; model 2, additionally adjusting for healthcare behaviour (GP consultation frequency). Second, we conducted a Mendelian randomisation (MR) study using data from the UK Biobank, Trans-

National Asthma Genetic Consortium (TAGC) and Coronary Artery Disease Genome-wide Replication and Meta-analysis consortium (CARDIoGRAM). Using 64 asthma single nucleotide polymorphisms, the effect of asthma on CHD was estimated with inverse variance-weighted meta-analysis and methods that adjust for pleiotropy.

Results: In our observational study (n=1 522 910), we found asthma was associated with 6% increased risk of CHD (model 1: HR 1.06, 95% CI 1.01-1.13); after accounting for healthcare behaviour, we found no association (model 2: HR 0.99, 95% CI 0.94-1.05). Asthma severity did not modify the association, but sex did (females: HR 1.11, 95% CI 1.01-1.21; males: HR 0.91, 95% CI 0.84-0.98). Our MR study (n=589 875) found no association between asthma and CHD (OR 1.01, 95% CI 0.98-1.04) and no modification by sex.

Conclusions: Our findings suggest that asthma is not a risk factor for CHD. Previous studies may have suffered from detection bias or residual confounding.

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Conflict of interest statement

Conflict of interest: C.A. Valencia-Hernández, F. Del Greco M, L. Portas, V. Sundaram and C. Minelli have no conflicts of interest to disclose. C.I. Bloom reports awards and grants from the National Institute for Health and Care Research and Asthma + Lung UK, outside the submitted work.

Comment in

- [An attack of asthma is not an attack of the heart: clarifying causal links between asthma and incident coronary heart disease.](#)
Morgan C, Higbee D. *Eur Respir J*. 2023 Nov 29;62(5):2302009. doi: 10.1183/13993003.02009-2023. Print 2023 Nov. PMID: 38035696 No abstract available.

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. 2023 Nov 28:102272.

doi: 10.1016/j.pupt.2023.102272. Online ahead of print.

Improvement of asthma control in adult patients using extrafine inhaled beclomethasone/formoterol fixed combination as maintenance therapy as well as maintenance and reliever therapy – control study

[Tomasz Dębowski](#)¹, [Monika Marko](#)², [Barbara Rogala](#)³, [Paweł Majak](#)⁴, [Rafał Pawliczak](#)⁵

Affiliations expand

- PMID: 38036258
- DOI: [10.1016/j.pupt.2023.102272](https://doi.org/10.1016/j.pupt.2023.102272)

Abstract

Introduction: Extrafine formulation of beclomethasone/formoterol fixed combination (BDP/F pMDI HFA) is approved for both fixed maintenance and maintenance and reliever therapy (MART) of asthma, and recent data has proven that BDP/F pMDI HFA maintenance and reliever therapy is an effective alternative to other regimens.

Objective: This study aimed to assess the level of asthma control in a real-life setting in adult patients using extrafine BDP/F pMDI HFA fixed combination in a pressurized metered-dose inhaler (pMDI) as fixed maintenance dosing as well as maintenance and maintenance and reliever therapy. Additionally, we examined patients' satisfaction with the inhaler device and compliance with therapy as essential factors determining asthma control.

Methods: This multicenter prospective non-interventional observational study lasted 4 months with 3 patient visits. We used the Asthma Control Questionnaire 7 (ACQ-7) to evaluate the degree of asthma control and Morisky Medication Adherence Scale (MMAS-4)

to assess compliance. A self-developed questionnaire was used to assess satisfaction with the inhaler device.

Results: 2179 patients using BDP/F pMDI HFA fixed combination as maintenance and reliever therapy or BDP/F pMDI HFA as maintenance therapy and SABA (short-acting beta₂-agonist) as a reliever for at least 2 months were included. During the prospective follow-up, we observed an upward trend in the FEV1% (forced expiratory volume in 1 s) predicted values, improvement in the control of symptoms as indicated by a decline in the mean ACQ-7 score was noted (1.62 at Visit 1 vs. 1.21 at Visit 2 vs. 0.94 at Visit 3, $p < 0.001$) and increase in patients' compliance (the number of patients that reported forgetting at times to take their medication was reduced from 49.7 % to 27.1 %, $p < 0.001$). At the same time, we noted a reduction in the number of as-needed doses used for symptom relief ($p < 0.001$). Most patients were satisfied with the pMDI, considered it easy and convenient to use, and preferred it to a dry powder inhaler ($p < 0.001$).

Conclusions: The use of extrafine BDP/F pMDI HFA as maintenance as well as reliever therapy seems to be associated with increased asthma control and better compliance to therapy.

Keywords: Asthma control; Compliance; Extrafine beclomethasone/formoterol; pMDI.

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Conflict of interest statement

Declaration of competing interest Tomasz Dębowski is an employee of Chiesi Poland sp. z o.o. Monika Marko declared no competing interest. Barbara Rogala declared no competing interest. Paweł Majak declared no competing interest. Rafał Pawliczak received travel grants and lecture honoraria from Chiesi Poland sp. z o.o. This work was supported by a grant from Chiesi Polska sp. z o.o.

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J Allergy Clin Immunol Pract

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. 2023 Nov 28:S2213-2198(23)01305-3.

doi: 10.1016/j.jaip.2023.11.036. Online ahead of print.

Associations of Breathing Pattern Disorder and Nijmegen Score with Clinical Outcomes in Difficult-to-treat Asthma

[Anna Freeman](#)¹, [Steevo Abraham](#)², [Latha Kadalayil](#)², [Judit Varkonyi-Sepp](#) CPsychol³, [Ben Ainsworth](#)⁴, [J J Hudson-Colby](#)⁵, [Clair Barber](#)⁶, [Paddy Dennison](#)⁷, [Adnan Azim](#)⁶, [Heena Mistry](#)⁶, [Peter Howarth](#)⁶, [Ratko Djukanovic](#)⁶, [Hongmei Zhang](#)⁸, [S Hasan Arshad](#)⁹, [Hans Michael Haitchi](#)¹⁰, [Ramesh J Kurukulaaratchy](#)¹¹

Affiliations expand

- PMID: 38036249
- DOI: [10.1016/j.jaip.2023.11.036](https://doi.org/10.1016/j.jaip.2023.11.036)

Abstract

Background: Breathing pattern disorder (BPD) reflects altered biomechanical patterns of breathing that drive breathing difficulty and commonly accompanies difficult-to-treat asthma. Diagnosis of BPD has no gold standard, but Nijmegen Questionnaire (NQ) >23 is commonly used.

Objectives: We sought to advance clinical characterisation of BPD and better understand clinical utility of NQ in difficult asthma, in patients from the Wessex AsThma CoHort of difficult asthma (WATCH) study.

Methods: Association between demographic and clinical factors in difficult asthma and BPD, ascertained by clinical diagnosis (yes/no, n=476), by NQ scores (≤ 23 : normal (no suggestion of BPD) and >23 : abnormal (suggested BPD), n=372, as well as the continuous raw NQ scores) were assessed in univariate models to identify significant risk factors associated with the three BPD outcomes. For the clinician-diagnosed and NQ-based BPD, associations of continuous factors were assessed using independent samples t-test or Mann-Whitney U test as appropriate for the data distribution or by Spearman correlation

test. Dichotomous associations were evaluated using chi-squared tests. Multivariable logistic (dichotomous outcomes) and linear regression models (continuous outcomes) were developed to identify predictive factors associated with clinician-diagnosed and NQ-based BPD, dichotomous and continuous. Patients with data on NQ scores were grouped into NQ quartiles (low, moderate, high, and very high). The patterns of association of the quartiles with four health-related questionnaire outcomes were assessed using linear regression analyses.

Results: Multivariable regression identified that clinically diagnosed BPD was associated with female sex (OR 1.85; 95% CI 1.07, 3.20), comorbidities (rhinitis (OR 2.46; 95% CI 1.45, 4.17), GORD (OR 2.77; 95% CI 1.58, 4.84), ILO (OR 4.37; 95% CI 2.01, 9.50) and any psychological co-morbidity (OR 1.86; 95% CI 1.13, 3.07)) and healthcare usage (exacerbations (OR 1.07; 95% CI 1.003, 1.14) and previous ICU admissions (OR 2.03; 95% CI 1.18, 3.47)). Abnormal NQ-based BPD diagnosis was associated with history of eczema (OR 1.83; 95% CI 1.07, 3.14), GORD (OR 1.94; 95% CI 1.15, 3.27) or any psychological comorbidity (OR 4.29; 95% CI 2.64, 6.95) at multivariable regression. Differences between clinical and NQ-based BPD traits were also found with 42% discordance in BPD-state between these definitions. Multivariable linear regression analysis with NQ as a continuous outcome showed positive association with worse asthma outcomes (admission to ICU, $p=0.037$), different phenotypic traits (female sex $p=0.001$, ever smoker, $p=0.025$) and greater multimorbidity (GORD, $p=0.002$, sleep apnoea, $p=0.040$, any psychological comorbidity, $p<0.0001$).

Conclusion: BPD is associated with worse health outcomes and negative health impacts in difficult asthma within a multimorbidity disease model. It therefore merits better recognition and prompt treatment. Clinical diagnosis and NQ offer different perspectives on BPD, so this goal may be best addressed by considering clinical features alongside magnitude of NQ.

Keywords: Breathing-pattern-disorder (BPD); Nijmegen questionnaire (NQ); difficult asthma; multimorbidity; treatable trait.

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[A mobile health intervention for improving the technique of inhaled medications among children with asthma: A pilot study](#)

[Mary Jane Smith](#)^{1,2}, [Zhiwei Gao](#)¹, [Roger Chafe](#)¹, [Meshari Alwashmi](#)³

Affiliations expand

- PMID: 38033513
- PMCID: [PMC10685774](#)
- DOI: [10.1177/20552076231216589](#)

Abstract

Objective: BreatheSuite MDI is a Bluetooth-enabled inhaler attachment and mobile application which aims to improve asthma control. The objective was to compare pressurized metered dose inhaler (pMDI) technique and asthma control test (ACT) scores pre- and post-use of the device and mobile application. Secondary objectives were to assess user satisfaction and therapy adherence.

Methods: Patients between the ages of 8 and 18 were recruited from several pediatric asthma clinics. Technique and ACT scores were assessed at baseline. Users were given no prompts on technique during the first month of device use. For the subsequent three months, users were given technique scores through the mobile application after each inhaler use and provided weekly performance summaries. At the end of the study, technique and ACT scores were analyzed and an exit survey was completed. Conditional logistic regression was used to examine the association between well-controlled asthma (ACT score > 19) and the intervention.

Results: 24 patients completed the study. Technique scores improved following the use of BreatheSuite (44.19 vs. 62.54; $P = 0.01$). Well-controlled asthma did not significantly improve (OR = 1.20 [0.4-3.9], $P = 0.76$). 87% of study subjects agreed or strongly agreed that their asthma control improved while using BreatheSuite; 79% were satisfied with the device and mobile application; and 91% preferred using the device compared to a standard logbook to track inhaler usage.

Conclusions: In this pilot study, the use of BreatheSuite device was associated with improved technique scores. These results need to be confirmed by a randomized controlled trial. There was high user satisfaction with the BreatheSuite device.

Keywords: Canada; Mobile health; asthma; intervention; patient satisfaction; pediatric care.

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Conflict of interest statement

MA was a full-time employee at BreatheSuite, Inc. during the study. MA was not involved in data analysis. BreatheSuite MDI devices were purchased directly from BreatheSuite Inc. for the purpose of this study. The company had no other involvement with the study. None of the other authors report any potential conflicts of interest.

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

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Am J Respir Crit Care Med

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. 2023 Nov 28.

doi: 10.1164/rccm.202305-0808OC. Online ahead of print.

Association Between T2-related Comorbidities and Effectiveness of Biologics in Severe Asthma

[Michael E Wechsler](#)¹, [Ghislaine Scelo](#)^{2,3}, [Désirée E S Larenas-Linnemann](#)⁴, [Carlos A Torres-Duque](#)^{5,6}, [Jorge Maspero](#)⁷, [Trung N Tran](#)⁸, [Ruth B Murray](#)³, [Neil Martin](#)^{9,10}, [Andrew N Menzies-Gow](#)^{11,12}, [Mark Hew](#)^{13,14}, [Matthew J Peters](#)¹⁵, [Peter G Gibson](#)^{16,17}, [George C Christoff](#)¹⁸, [Todor A Popov](#)¹⁹, [Andréanne Côté](#)²⁰, [Celine Bergeron](#)^{21,22}, [Delbert Dorscheid](#)²³, [J Mark FitzGerald](#)²⁴, [Kenneth R Chapman](#)²⁵, [Louis Philippe Boulet](#)²⁶, [Mohit Bhutani](#)²⁷, [Mohsen Sadatsafavi](#)²⁸, [Libardo Jiménez-Maldonado](#)²⁹, [Mauricio Duran-Silva](#)³⁰, [Bellanid Rodriguez](#)³¹, [Carlos Andres Celis-Preciado](#)^{32,33}, [Diana Jimena Cano-Rosales](#)³¹, [Ivan Solarte](#)^{32,34}, [Maria Jose Fernandez-Sanchez](#)^{32,33}, [Patricia Parada-Tovar](#)³⁵, [Anna von Bülow](#)³⁶, [Anne Sofie Bjerrum](#)³⁷, [Charlotte S Ulrik](#)³⁸, [Karin Dahl Assing](#)³⁹, [Linda Makowska Rasmussen](#)⁴⁰, [Susanne Hansen](#)^{41,42}, [Alan Altraja](#)⁴³, [Arnaud Bourdin](#)⁴⁴, [Camille Taille](#)⁴⁵, [Jeremy Charriot](#)⁴⁶, [Nicolas Roche](#)⁴⁷, [Andriana I Papaioannou](#)⁴⁸, [Konstantinos Kostikas](#)⁴⁹, [Nikolaos G Papadopoulos](#)^{50,51}, [Sundeep Salvi](#)⁵², [Deirdre Long](#)⁵³, [Patrick D Mitchell](#)⁵⁴, [Richard Costello](#)⁵⁵, [Concetta Sirena](#)⁵⁶, [Cristina Cardini](#)⁵⁷, [Enrico Heffler](#)^{58,59}, [Francesca Puggioni](#)⁵⁸, [Giorgio Walter Canonica](#)^{60,61}, [Giuseppe Guida](#)⁶², [Takashi Iwanaga](#)⁶³, [Mona Al-Ahmad](#)⁶⁴, [Ulises García](#)⁶⁵, [Piotr Kuna](#)⁶⁶, [João A Fonseca](#)⁶⁷, [Riyad Al-Lehebi](#)^{68,69}, [Mariko S Koh](#)⁷⁰, [Chin Kook Rhee](#)⁷¹, [Borja G Cosio](#)⁷², [Luis Perez de Llano](#)⁷³, [Diahn-Warng Perng](#)^{74,75}, [Erick Wan-Chun Huang](#)⁷⁶, [Hao-Chien Wang](#)⁷⁷, [Ming-Ju Tsai](#)^{78,79}, [Bassam Mahboub](#)⁸⁰, [Laila Ibraheem Jaber Salameh](#)⁸¹, [David J Jackson](#)⁸², [John Busby](#)⁸³, [Liam G Heaney](#)⁸⁴, [Paul E Pfeffer](#)^{85,86}, [Amanda Grippen](#)⁸⁷, [Eileen Wang](#)⁸⁸, [Flavia C L Hoyte](#)⁸⁹, [Nicholas M Chapman](#)⁹⁰, [Rohit Katial](#)⁸⁹, [Victoria Carter](#)^{3,2}, [Lakmini Bulathsinhala](#)^{2,91}, [Neva Eleangovan](#)^{2,92}, [Con Ariti](#)^{2,92}, [Juntao Lyu](#)⁹³, [Celeste Porsbjerg](#)⁹⁴, [David B Price](#)^{2,95,96}

Affiliations expand

- PMID: 38016003
- DOI: [10.1164/rccm.202305-0808OC](https://doi.org/10.1164/rccm.202305-0808OC)

Abstract

Rationale: Previous studies investigating comorbidity impact on biologic effectiveness have been relatively small, of short duration, and have not compared biologic classes.

Objectives: To determine the association between T2-related comorbidities and biologic effectiveness in adults with severe asthma (SA).

Methods: This cohort study used International Severe Asthma Registry data (n=21 countries, 2017-2022) to quantify pre- to post-biologic change for four outcomes (annual asthma exacerbation rate, % predicted FEV₁ (ppFEV₁), asthma control, and long-term oral

corticosteroid daily dose [LTOCS]) in patients with/without allergic rhinitis (AR), chronic rhinosinusitis +/- nasal polyps (CRS+/-NP), NP, or eczema/atopic dermatitis (AD).

Main results: Of 1765 patients, 1257, 421, and 87 initiated anti-IL-5/5R, anti-IgE, and anti-IL-4/13 therapies, respectively. In general, pre- to post-biologic improvements were noted in all four asthma outcomes assessed, irrespective of comorbidity status. However, patients with comorbid CRS+/-NP experienced 23% (95% CI 10-35%, $p<0.001$) fewer exacerbations/year and had 59% (95% CI: 26-102%, $p<0.001$) higher odds of better post-biologic control than those without CRS+/-NP. Similar estimates were noted for those with comorbid NP (22% less exacerbations and 56% higher odds of better post-biologic control). Patients with SA and CRS+/-NP had an additional ppFEV₁ improvement of 3.2% (95% CI: 1.0-5.3; $p=0.004$), a trend that was also noted in those with comorbid NP. The presence of AR or AD were not associated with pre- to post-biologic effect for any outcome assessed.

Conclusions: These findings highlight the importance of systematic comorbidity evaluation. The presence of CRS+/-NP or NP may be considered a predictor of biologic effectiveness in patients with severe asthma.

Keywords: allergic rhinitis; chronic rhinosinusitis; nasal polyposis.

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. 2023 Nov 28.

doi: 10.1002/ppul.26780. Online ahead of print.

Higher levels of insulin-like growth factor-1 in cord blood associate with risk of asthma at age 3

[Jose A Castro-Rodriguez¹](#), [Oslando Padilla²](#), [Paola Casanello³](#), [Erick Forno⁴](#)

Affiliations expand

- PMID: 38014590
- DOI: [10.1002/ppul.26780](https://doi.org/10.1002/ppul.26780)

Abstract

Rationale: Experimental studies and epidemiological data in adults suggest that somatomedin-C (insulin-like growth factor-1, IGF-1) may play a role in asthma by modulating airway inflammation, bronchial hyperreactivity, and airway smooth muscle hyperplasia. However, its role in children with asthma is not well understood.

Methods: We established a birth cohort with 339 Chilean pregnant mothers enrolled at the time of delivery from December 2014 to January 2016. We obtained cord blood at birth and followed the offspring every 6 months until 30 months of age, recording data on atopy, wheezing, and other respiratory illnesses. We measured IGF-1 in cord blood and determined the Asthma Predictive Index (API) at 30 months. The cohort was divided according to the API.

Results: Complete data were available for 307/339 (91%) dyads, including 44 preschoolers with API+ and 263 with API-. Demographic characteristics were similar between groups, but mothers of API+ children had a higher prevalence of obesity, previous use of oral contraceptives, and higher education than those of API- children. API+ children had higher birth weight and significantly higher IGF-1 in cord blood (37.4 ± 13.2 in API+ vs. 30.5 ± 13.0 ng/ml in API-, $p = .01$). In the multivariable analysis, IGF-1 in cord blood remained independently associated with a higher risk of asthma (adjusted OR for API+ per ng/ml higher IGF-1 = 1.03 [1.0-1.06], $p = .015$).

Conclusions: Higher insulin-like growth factor-1 in cord blood is associated with asthma risk in the preschool years.

Keywords: IGF-1; asthma; children; cord blood; somatomedin.

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. 2023 Nov 27;9(6):00383-2023.

doi: 10.1183/23120541.00383-2023. eCollection 2023 Nov.

Benralizumab in severe eosinophilic asthma in real life: confirmed effectiveness and contrasted effect on sputum eosinophilia versus exhaled nitric oxide fraction – PROMISE

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Affiliations [expand](#)

- PMID: 38020567

- PMCID: [PMC10680030](#)
- DOI: [10.1183/23120541.00383-2023](#)

Abstract

Background: Randomised controlled trials have shown that benralizumab, an anti-interleukin-5 receptor monoclonal antibody, reduces exacerbations and oral corticosteroid dose and improves asthma control and lung function in severe eosinophilic asthma. The aim of this study was to confirm results of randomised controlled trials in real life in a population of 73 patients with severe eosinophilic asthma treated with benralizumab for at least 12 months.

Methods: Patients underwent careful monitoring of asthma exacerbations, exhaled nitric oxide fraction, lung function, asthma control and quality of life questionnaire responses and sputum induction, and gave a blood sample at baseline, after 6 months and then every year.

Results: We found significant reductions in exacerbations (by 92%, $p < 0.0001$) and oral corticosteroid dose (by 83%, $p < 0.001$) after 6 months that were maintained over time, with 78% of patients able to stop oral corticosteroid therapy. Patients improved their Asthma Control Test (ACT) score (from 11.7 ± 5.1 to 16.9 ± 5.35 , $p < 0.0001$), Asthma Control Questionnaire (ACQ) score (from 2.88 ± 1.26 to 1.77 ± 1.32 , $p < 0.0001$) and Asthma Quality of Life Questionnaire score ($+1.04$, $p < 0.0001$) at 6 months and this was maintained during follow-up. Only 35% and 43% of patients reached asthma control according to an ACT score ≥ 20 and ACQ score < 1.5 , respectively. We observed stable post-bronchodilation lung function over time and a significant reduction in sputum eosinophil count, with 85% of patients exhibiting sputum eosinophil counts $< 3\%$ after 6 months ($p < 0.01$) with no effect on exhaled nitric oxide fraction.

Conclusion: In our real-life study, we confirm the results published in randomised controlled trials showing a sharp reduction in exacerbations and oral corticosteroid therapy, an improvement in asthma control and quality of life, and a dramatic reduction in sputum eosinophil count.

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Conflict of interest statement

Conflict of interest: F. Schleich reports grants or contracts from GSK, AstraZeneca, Chiesi and Novartis, outside the submitted work; consulting fees from GSK, AstraZeneca, Chiesi and Novartis, outside the submitted work; and lectures for GSK, AstraZeneca, Chiesi and Novartis, outside the submitted work. Conflict of interest: A-L. Poirrier reports a speaker

honorarium from GlaxoSmithKline Pharmaceuticals SA outside the submitted work; and advisory board honoraria from GlaxoSmithKline Pharmaceuticals SA and Sanofi Aventis Belgium SA, outside the submitted work. Conflict of interest: R. Louis reports grants or contracts from GSK, AstraZeneca and Chiesi, outside the submitted work; payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from GSK, AstraZeneca, Chiesi and TEVA, outside the submitted work; and participation on a data safety monitoring or advisory board for GSK and AstraZeneca, outside the submitted work. Conflict of interest: The remaining authors have nothing to disclose.

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

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An Pediatr (Engl Ed)

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. 2023 Nov 27:S2341-2879(23)00255-7.

doi: 10.1016/j.anpede.2023.09.014. Online ahead of print.

[Implementation of programmes for the transition of adolescents to adult care](#)

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Affiliations expand

- PMID: 38016858

- DOI: [10.1016/j.anpede.2023.09.014](https://doi.org/10.1016/j.anpede.2023.09.014)

Abstract

Up to 15-20% of adolescents have a chronic health problem. Adolescence is a period of particular risk for the development or progression of chronic diseases for both individuals with more prevalent conditions and those affected by rare diseases. The transition from paediatric to adult care begins with preparing and training the paediatric patient, accustomed to supervised care, to assume responsibility for their self-care in an adult care setting. The transition takes place when the young person is transferred to adult care and discharged from paediatric care services. It is only complete when the youth is integrated and functioning competently within the adult care system. Adult care providers play a crucial role in welcoming and integrating young adults. A care transition programme can involve transitions of varying complexity, ranging from those required for common and known diseases such as asthma, whose management is more straightforward, to rare complex disorders requiring highly specialized personnel. The transition requires teamwork with the participation of numerous professionals: paediatricians and adult care physicians, nurses, clinical psychologists, health social workers, the pharmacy team and administrative staff. It is essential to involve adolescents in decision-making and for parents to let them take over gradually. A well-structured transition programme can improve health outcomes, patient experience, the use of health care resources and health care costs.

Keywords: Adolescentes; Adolescents; Adultos jóvenes; Chronic diseases; Cuidados apropiados al desarrollo; Developmentally appropriate healthcare; Enfermedades crónicas; Enfermedades raras; Rare diseases; Transición; Transition; Young adults.

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Clin Exp Allergy

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. 2023 Nov 27.

doi: 10.1111/cea.14425. Online ahead of print.

Role of epithelial barrier function in inducing type 2 immunity following early-life viral infection

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Affiliations expand

- PMID: 38011856
- DOI: [10.1111/cea.14425](https://doi.org/10.1111/cea.14425)

Abstract

Background: Preschool wheeze attacks triggered by recurrent viral infections, including respiratory syncytial virus (RSV), are associated with an increased risk of childhood asthma. However, mechanisms that lead to asthma following early-life viral wheezing remain uncertain.

Methods: To investigate a causal relationship between early-life RSV infections and onset of type 2 immunity, we developed a neonatal murine model of recurrent RSV infection, in vivo and in silico, and evaluated the dynamical changes of altered airway barrier function and downstream immune responses, including eosinophilia, mucus secretion and type 2 immunity.

Results: RSV infection of neonatal BALB/c mice at 5 and 15 days of age induced robust airway eosinophilia, increased pulmonary CD4⁺ IL-13⁺ and CD4⁺ IL-5⁺ cells, elevated levels of IL-13 and IL-5 and increased airway mucus at 20 days of age. Increased bronchoalveolar lavage albumin levels, suggesting epithelial barrier damage, were present and persisted following the second RSV infection. Computational in silico simulations demonstrated that recurrent RSV infection resulted in severe damage of the airway barrier (epithelium), triggering the onset of type 2 immunity. The in silico results also demonstrated that recurrent infection is not always necessary for the development of type 2 immunity, which could also be triggered with single infection of high viral load or when the epithelial barrier repair is compromised.

Conclusions: The neonatal murine model demonstrated that recurrent RSV infection in early life alters airway barrier function and promotes type 2 immunity. A causal relationship between airway barrier function and type 2 immunity was suggested using in silico model simulations.

Keywords: in silico modelling; neonatal murine model; pre-school wheeze; recurrent viral infections; respiratory syncytial virus.

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J Asthma

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. 2023 Nov 27:1-21.

doi: 10.1080/02770903.2023.2289158. Online ahead of print.

[Exploring the Relationship Between Asthma, Its Severity and Anxiety Symptoms in Pediatric Patients: A Case-Control Study](#)

[Sheykhi Mahdi](#)¹, [Ali Pourvali](#)², [Yazdan Ghandi](#)², [Anita Alaghmand](#)³, [Maryam Zamanian](#)⁴, [Tina Eslambeik](#)¹, [Amin Tajerian](#)¹

Affiliations expand

- PMID: 38009701
- DOI: [10.1080/02770903.2023.2289158](https://doi.org/10.1080/02770903.2023.2289158)

Abstract

Background: Asthma is a global health concern, especially among children, and is associated with various underlying mechanisms. Childhood exposure to early life stress and anxiety can potentially exacerbate asthma symptoms and complicate its management. While some studies have suggested the benefits of psychological therapies as adjuncts to medication in asthma management, evidence remains inconsistent, emphasizing the need for rigorous evaluation.

Method: This case-control study involved 120 children aged 5-15, with 60 children having asthma and 60 healthy controls. Asthma severity was assessed based on EPR3 guidelines, while anxiety symptoms were measured using the Spence Children's Anxiety Scale (SCAS). Demographic data and asthma-related information were collected via questionnaires. Statistical analyses were conducted to explore the relationship between asthma and anxiety.

Results: Children with asthma exhibited significantly higher anxiety symptoms compared to those without asthma ($P < 0.001$). Subdomain analysis revealed elevated scores in separation anxiety ($P = 0.025$), social phobia ($P < 0.001$), agoraphobia ($P = 0.004$), and fears of physical injury ($P < 0.001$) in children with asthma. Furthermore, increased need for SABA, frequency of nocturnal symptoms, and asthma severity were associated with higher anxiety levels in pediatric asthma patients.

Conclusion: This study highlights a significant association between asthma and heightened anxiety symptoms in children, particularly in domains such as separation anxiety, social phobia, agoraphobia, and fears related to physical injury. However, limitations include reliance on self-evaluation questionnaires and the observational nature of the study, emphasizing the need for cautious interpretation.

Keywords: Anxiety; Asthma; Children.

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Cureus

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. 2023 Nov 26;15(11):e49430.

doi: 10.7759/cureus.49430. eCollection 2023 Nov.

Role of Screening Lung Function Tests in a Routine Health Checkup

[Shankar Iyer](#)¹, [S P Rai](#)¹, [Sumeet Singhania](#)¹, [Caroline Simon](#)¹

Affiliations [expand](#)

- PMID: 38024041
- PMCID: [PMC10679964](#)
- DOI: [10.7759/cureus.49430](#)

Abstract

Background and objectives The lung function test is a gold standard, guideline-recommended test to detect obstructive airway diseases like asthma and COPD. It is of considerable value in detecting the presence and severity of airflow obstruction in patients with respiratory symptoms. However, the role of spirometry in a routine health checkup is controversial. Spirometry, when used in routine health checkup settings as a case-finding tool for all adults with persistent respiratory symptoms or having a history of exposure to risk factors, is likely to label a relatively large proportion of individuals as diseased with airflow obstruction. Conversely, spirometry is normal in a relatively large percentage of adults who report respiratory symptoms including dyspnea, the respiratory symptom having the greatest impact on quality of life. The objective of this study is to determine the

utility of spirometry as a screening test to detect airflow obstruction in otherwise healthy subjects undergoing a routine health checkup. **Methods** This observational study was conducted with 538 health checkup individuals aged 18 and over. A brief history was taken prior to the test. Lung function tests were performed and interpreted as per the Global Initiative for Chronic Obstructive Lung Disease criteria. The anthropometric and spirometric data obtained were compared to other population-based spirometric studies to compare the prevalence of airflow limitation, the risk factors, and smoking history. **Results** Of the total 538 subjects incorporated in the study, 305 (57%) were males and 233 (43%) were females aged between 18 to 80 years with a mean age of 45 years. The male-to-female ratio was 1.3:1 with a mean BMI of 25.9. The overall yield from lung function tests in detecting airflow obstruction was 63 subjects (11.7%), of which 36 (11.8%) were males and 27 (11.5%) were females. Seventy-three subjects (13.5%) were classified as having a small airway obstruction, of which 34 were males (46.6%), and 39 were females (53.4%). The distribution of airflow obstruction by age was with eight subjects (5.4%) in the 18-35 group, 21 subjects (7.8%) in the 36-55 group, and 34 (25%) in the elderly (>55) age group. Although overall smoking history showed no significant association with developing airflow obstruction, significant association with smoking was found in the elderly (>55) age group. **Interpretation and conclusions** The results of the study suggest that lung function tests should be included in routine health checkups in the subset of individuals greater than 35 years of age with or without a history of smoking, in all age groups with a family history of asthma, in individuals with respiratory symptoms and in individuals greater than 55 years of age with a moderate history of smoking.

Keywords: "spirometry"; air flow obstruction; health checkup; lung function test; obstructive airway diseases; smoking.

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Conflict of interest statement

The authors have declared that no competing interests exist.

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

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

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. 2023 Dec 1;152(Suppl 3):S20-S21.

doi: 10.1542/peds.2023-064344GA.

YouTube as a Source of (Mis)Information on Allergic Rhinitis

[Aiden C Bingemann¹](#), [Theresa A Bingemann¹](#)

Affiliations expand

- PMID: 38038561
- DOI: [10.1542/peds.2023-064344GA](https://doi.org/10.1542/peds.2023-064344GA)

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Pediatrics

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. 2023 Dec 1;152(Suppl 3):S19-S20.

doi: 10.1542/peds.2023-064344G.

Allergic Rhinitis Comorbidity on Asthma Outcomes in City School Children

[Dexter Matrana](#)¹, [Andrew Abreo](#)¹

Affiliations expand

- PMID: 38038557
- DOI: [10.1542/peds.2023-064344G](https://doi.org/10.1542/peds.2023-064344G)

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. 2023 Dec 1;152(Suppl 3):S23.

doi: [10.1542/peds.2023-064344HB](https://doi.org/10.1542/peds.2023-064344HB).

Evolution of Eczema, Wheeze, and Rhinitis From Infancy to Early Adulthood: Four Birth Cohort Studies

[Samantha K Knox](#)¹, [Todd A Mahr](#)¹

Affiliations expand

- PMID: 38038546
- DOI: [10.1542/peds.2023-064344HB](https://doi.org/10.1542/peds.2023-064344HB)

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Saudi Med J

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. 2023 Dec;44(12):1254-1259.

doi: 10.15537/smj.2023.44.12.20230396.

[Risk factors for recurrence of chronic rhinosinusitis with nasal polyps after endoscopic sinus surgery: A retrospective study](#)

[Yahya A Fageeh](#)¹, [Mohammed A Basurrah](#)¹, [Khalid T Hakami](#)¹, [Zohour A Almalki](#)¹, [Farah S Alnemari](#)¹, [Wahaj A Altalhi](#)¹

Affiliations expand

- PMID: 38016740

- DOI: [10.15537/smj.2023.44.12.20230396](https://doi.org/10.15537/smj.2023.44.12.20230396)

Free article

Abstract

Objectives: To assess the pathophysiological factors leading to chronic rhinosinusitis (CRS) recurrence with nasal polyps (CRSwNP) after endoscopic sinus surgery (ESS) and compare the clinical and imaging findings between both groups.

Methods: A retrospective study was carried out at a tertiary hospital. Patients with recurrent nasal polyps were compared to those with no recurrence by demographics, risk factors, anatomical abnormalities, clinical features, and Lund-Mackey (LM) scores. Both groups were followed up for 24 months after the primary surgery to detect recurrence.

Results: Among the 134 patients who underwent ESS for CRSwNP, 69 patients were in the recurrence group and 65 in the non-recurrence group. No significant difference was found in demographics, comorbidities, and anatomical abnormalities between both groups. However, asthma was more prevalent in the recurrence group (73.9% vs. 29.2%; $p < 0.01$). All clinical features were similar between both groups. However, the recurrence group had more patients with bilateral polyps than non-recurrence (95.7% vs. 80%; $p < 0.01$). We found that 26.1% ($n = 18$) of the 69 patients with recurrence needed revision surgery. Smoking rates were significantly different between reoperated vs. non-reoperated patients (16.7% (3/18) vs. 2% (1/51); $p = 0.02$), and the extent of primary ESS was different between them.

Conclusion: Asthma is a significant risk factor for CRS recurrence. Furthermore, smoking and inadequate primary surgery increase the chance of revision surgery in case of recurrence.

Keywords: chronic rhinosinusitis; endoscopic sinus surgery; nasal polyps.

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MeSH termsexpand

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Int Forum Allergy Rhinol

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. 2023 Dec;13(12):2262-2263.

doi: 10.1002/alr.23286. Epub 2023 Oct 10.

Letter to the editor regarding "Long-term treatment outcomes in refractory rhinitis medicamentosa managed with nasal surgery"

[Xiao Cui](#)¹, [Sai Wang](#)¹, [Liyin Wang](#)²

Affiliations expand

- PMID: 37817466
- DOI: [10.1002/alr.23286](https://doi.org/10.1002/alr.23286)

No abstract available

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Int Forum Allergy Rhinol

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. 2023 Dec;13(12):2264-2265.

doi: 10.1002/alr.23287. Epub 2023 Oct 10.

Response to letter to the editor regarding "Long-term treatment outcomes in refractory rhinitis medicamentosa managed with nasal surgery"

[William Li](#)¹, [Richard John Harvey](#)^{1,2}, [Larry Kalish](#)^{1,3}

Affiliations expand

- PMID: 37817418
- DOI: [10.1002/alr.23287](https://doi.org/10.1002/alr.23287)

No abstract available

Keywords: Chronic Disease; Rhinitis; SNOT-22.

- [4 references](#)

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Observational Study

Adv Ther

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. 2023 Dec;40(12):5366-5382.

doi: 10.1007/s12325-023-02644-5. Epub 2023 Oct 6.

Baseline Demographics, Comorbidities, Treatment Patterns and Burden of Atopic Dermatitis in Adults and Adolescents from the GLOBOSTAD Long-Term Observational Study

[Piergiacomo Calzavara-Pinton](#)¹, [Jarmila Čelakovská](#)², [Hilde Lapeere](#)³, [Gregor Holzer](#)⁴, [Mona Al-Ahmad](#)⁵, [Chia-Yu Chu](#)⁶, [Silvia M Ferrucci](#)⁷, [Yoko Kataoka](#)⁸, [Mariateresa Rossi](#)⁹, [Daria S Fomina](#)^{10 11}, [Wen-Hung Chung](#)¹², [Thrasyvoulos Tzellos](#)¹³, [Anne-Claire Fougerousse](#)^{14 15}, [Jiangming Wu](#)¹⁶, [Marius Ardeleanu](#)¹⁷, [Zafer E Ozturk](#)¹⁸

Affiliations expand

- PMID: 37801232
- PMCID: [PMC10611842](#)
- DOI: [10.1007/s12325-023-02644-5](#)

Free PMC article

Abstract

Introduction: Insights into real-world treatment of atopic dermatitis (AD) are relevant to clinical decision making. The aim of this analysis was to characterize patients who receive dupilumab for AD in a real-world setting.

Methods: The GLOBOSTAD registry is an ongoing, longitudinal, prospective, observational study of patients with AD who receive dupilumab according to country-specific prescribing information. We report baseline characteristics, comorbidities and treatment patterns for patients enrolled from July 11, 2019 to March 31, 2022. Analyses are descriptive; no formal statistical comparisons were performed.

Results: Nine hundred fifty-two adults and adolescents were enrolled in GLOBOSTAD. Patients had a high disease burden before starting dupilumab: (mean [standard deviation]) percent body surface area affected (44.8 [24.42]), Eczema Area and Severity Index total score (24.8 [12.95]), SCORing Atopic Dermatitis total score (60.5 [16.34]), Patient-Oriented Eczema Measure total score (19.7 [6.37]) and Dermatology Life Quality Index total score (13.7 [7.02]). Overall, 741 (77.8%) patients reported ≥ 1 type 2 inflammatory comorbidities, most frequently allergic rhinitis (492 [51.7%]), asthma (323 [33.9%]), food allergy (294 [30.9%]) or another allergy (274 [28.8%]). In the previous 12 months, 310 (32.6%) patients had received systemic non-steroidal immunosuppressants and 169 (17.8%) systemic corticosteroids; 449 (47.2%) had received topical corticosteroids, most commonly potent topical corticosteroids; 141 (14.8%) had received topical calcineurin inhibitors and 32 (3.4%) ultraviolet therapy. Most (713 [74.9%]) patients started dupilumab because of prior treatment failure.

Conclusion: Patients enrolled in GLOBOSTAD demonstrated considerable multidimensional burden of disease across AD signs, symptoms and quality of life despite previous use of systemic and non-systemic AD treatments.

Clinical trial registration: ClinicalTrials.gov identifier [NCT03992417](https://clinicaltrials.gov/ct2/show/study/NCT03992417). Video Abstract.

Keywords: Atopic dermatitis; Comorbidities; Disease burden; Observational study; Treatment patterns.

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Conflict of interest statement

Piergiacomo Calzavara-Pinton is an advisory board member for AbbVie, Almirall, Galderma, LEO Pharma, Meda and Sanofi. Jarmila Čelakovská has nothing to disclose. Hilde Lapeere is on the advisory boards of AbbVie, LEO Pharma, Eli Lilly, Pfizer and Sanofi. Gregor Holzer is an advisory board member for AbbVie, Almirall, Eli Lilly, Galderma, LEO Pharma and Sanofi. Mona Al-Ahmad is an advisory board member and speaker for AstraZeneca, GSK and Novartis. Chia-Yu Chu is an investigator for AbbVie, Dermira, Eli Lilly, Novartis, Oneness

Biotech, Pfizer, Regeneron Pharmaceuticals Inc., Roche and Sanofi; a consultant for AbbVie, Eli Lilly, Novartis, Pfizer, Roche and Sanofi; a speaker for AbbVie, Eli Lilly, Mylan, Novartis, Pfizer, Roche, Sanofi and Viartis; and an advisory board member for Mylan, Pfizer, Roche and Sanofi. Silvia M. Ferrucci is an advisory board member for AbbVie, Eli Lilly and Sanofi; a Principal Investigator for Almirall, Menarini and Pfizer; and reports honoraria for lectures and research grants from Novartis. Yoko Kataoka reports lecturer honoraria from AbbVie, Pfizer and Sanofi; and research funding from AbbVie, Amgen, LEO Pharma, Lilly, Maruho, Otsuka, Pfizer, Sanofi and Taiho. Mariateresa Rossi is a speaker for AbbVie, Galderma, La Roche Posay, LEO Pharma, Pfizer and Sanofi. Daria S. Fomina reports honoraria from CSL Behring, Novartis, Sanofi and Shire. Wen-Hung Chung has nothing to disclose. Thrasyvoulos Tzellos has received honoraria from and is an advisory board member and speaker for AbbVie; and has received honoraria from and is an advisory board member for Boehringer Ingelheim and Sanofi. Anne-Claire Fougousse is a consultant for AbbVie, Lilly and Sanofi. Jiangming Wu and Zafer E. Ozturk are employees of Sanofi and may hold stock and/or stock options in the company. Marius Ardeleanu is an employee and shareholder of Regeneron Pharmaceuticals Inc.

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

SUPPLEMENTARY INFO

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[Multicenter Study](#)

Eur Arch Otorhinolaryngol

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. 2023 Dec;280(12):5417-5431.

The efficacy of steroid-eluting stents on the local inflammation of chronic rhinosinusitis with nasal polyposis after endoscopic sinus surgery: a multicenter prospective longitudinal study

[Li Zheng](#)^{#1,2}, [Zhe Chen](#)^{#3}, [Jing Jin](#)^{1,2}, [Yuqin Deng](#)^{1,2}, [Lisheng Fu](#)^{1,2}, [Wei Zhang](#)^{1,2}, [Rong Xiang](#)^{1,2}, [Bei Guo](#)⁴, [Zezhang Tao](#)^{5,6}, [Yu Xu](#)^{7,8}

Affiliations expand

- PMID: 37665343
- DOI: [10.1007/s00405-023-08158-8](https://doi.org/10.1007/s00405-023-08158-8)

Abstract

Purpose: Attenuating local inflammation of chronic rhinosinusitis with nasal polyps (CRSwNP) after endoscopic sinus surgery (ESS) was crucial. Corticosteroids were generally exploited to ameliorate the postoperative state of CRSwNP. This study aims to verify the efficacy of steroid-eluting stents on the local inflammation of CRSwNP following ESS.

Methods: 57 CRSwNP were enrolled from September 2021 to April 2022. 30 were with stents, and 27 were without stents after ESS. Eosinophilic cationic protein (ECP), myeloperoxidase (MPO), eosinophil, and neutrophil levels in nasal secretions, as well as visual analog scale (VAS) and modified perioperative sinus endoscopy (POSE) scores, were assessed preoperatively and after 2, 4, 8, and 12 weeks.

Results: All subjects of CRSwNP exhibited reduced results of eosinophil levels, neutrophil levels, nasal obstruction, nasal discharge, loss of smell, and total VAS scores after 12 weeks compared to the preoperative ones ($p < 0.05$). Compared with control subjects, CRSwNP with stents acquired lower levels of ECP, MPO, loss of smell, total VAS, and POSE scores at four follow-up visits, as well as reduced eosinophil and neutrophil levels in nasal secretions after 12 weeks ($p < 0.05$). Correlation analysis revealed that postoperative ECP and MPO levels of CRSwNP in nasal secretions correlated strongly with eosinophil and neutrophil levels, respectively, as well as POSE scores ($r > 0.6$).

Conclusion: These findings indicated that steroid-eluting stents might be an acclaimed option for CRSwNP in alleviating local inflammation to acquire a superior state after ESS.

Keywords: Chronic rhinosinusitis with nasal polyps; Eluting stent; Eosinophilic cationic protein; Inflammation; Myeloperoxidase.

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- [45 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grants and fundingexpand

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Review

Otolaryngol Head Neck Surg

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. 2023 Dec;169(6):1424-1435.

doi: 10.1002/ohn.461. Epub 2023 Aug 7.

[Systematic Review and Meta-analysis: Macrolide in the Treatment of Chronic Rhinosinusitis After Endoscopic Sinus Surgery](#)

[Fu Shu](#)¹, [Chan-Xiu Li](#)², [Feng Zhang](#)³, [Mingwei Peng](#)⁴, [Lei Shi](#)⁵, [Linglong Li](#)³, [Juan Xiong](#)³, [Zengyi Mu](#)², [Yaping Wang](#)³, [Dehong Mao](#)³

Affiliations expand

- PMID: 37548067
- DOI: [10.1002/ohn.461](https://doi.org/10.1002/ohn.461)

Abstract

Objectives: To evaluate the efficacy and safety of macrolide antibiotics therapy in patients with chronic rhinosinusitis (CRS) receiving endoscopic sinus surgery.

Data sources: PubMed, Web of Science, Embase, and Cochrane Library.

Review methods: The electronic databases were comprehensively searched on June 2, 2022, for randomized controlled trials on macrolide antibiotics in the treatment of patients undergoing CRS endoscopic surgery. The primary outcome measures were the sinonasal outcome test (SNOT) score and the visual analog scale (VAS) score. The secondary outcome measures were the nasal endoscopy score (NES), the sinus computed tomography score, and adverse events.

Results: A total of 8 studies were included, involving 606 patients who used macrolide for a long time. Meta-analysis showed that no significant difference was observed in SNOT (standardized mean difference [SMD] = -0.13; 95% confidence interval [CI]: -0.38 to 0.13, $I^2 = 0\%$) and VAS (SMD = -0.10; 95% CI, -0.88 to 0.68, $I^2 = 81\%$) between the macrolide and placebo groups. However, macrolide outperformed the placebo in improving NES (SMD = -0.32; 95% CI, -0.62 to -0.03, $I^2 = 21\%$). The use of macrolide did not increase the incidence of adverse events.

Conclusion: Long-term use of macrolide after CRS surgery may not significantly improve the quality of life and disease severity of the patients but may play a role in improving postoperative NES in patients with CRS. There is still no sufficient evidence to determine whether the disease phenotype of CRS or the patient's race will affect the efficacy of long-term use of macrolide after CRS.

Keywords: chronic rhinosinusitis; macrolide antibiotics; meta-analysis; postendoscopic sinus surgery.

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- [48 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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J Asthma

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. 2023 Dec;60(12):2224-2232.

doi: 10.1080/02770903.2023.2231078. Epub 2023 Jul 10.

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](https://doi.org/10.1080/02770903.2023.2231078)

Abstract

Objective: Adult-onset asthma is a recognized but heterogeneous phenotype and has been described to associate with poor asthma control. Knowledge about associations between clinical characteristics including comorbidities and control of adult-onset asthma is limited, especially in older populations. We aimed to study how clinical biomarkers and comorbidities 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 ($ACT \leq 19$) was significantly associated with a blood neutrophil count $\geq 5/\mu\text{l}$, BMI ≥ 30 , and several comorbidities. In multivariable regression analysis, uncontrolled asthma was associated with neutrophils $\geq 5/\mu\text{l}$ (OR 2.35; 95% CI 1.11-4.99). In age-stratified analysis, BMI ≥ 30 (OR 3.04; 1.24-7.50), eosinophils $\geq 0.3/\mu\text{l}$ (OR 3.17; 1.20-8.37), neutrophils $\geq 5/\mu\text{l}$ (OR 4.39; 1.53-12.62) and allergic rhinitis (OR 5.10; 1.59-16.30) were associated with uncontrolled asthma among the middle-aged. Among the older adults, uncontrolled asthma was only associated with comorbidities: chronic rhinitis (OR 4.08; 1.62-10.31), ischemic heart disease (OR 3.59; 1.17-10.98), malignancy (OR 3.10; 1.10-8.73), and depression/anxiety (OR 16.31; 1.82-146.05).

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

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

SUPPLEMENTARY INFO

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Effect of second-generation antihistamines on nighttime sleep and daytime sleepiness in patients with allergic rhinitis

[Teruyuki Sato](#)¹, [Youji Tareishi](#)², [Takahiro Suzuki](#)³, [Nanako Ansai](#)³, [Chikara Asaka](#)², [Nobuo Ohta](#)³

Affiliations expand

- PMID: 37382850
- DOI: [10.1007/s11325-023-02857-6](https://doi.org/10.1007/s11325-023-02857-6)

Abstract

Background: The daytime tiredness experienced by the vast majority of allergic rhinitis (AR) sufferers is directly related to the fact that they experience disrupted sleep at night. This study compared the effects of recently marketed second-generation H1 antihistamines (SGAs) on nighttime sleep and daytime sleepiness in patients with AR, with patients grouped into those taking non-brain-penetrating antihistamines (NBP group) and those taking brain-penetrating antihistamines (BP group).

Methods: Patients with AR completed self-administered questionnaire-based surveys to determine Pittsburgh Sleep Quality Index (PSQI) before and after taking SGAs. Statistical analysis was performed on each evaluation item.

Results: Of 53 Japanese patients with AR between 6 and 78 years old, median (SD) age was 37.0 (22.4) years old and 21 were men (40%). Of the 53 patients, 34 were the NBP group and 19 were the BP group. In the NBP group, mean (SD) subjective sleep quality score after medication was 0.76 (0.50), which was significantly lower (better) than the score of 0.97 (0.52) before medication ($p = 0.020$). In the BP group, mean (SD) subjective sleep quality score after medication was 0.79 (0.54), which was not significantly different from

the score of 0.74 (0.56) before medication ($p = 0.564$). In the NBP group, mean (SD) global PSQI score was 3.47 (1.71) after medication, which was significantly lower (better) than the score of 4.35 (1.92) before medication ($p = 0.011$). In the BP group, mean (SD) global PSQI score was 2.47 (2.39) after medication, which was not significantly different from the score of 3.00 (2.71) before medication ($p = 0.125$).

Conclusion: Subjective sleep quality and global PSQI score were improved only in the group taking non-brain-penetrating SGAs.

Keywords: Allergic rhinitis; Daytime sleepiness; Nighttime sleep; Questionnaire self-survey; Second-generation H1 antihistamine; Sleep quality.

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- [19 references](#)

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Int Forum Allergy Rhinol

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. 2023 Dec;13(12):2244-2247.

doi: 10.1002/alr.23212. Epub 2023 Jul 1.

Early increase in eosinophil count may predict long-term hypereosinophilia

during dupilumab treatment: a 2-year observational study

[Andrea Rampi](#)^{1,2}, [Umberto Tanzini](#)^{1,2}, [Alessandro Vinciguerra](#)³, [Giulia Danè](#)¹, [Luca Moroni](#)^{2,4}, [Mona-Rita Yacoub](#)⁴, [Matteo Trimarchi](#)^{1,2,5}

Affiliations expand

- PMID: 37316962
- DOI: [10.1002/alr.23212](https://doi.org/10.1002/alr.23212)

Abstract

In a limited subset of patients, dupilumab-induced hypereosinophilia is persistent. Two-month follow-up eosinophil count may predict long-lasting hypereosinophilia.

Keywords: chronic rhinosinusitis; eosinophilic rhinitis and nasal polyposis; paranasal sinus diseases; therapeutics.

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- [10 references](#)

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Randomized Controlled Trial

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. 2023 Dec;132(12):1631-1637.

doi: 10.1177/00034894231176327. Epub 2023 Jun 4.

Intranasal Schirmer Test in Allergic Rhinitis: Relationship to Symptom Scores and Role in Determining Response to Treatment

[Ozlem Onerci Celebi](#)¹, [Ela Araz Server](#)¹, [Tolga Kirgezen](#)¹, [Ozgur Yigit](#)¹, [Ecem Sevim Aki](#)¹

Affiliations expand

- PMID: 37271974
- DOI: [10.1177/00034894231176327](https://doi.org/10.1177/00034894231176327)

Abstract

Objectives: The Intranasal Schirmer test (INS) is an easy to administer test that can yield objective measurement of the quantity of nasal secretion and has been studied in patients with various nasal and systemic pathologies; however, the role of INS in patients with allergic rhinitis remains unclear. Our aim was to determine the relationship between various allergic symptoms and the Intranasal Schirmer Test (INS) score and to evaluate the utility of INS in determining treatment effect in patients with allergic rhinitis.

Methods: This prospective study included patients with allergic rhinitis who were randomly divided into 3 treatment groups (nasal steroid only, oral antihistamine only, nasal steroid and oral antihistamine). For all patients, Total Nasal Symptom Score (TNSS) was used to measure symptom severity and INS was administered before and after treatment. Pre-treatment and post treatment TNSS and INS scores were compared between different treatment groups and within each group.

Results: The study included 120 patients, with 40 patients in each group. There were significant differences both in pre-treatment and post-treatment symptom severity score with changes of INS scores between treatment groups ($P < .001$ and $P = .002$, respectively). There was a significant difference between pre-treatment and post-treatment symptom

severity scores and the INS score in each treatment group ($P < .001$). There was also a significant positive correlation between INS score and TNSS ($r = .591$ and $P < .001$).

Conclusion: The Intranasal Schirmer Test can be used as an objective tool for patients with allergic rhinitis as an adjunct to subjective patient symptom reports and can also be used to determine the response to treatment.

Keywords: Intranasal Schirmer test; allergic rhinitis; nasal steroids; oral antihistamines.

Conflict of interest statement

Declaration of Conflicting InterestsThe author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Laryngoscope

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. 2023 Dec;133(12):3299-3303.

doi: 10.1002/lary.30685. Epub 2023 Apr 5.

The Long-Term Implications of Rhinitis and Chronic Rhinosinusitis in Young Adults

[Yoni Shopen](#)^{1,2}, [Nir Tsur](#)^{1,2,3}, [Ethan Soudry](#)^{1,2}

Affiliations expand

- PMID: 37017253
- DOI: [10.1002/lary.30685](https://doi.org/10.1002/lary.30685)

Abstract

Background: The long-term impact of rhinitis and chronic rhinosinusitis (CRS) on general health and medical services utilization in young adults have been limitedly studied.

Methods: A case-control study in the Israeli Defense Forces, between the years 2005 and 2019, of all individuals with either rhinitis or CRS and a matched cohort of healthy individuals with a minimum of 5 years of consecutive follow-up.

Results: The study groups included 617 patients with rhinitis and 296 patients with CRS and 2739 healthy controls with an average age of 28 years. During a mean follow-up of 8 years, a significant fraction of patients in both study groups were diagnosed with asthma compared to the control group, (26.1% and 23.3% vs. 3.7%, respectively; CI 95%: 12.1%-14.9%, $p < 0.0001$). 7.6% of patients with rhinitis developed CRS. Significantly increased loss of productivity and medical system utilization were noted in the study groups compared to controls ($p < 0.0001$). Moreover, deterioration in general health, manifested as loss of physical fitness for combative service was observed in a third of patients during follow-up.

Conclusions: Rhinitis and CRS significantly impact productivity and medical service utilization in young adults, as well as general health associated with development of asthma and impairment of physical fitness. A minority of rhinitis patients develop CRS overtime, further affecting this patient group. These patients should be followed up and managed to improve disease control and associated outcomes.

Level of evidence: 3 Laryngoscope, 133:3299-3303, 2023.

Keywords: asthma; chronic rhinitis; chronic rhinosinusitis; health-care burden; productivity; young adults.

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- [Cited by 1 article](#)
- [16 references](#)

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Editorial

Int Forum Allergy Rhinol

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. 2023 Nov 29.

doi: 10.1002/alr.23289. Online ahead of print.

[Reply to: "Air pollution exposure is associated with rhinitis in older US adults via specific immune mechanisms"](#)

[Henrique Ochoa Scussiatto](#)¹, [Kristen E Wroblewski](#)², [Kristina L Page](#)³, [L Philip Schumm](#)², [Martha K McClintock](#)⁴, [Murray Ramanathan Jr](#)⁵, [Helen H Suh](#)⁶, [Jayant M Pinto](#)¹

Affiliations expand

- PMID: 38018794

- DOI: [10.1002/alr.23289](https://doi.org/10.1002/alr.23289)

No abstract available

- [6 references](#)

SUPPLEMENTARY INFO

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Pol Arch Intern Med

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. 2023 Nov 29;133(11):16611.

doi: 10.20452/pamw.16611. Epub 2023 Nov 21.

Recent guidelines addressing chronic rhinosinusitis with nasal polyps: practical aspects

[Matthew A Rank](#), [Alex M Wonnapharhown](#), [Catherine M Freeman](#)

- PMID: 37987636
- DOI: [10.20452/pamw.16611](https://doi.org/10.20452/pamw.16611)

Free article

Abstract

Chronic rhinosinusitis (CRS) is common in adults. It is diagnosed based on a high index of suspicion alongside objective means of assessing sinus inflammation. Determining the impact of CRS on patient quality of life is an important starting point for discussions

regarding treatment, and is critical for longitudinal assessment of response to specific treatments. CRS can be further categorized by the presence or absence of nasal polyps. Recent Joint Task Force on Practice Parameters Grading of Recommendations Assessment, Development, and Evaluation guidelines for the management of CRS with nasal polyps (CRSwNP) focused on 3 treatment options: intranasal corticosteroids with multiple delivery methods, biologics (monoclonal antibodies targeting type 2 inflammation), and aspirin therapy after desensitization, which only applies to the subset of patients with CRSwNP who experience acute respiratory reactions following nonsteroidal anti-inflammatory drug ingestion. The authors of the guidelines made conditional recommendations in favor of each of these 3 treatment options, highlighting the importance of shared decision-making when choosing appropriate therapy for individuals with CRSwNP.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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J Allergy Clin Immunol Pract

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. 2023 Nov 28:S2213-2198(23)01305-3.

doi: 10.1016/j.jaip.2023.11.036. Online ahead of print.

[Associations of Breathing Pattern Disorder and Nijmegen Score with Clinical Outcomes in Difficult-to-treat Asthma](#)

[Anna Freeman](#)¹, [Steevo Abraham](#)², [Latha Kadalayil](#)², [Judit Varkonyi-Sepp](#) CPsychol³, [Ben Ainsworth](#)⁴, [J J Hudson-Colby](#)⁵, [Clair Barber](#)⁶, [Paddy Dennison](#)⁷, [Adnan Azim](#)⁶, [Heena Mistry](#)⁶, [Peter Howarth](#)⁶, [Ratko Djukanovic](#)⁶, [Hongmei Zhang](#)⁸, [S Hasan Arshad](#)⁹, [Hans Michael Haitchi](#)¹⁰, [Ramesh J Kurukulaaratchy](#)¹¹

Affiliations expand

- PMID: 38036249
- DOI: [10.1016/j.jaip.2023.11.036](https://doi.org/10.1016/j.jaip.2023.11.036)

Abstract

Background: Breathing pattern disorder (BPD) reflects altered biomechanical patterns of breathing that drive breathing difficulty and commonly accompanies difficult-to-treat asthma. Diagnosis of BPD has no gold standard, but Nijmegen Questionnaire (NQ) >23 is commonly used.

Objectives: We sought to advance clinical characterisation of BPD and better understand clinical utility of NQ in difficult asthma, in patients from the Wessex AsThma CoHort of difficult asthma (WATCH) study.

Methods: Association between demographic and clinical factors in difficult asthma and BPD, ascertained by clinical diagnosis (yes/no, n=476), by NQ scores (≤ 23 : normal (no suggestion of BPD) and >23 : abnormal (suggested BPD), n=372, as well as the continuous raw NQ scores) were assessed in univariate models to identify significant risk factors associated with the three BPD outcomes. For the clinician-diagnosed and NQ-based BPD, associations of continuous factors were assessed using independent samples t-test or Mann-Whitney U test as appropriate for the data distribution or by Spearman correlation test. Dichotomous associations were evaluated using chi-squared tests. Multivariable logistic (dichotomous outcomes) and linear regression models (continuous outcomes) were developed to identify predictive factors associated with clinician-diagnosed and NQ-based BPD, dichotomous and continuous. Patients with data on NQ scores were grouped into NQ quartiles (low, moderate, high, and very high). The patterns of association of the quartiles with four health-related questionnaire outcomes were assessed using linear regression analyses.

Results: Multivariable regression identified that clinically diagnosed BPD was associated with female sex (OR 1.85; 95% CI 1.07, 3.20), comorbidities (rhinitis (OR 2.46; 95% CI 1.45, 4.17), GORD (OR 2.77; 95% CI 1.58, 4.84), ILO (OR 4.37; 95% CI 2.01, 9.50) and any psychological co-morbidity (OR 1.86; 95% CI 1.13, 3.07)) and healthcare usage (exacerbations (OR 1.07; 95% CI 1.003, 1.14) and previous ICU admissions (OR 2.03; 95% CI 1.18, 3.47)). Abnormal NQ-based BPD diagnosis was associated with history of eczema (OR 1.83; 95% CI 1.07, 3.14), GORD (OR 1.94; 95% CI 1.15, 3.27) or any psychological

comorbidity (OR 4.29; 95% CI 2.64, 6.95) at multivariable regression. Differences between clinical and NQ-based BPD traits were also found with 42% discordance in BPD-state between these definitions. Multivariable linear regression analysis with NQ as a continuous outcome showed positive association with worse asthma outcomes (admission to ICU, $p=0.037$), different phenotypic traits (female sex $p=0.001$, ever smoker, $p=0.025$) and greater multimorbidity (GORD, $p=0.002$, sleep apnoea, $p=0.040$, any psychological comorbidity, $p<0.0001$).

Conclusion: BPD is associated with worse health outcomes and negative health impacts in difficult asthma within a multimorbidity disease model. It therefore merits better recognition and prompt treatment. Clinical diagnosis and NQ offer different perspectives on BPD, so this goal may be best addressed by considering clinical features alongside magnitude of NQ.

Keywords: Breathing-pattern-disorder (BPD); Nijmegen questionnaire (NQ); difficult asthma; multimorbidity; treatable trait.

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Am J Respir Crit Care Med

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. 2023 Nov 28.

doi: 10.1164/rccm.202305-0808OC. Online ahead of print.

[Association Between T2-related Comorbidities and Effectiveness of Biologics in Severe Asthma](#)

Michael E Wechsler¹, Ghislaine Scelo^{2,3}, Désirée E S Larenas-Linnemann⁴, Carlos A Torres-Duque^{5,6}, Jorge Maspero⁷, Trung N Tran⁸, Ruth B Murray³, Neil Martin^{9,10}, Andrew N Menzies-Gow^{11,12}, Mark Hew^{13,14}, Matthew J Peters¹⁵, Peter G Gibson^{16,17}, George C Christoff¹⁸, Todor A Popov¹⁹, Andréanne Côté²⁰, Celine Bergeron^{21,22}, Delbert Dorscheid²³, J Mark FitzGerald²⁴, Kenneth R Chapman²⁵, Louis Philippe Boulet²⁶, Mohit Bhutani²⁷, Mohsen Sadatsafavi²⁸, Libardo Jiménez-Maldonado²⁹, Mauricio Duran-Silva³⁰, Bellanid Rodriguez³¹, Carlos Andres Celis-Preciado^{32,33}, Diana Jimena Cano-Rosales³¹, Ivan Solarte^{32,34}, Maria Jose Fernandez-Sanchez^{32,33}, Patricia Parada-Tovar³⁵, Anna von Bülow³⁶, Anne Sofie Bjerrum³⁷, Charlotte S Ulrik³⁸, Karin Dahl Assing³⁹, Linda Makowska Rasmussen⁴⁰, Susanne Hansen^{41,42}, Alan Altraja⁴³, Arnaud Bourdin⁴⁴, Camille Taille⁴⁵, Jeremy Charriot⁴⁶, Nicolas Roche⁴⁷, Andriana I Papaioannou⁴⁸, Konstantinos Kostikas⁴⁹, Nikolaos G Papadopoulos^{50,51}, Sundeep Salvi⁵², Deirdre Long⁵³, Patrick D Mitchell⁵⁴, Richard Costello⁵⁵, Concetta Sirena⁵⁶, Cristina Cardini⁵⁷, Enrico Heffler^{58,59}, Francesca Puggioni⁵⁸, Giorgio Walter Canonica^{60,61}, Giuseppe Guida⁶², Takashi Iwanaga⁶³, Mona Al-Ahmad⁶⁴, Ulises García⁶⁵, Piotr Kuna⁶⁶, João A Fonseca⁶⁷, Riyadh Al-Lehebi^{68,69}, Mariko S Koh⁷⁰, Chin Kook Rhee⁷¹, Borja G Cosío⁷², Luis Perez de Llano⁷³, Diahn-Warng Perng^{74,75}, Erick Wan-Chun Huang⁷⁶, Hao-Chien Wang⁷⁷, Ming-Ju Tsai^{78,79}, Bassam Mahboub⁸⁰, Laila Ibraheem Jaber Salameh⁸¹, David J Jackson⁸², John Busby⁸³, Liam G Heaney⁸⁴, Paul E Pfeffer^{85,86}, Amanda Grippen Goddard⁸⁷, Eileen Wang⁸⁸, Flavia C L Hoyte⁸⁹, Nicholas M Chapman⁹⁰, Rohit Katial⁸⁹, Victoria Carter^{3,2}, Lakmini Bulathsinhala^{2,91}, Neva Eleangovan^{2,92}, Con Ariti^{2,92}, Juntao Lyu⁹³, Celeste Porsbjerg⁹⁴, David B Price^{2,95,96}

Affiliations expand

- PMID: 38016003
- DOI: [10.1164/rccm.202305-0808OC](https://doi.org/10.1164/rccm.202305-0808OC)

Abstract

Rationale: Previous studies investigating comorbidity impact on biologic effectiveness have been relatively small, of short duration, and have not compared biologic classes.

Objectives: To determine the association between T2-related comorbidities and biologic effectiveness in adults with severe asthma (SA).

Methods: This cohort study used International Severe Asthma Registry data (n=21 countries, 2017-2022) to quantify pre- to post-biologic change for four outcomes (annual asthma exacerbation rate, % predicted FEV₁ (ppFEV₁), asthma control, and long-term oral corticosteroid daily dose [LTOCS]) in patients with/without allergic rhinitis (AR), chronic rhinosinusitis +/- nasal polyps (CRS+/-NP), NP, or eczema/atopic dermatitis (AD).

Main results: Of 1765 patients, 1257, 421, and 87 initiated anti-IL-5/5R, anti-IgE, and anti-IL-4/13 therapies, respectively. In general, pre- to post-biologic improvements were noted in all four asthma outcomes assessed, irrespective of comorbidity status. However, patients with comorbid CRS+/-NP experienced 23% (95% CI 10-35%, p<0.001) fewer

exacerbations/year and had 59% (95% CI: 26-102%, $p < 0.001$) higher odds of better post-biologic control than those without CRS+/-NP. Similar estimates were noted for those with comorbid NP (22% less exacerbations and 56% higher odds of better post-biologic control). Patients with SA and CRS+/-NP had an additional ppFEV₁ improvement of 3.2% (95% CI: 1.0-5.3; $p = 0.004$), a trend that was also noted in those with comorbid NP. The presence of AR or AD were not associated with pre- to post-biologic effect for any outcome assessed.

Conclusions: These findings highlight the importance of systematic comorbidity evaluation. The presence of CRS+/-NP or NP may be considered a predictor of biologic effectiveness in patients with severe asthma.

Keywords: allergic rhinitis; chronic rhinosinusitis; nasal polyposis.

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Review

Am J Otolaryngol

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. 2023 Nov 26;45(2):104130.

doi: 10.1016/j.amjoto.2023.104130. Online ahead of print.

[An indirect comparative analysis of two posterior nasal nerve ablation techniques for treating chronic rhinitis: A systemic review and meta-analysis](#)

[Do Hyun Kim](#)¹, [Soo Whan Kim](#)¹, [Sung Won Kim](#)¹, [Gulnaz Stybayeva](#)², [Se Hwan Hwang](#)³

Affiliations expand

- PMID: 38039909
- DOI: [10.1016/j.amjoto.2023.104130](https://doi.org/10.1016/j.amjoto.2023.104130)

Abstract

Objectives: This systematic review and meta-analysis evaluates and compares the effects of two treatments that ablate the posterior nasal nerves for rhinitis-related symptoms: cryotherapy and radiofrequency neurolysis.

Methods: We reviewed studies retrieved from PubMed, SCOPUS, Embase, the Web of Science and the Cochrane database up to June 2023. Papers reporting quality-of-life and rhinitis-related symptom scores before and after cryotherapy, and sham-controlled studies, were analyzed.

Results: In total, 738 patients enrolled in 10 studies were evaluated. Both cryotherapy and radiofrequency neurolysis significantly improved rhinitis-related symptoms including congestion, itching, rhinorrhea, and sneezing, and quality of life during 12 months of follow-up. Radiofrequency neurolysis was significantly more effective than cryotherapy in terms of reducing total nasal symptom scores at up to 12 months postoperatively. In terms of individual symptoms, itching, rhinorrhea, and congestion were significantly alleviated or tended to be reduced more by radiofrequency neurolysis than by cryotherapy. The improvements in the minimal clinically important difference in total nasal symptom scores (1.0 point) after 3 months of cryotherapy and radiofrequency therapy were 81.8 % and 92.7 %, respectively.

Conclusions: Cryotherapy and radiofrequency neurolysis both improved rhinitis-symptom and quality-of-life scores. Especially, radiofrequency neurolysis showed the better effectiveness for improving the nasal symptoms related to the rhinitis than cryotherapy.

Keywords: Equipment and supplies; Meta-analysis; Nose; Quality of life; Rhinitis.

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Conflict of interest statement

Declaration of competing interest The authors declare that there are no competing interests.

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Chronic cough

1

Review

Lung

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. 2023 Dec;201(6):499-509.

doi: 10.1007/s00408-023-00659-x. Epub 2023 Nov 21.

Illuminating Airway Nerve Structure and Function in Chronic Cough

[James Kornfield](#) ^{#1}, [Ubaldo De La Torre](#) ^{#1}, [Emily Mize](#) ¹, [Matthew G Drake](#) ²

Affiliations [expand](#)

- PMID: 37985513
- PMCID: [PMC10673771](#)
- DOI: [10.1007/s00408-023-00659-x](#)

Free PMC article

Abstract

Airway nerves regulate vital airway functions including bronchoconstriction, cough, and control of respiration. Dysregulation of airway nerves underlies the development and

manifestations of airway diseases such as chronic cough, where sensitization of neural pathways leads to excessive cough triggering. Nerves are heterogeneous in both expression and function. Recent advances in confocal imaging and in targeted genetic manipulation of airway nerves have expanded our ability to visualize neural organization, study neuro-immune interactions, and selectively modulate nerve activation. As a result, we have an unprecedented ability to quantitatively assess neural remodeling and its role in the development of airway disease. This review highlights our existing understanding of neural heterogeneity and how advances in methodology have illuminated airway nerve morphology and function in health and disease.

Keywords: Asthma; Chronic cough; Confocal microscopy; Optogenetics; Parasympathetic nerve; Sensory nerve.

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Conflict of interest statement

Dr. Drake has received honorarium from Merck, Bellus, Astra Zeneca, and Chiesi.

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

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Lung

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. 2023 Dec;201(6):511-519.

doi: 10.1007/s00408-023-00660-4. Epub 2023 Nov 18.

Chronic Cough as a Genetic Neurological Disorder? Insights from Cerebellar Ataxia with Neuropathy and Vestibular Areflexia Syndrome (CANVAS)

[Richard D Turner](#)^{1,2}, [Barnaby Hiron](#)^{3,4}, [Andrea Cortese](#)^{5,6}, [Surinder S Birring](#)^{3,4}

Affiliations expand

- PMID: 37979058
- PMCID: [PMC10673766](#)
- DOI: [10.1007/s00408-023-00660-4](#)

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Abstract

Chronic cough is common, and in many cases unexplained or refractory to otherwise effective treatment of associated medical conditions. Cough hypersensitivity has developed as a paradigm that helps to explain clinical and research observations that frequently point towards chronic cough as a neuropathic disorder. Cerebellar ataxia with neuropathy and vestibular areflexia syndrome (CANVAS) is a recently described neurological condition whose clinical features include gait ataxia, unsteadiness, peripheral neuropathy, and autonomic dysfunction. Chronic cough is also a common feature of the syndrome, with features of hypersensitivity, often preceding core neurological symptoms by up to 30 years or more. The genetic basis in a majority of cases of CANVAS appears to be biallelic variable repeat intron expansion sequences within RFC1, a gene normally involved in the regulation of DNA replication and repair. The same polymorphism has now been identified at an increased frequency in patients with unexplained or refractory chronic cough in the absence of defining clinical features of CANVAS. This review expands on

these points, aiming to increase the awareness of CANVAS amongst clinicians and researchers working with chronic cough. We discuss the implications of a link between RFC1 disease and cough. Improved understanding of CANVAS may lead to an enhanced grasp of the pathophysiology of chronic cough, and new approaches to antitussive treatments.

Keywords: CANVAS; Chronic cough; RFC1.

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Conflict of interest statement

BH, RT, SB declare no conflicts of interest in relation to this manuscript. AC has declared funding from the Medical Research Council (MR/T001712/1) and Fondazione Cariplo (Grant No. 2019-1836) which are unrelated to this manuscript.

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

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. 2023 Dec;201(6):545-553.

doi: 10.1007/s00408-023-00654-2. Epub 2023 Nov 14.

Recurrent Cough in the Elderly: A Forgotten Entity

[Johanna Tuulikki Kaulamo](#)^{1,2}, [Anne Marika Lätti](#)^{3,4}, [Heikki Olavi Koskela](#)^{3,4}

Affiliations expand

- PMID: 37964136
- PMCID: [PMC10673973](#)
- DOI: [10.1007/s00408-023-00654-2](#)

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Abstract

Introduction: Recurrent cough is little researched in adults. We investigated the prevalence, risk factors, and consequences of recurrent cough, and compared the results to those of isolated chronic cough.

Methods: Cross-sectional email survey in an elderly community-based population. Recurrent cough was defined as ≥ 3 cough episodes within one year (each lasting ≥ 1 week) and no current chronic cough. Isolated chronic cough was defined as current cough lasting ≥ 8 weeks and no recurrent cough.

Results: The prevalence of recurrent cough was 3.8% among all respondents ($n = 5983$). Recurrent cough was associated with asthma (aOR 3.32 (95% CI 2.13-5.18)), chronic rhinosinusitis (2.91 (1.89-4.46)), family history of chronic cough (2.59 (1.88-3.56)), analgesic intolerance (2.13 (1.27-3.57)), male gender (1.92 (1.39-2.66)), gastro-esophageal reflux disease (1.73 (1.21-2.47)), obstructive sleep apnoea (1.69 (1.23-2.32)), symptom sum (1.12 per symptom (1.03-1.22)), and younger age (0.96 per year (0.93-1.00)). Isolated chronic cough was associated with chronic rhinosinusitis (3.45 (2.39-4.97)), asthma (2.17 (1.38-3.41)), gastro-esophageal reflux disease (1.80 (1.32-2.47)), family history of chronic cough (1.80 (1.35-2.41)), obstructive sleep apnoea (1.49 (1.12-2.00)), symptom sum (1.18 per symptom (1.10-1.27)), and body mass index (0.96 per unit (0.93-1.00)). Among subjects with recurrent and isolated chronic cough, the prevalence of depressive symptoms were 7.7% and 4.2%, $p = 0.11$, the Leicester Cough Questionnaire total scores 15.2 (14.6-15.8) and 16.3 (16.0-16.6), $P = 0.001$, and the mean number of yearly cough-related doctor's visits 0.58 (0.45-0.71) and 0.36 (0.19-0.53), $P = 0.007$, respectively.

Conclusion: The risk factors and consequences of recurrent and isolated chronic cough were comparable. Recurrent cough seems beneficial to address in cough evaluation.

Keywords: Chronic cough; Epidemiology; Quality of life; Recurrent cough; Risk factors.

© 2023. The Author(s).

Conflict of interest statement

JTK has received grants from Kuopion Seudun Hengityssäätiö, Hengityssairauksien Tutkimussäätiö, Suomen Tuberkuloosin vastustamisyhdistyksen Säätiö, Väinö ja Laina Kiven Säätiö, and Suomen Kulttuurirahasto foundations. AML has received grants from Kuopion Seudun Hengityssäätiö, Hengityssairauksien Tutkimussäätiö, KYS:n Tutkimussäätiö, Suomen Tuberkuloosin Vastustamisyhdistyksen Säätiö, and Väinö ja Laina Kiven Säätiö Foundations, meeting attendance support from Boehringer Ingelheim and Novartis, and payment for lectures/group input meetings from Farmasian oppimiskeskus, Hengitysliitto, Duodecim, MSD, Chiesi and GlaxoSmithKline. HOK has received grants from Kuopion Seudun Hengityssäätiö and Hengityssairauksien Tutkimussäätiö Foundations, payments for lectures from Boehringer Ingelheim and MSD, and owns shares of a medical company Orion. The authors have no other financial or non-financial competing interests.

- [38 references](#)
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. 2023 Dec;201(6):531-544.

doi: 10.1007/s00408-023-00653-3. Epub 2023 Nov 7.

Assessment and Management of Cough in Idiopathic Pulmonary Fibrosis: A Narrative Review

[Shangxiang Liu](#)¹, [Xu Ye](#)²

Affiliations expand

- PMID: 37934241
- DOI: [10.1007/s00408-023-00653-3](https://doi.org/10.1007/s00408-023-00653-3)

Abstract

Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive, and fatal disease with an unknown cause. It is characterized by symptoms such as cough and breathlessness, which significantly impact patients' quality of life. Cough, in particular, has emerged as a burdensome symptom for individuals with IPF. The etiology of cough in IPF patients is believed to be complex, involving factors related to the disease itself, such as increased sensitivity of cough nerves, lung structural changes, inflammation, and genetic factors, as well as comorbidities and medication effects. Unfortunately, effective treatment options for cough in IPF remain limited, often relying on empirical approaches based on studies involving chronic cough patients in general and the personal experience of physicians. Medications such as opioids and neuromodulators are commonly prescribed but have shown suboptimal efficacy, imposing significant physical, psychological, and economic burdens on patients. However, there is hope on the horizon, as specific purinergic P2 receptor ligand-gated ion channel (P2X3) inhibitors have demonstrated promising antitussive effects in ongoing clinical trials. This review aims to provide a comprehensive overview of the evaluation and management of cough in IPF patients, as well as highlight emerging pharmacological and non-pharmacological approaches that target the cough reflex and are currently being investigated in clinical settings.

Keywords: Assessment; Cough; Idiopathic pulmonary fibrosis; Management; Pulmonary fibrosis.

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. 2023 Dec;201(6):555-564.

doi: 10.1007/s00408-023-00647-1. Epub 2023 Oct 13.

[Feasibility and Utility of a Smartphone Application–Based Longitudinal Cough Monitoring in Chronic Cough Patients in a Real–World Setting](#)

[Seung-Eun Lee¹](#), [Matthew Rudd^{2,3}](#), [Tae-Hwa Kim¹](#), [Ji-Yoon Oh⁴](#), [Ji-Hyang Lee⁴](#), [Lola Jover³](#), [Peter M Small^{3,5}](#), [Kian Fan Chung⁶](#), [Woo-Jung Song⁷](#)

Affiliations expand

- PMID: 37831232

- DOI: [10.1007/s00408-023-00647-1](https://doi.org/10.1007/s00408-023-00647-1)

Abstract

Purpose: This study evaluated the feasibility and utility of longitudinal cough frequency monitoring with the Hyfe Cough Tracker, a mobile application equipped with cough-counting artificial intelligence algorithms, in real-world patients with chronic cough.

Methods: Patients with chronic cough (> 8-week duration) were monitored continuously for cough frequency with the Hyfe app for at least one week. Cough was also evaluated using the Leicester Cough Questionnaire (LCQ) and daily cough severity scoring (0-10). The study analyzed adherence rate, the correlation between objective cough frequency and subjective scores, day-to-day variability, and patient experience.

Results: Of 65 subjects consecutively recruited, 43 completed the study. The median cough monitoring duration was 13.9 days, with a median adherence of 91%. Study completion was associated with baseline cough severity, and the adherence rate was higher in younger subjects. Cross-sectional correlation analyses showed modest correlations between objective and subjective cough measures at the group level. However, in time series correlation analyses, correlations between objective and subjective measures widely varied across individuals. Cough frequency had greater day-to-day variability than daily cough severity scores in most subjects. A patient experience survey found that 70% of participants found the cough monitoring helpful, 86% considered it acceptable, and 84% felt it was easy to use.

Conclusion: Monitoring cough frequency longitudinally for at least one week may be feasible. The substantial day-to-day variability in objective cough frequency highlights the need for continuous monitoring. Grasping the implications of daily cough variability is crucial in both clinical practice and clinical trials.

Keywords: Chronic cough; Cough frequency; Cough monitor; Patient-reported outcome.

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Observational Study

Pediatr Pulmonol

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. 2023 Dec;58(12):3466-3477.

doi: 10.1002/ppul.26677. Epub 2023 Sep 22.

Factors influencing behavioral cough suppression therapy in children with nonspecific chronic cough

[Robert Brinton Fujiki](#)¹, [Miranda L Wright](#)^{2,3}, [Amanda E Fujiki](#)⁴, [Susan L Thibeault](#)¹

Affiliations expand

- PMID: 37737562
- DOI: [10.1002/ppul.26677](https://doi.org/10.1002/ppul.26677)

Abstract

Background: Behavioral cough suppression therapy (BCST) with a speech-language pathologist is a common treatment for chronic nonspecific cough (a.k.a., tic cough) in children. Yet, the outcomes and duration of pediatric BCST have eluded formal investigation. This study examined whether BCST improves cough in children with nonspecific cough and factors that predict the course of treatment. Additionally, the cough characteristics and comorbidities associated with the condition were examined.

Methods: A retrospective, observational cohort design was utilized. Cough characteristics, medical history, and BCST treatment details and outcomes for 151 children were extracted from the electronic medical record of a large outpatient pediatric otolaryngology clinic.

Results: Cough was dry and onset unaccompanied by illness in most cases. Roughly half of patients reported gradual onset and cough proceeded by tickle. On average, patients experienced symptoms for 19 months (SD = 20.09) before diagnosis. Rates of comorbid General Anxiety Disorder were elevated compared to pediatric norms. Additionally, high rates of asthma (22.1%), reflux (62.3%), and disordered sleep breathing (19.2%) were observed. Common findings on laryngoscopy included interarytenoid edema and erythema. Vocal fold changes were observed in 22.9% of children. BCST reduced cough in 92.5% of patients following an average of 1.7 sessions. Comorbid behavioral health diagnoses ($p = 0.013$) or induced laryngeal obstruction symptoms ($p = 0.025$) were significant predictors of increased therapy sessions. Cough proceeded by tickle significantly predicted fewer sessions in therapy ($p = 0.011$).

Interpretation: Although randomized clinical trials are needed, these data suggest that BCST is a low-risk, effective treatment for children with nonspecific cough.

Keywords: chronic cough; pediatrics; tic cough.

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- [56 references](#)

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. 2023 Dec;39(12):1823-1839.

doi: 10.1007/s12264-023-01104-y. Epub 2023 Aug 22.

Neural Mechanisms Underlying the Coughing Reflex

[Haicheng Lu](#)^{1,2}, [Peng Cao](#)^{3,4}

Affiliations expand

- PMID: 37606821
- PMCID: PMC10661548 (available on 2024-12-01)
- DOI: [10.1007/s12264-023-01104-y](https://doi.org/10.1007/s12264-023-01104-y)

Abstract

Breathing is an intrinsic natural behavior and physiological process that maintains life. The rhythmic exchange of gases regulates the delicate balance of chemical constituents within an organism throughout its lifespan. However, chronic airway diseases, including asthma and chronic obstructive pulmonary disease, affect millions of people worldwide. Pathological airway conditions can disrupt respiration, causing asphyxia, cardiac arrest, and potential death. The innervation of the respiratory tract and the action of the immune system confer robust airway surveillance and protection against environmental irritants and pathogens. However, aberrant activation of the immune system or sensitization of the nervous system can contribute to the development of autoimmune airway disorders. Transient receptor potential ion channels and voltage-gated Na⁺ channels play critical roles in sensing noxious stimuli within the respiratory tract and interacting with the immune system to generate neurogenic inflammation and airway hypersensitivity. Although recent studies have revealed the involvement of nociceptor neurons in airway diseases, the further neural circuitry underlying airway protection remains elusive. Unraveling the mechanism underpinning neural circuit regulation in the airway may provide precise therapeutic strategies and valuable insights into the management of airway diseases.

Keywords: Airway disease; Cough; Na⁺ channel; Neural circuit; Transient receptor potential; Treatment.

Conflict of interest statement

All authors claim that there are no conflicts of interest.

- [136 references](#)

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. 2023 Dec;20(1):126-134.

doi: 10.1080/15412555.2023.2169120.

Incidence and Healthcare Burden of Pertussis among Older Adults with and without Pre-Existing Chronic Obstructive Pulmonary Disease or Asthma in South Korea

[Jing Chen](#)¹, [Ju-Young Shin](#)^{2,3}, [Hyungwoo Kim](#)⁴, [Ju Hwan Kim](#)², [Ahhyung Choi](#)², [Hee Jin Cheong](#)⁵, [Yeon-Mok Oh](#)⁶, [Adrienne Guignard](#)⁷, [Sumitra Shantakumar](#)¹

Affiliations expand

- PMID: 37093711
- DOI: [10.1080/15412555.2023.2169120](https://doi.org/10.1080/15412555.2023.2169120)

Abstract

A retrospective cohort study was conducted to examine trends in the incidence and burden of pertussis among adults ≥ 50 years in South Korea, with/without pre-existing chronic obstructive pulmonary disease (COPD) or asthma. The nationwide Health Insurance Review and Assessment Service (HIRA) database was used to identify patients ≥ 50 years diagnosed with pertussis (2009-2018). Mean annual incidence of pertussis per 100 000 persons and overall mean incidence rate ratios (IRR) were calculated for patients with pre-existing COPD or asthma versus those with neither. Incremental healthcare costs (all-cause and pertussis-related) and healthcare utilisation (number of outpatient visits, emergency room visits, and number and length of hospitalisations) up to 12 months after, compared to 3 months before pertussis diagnosis, were also measured for each group (matched on sex, age, and Charlson Comorbidity Index). Of 1011 pertussis cases, 175 had asthma, 96 had COPD (not mutually exclusive), and 796 had neither. Overall mean pertussis incidence was 2.5, 3.4, and 0.5 for adults with pre-existing COPD, asthma, and those with neither. IRR (95% confidence interval) of pertussis for adults with pre-existing COPD and asthma was 4.9 (4.0-6.1) and 6.7 (5.7-7.9). Both COPD-pertussis and asthma-pertussis groups had higher mean incremental all-cause costs and length of hospitalisations than the general-pertussis group 3 months following pertussis diagnosis. In conclusion, individuals ≥ 50 years in South Korea with pre-existing COPD or asthma were at an increased risk of being diagnosed with pertussis and had higher healthcare resource utilisation than those without these conditions.

Keywords: Adult; COPD; South Korea; asthma; pertussis; vaccination; whooping cough.

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Expert Opin Emerg Drugs

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. 2023 Dec;28(2):67-77.

doi: 10.1080/14728214.2023.2203912. Epub 2023 Apr 24.

Emerging drugs in the treatment of chronic cough

[Danica Brister](#)¹, [Mustafaa Wahab](#)¹, [Moaaz Rashad](#)¹, [Nermin Diab](#)¹, [Martin Kolb](#)^{1,2}, [Imran Satia](#)^{1,2}

Affiliations expand

- PMID: 37060576
- DOI: [10.1080/14728214.2023.2203912](https://doi.org/10.1080/14728214.2023.2203912)

Abstract

Introduction: Chronic cough is a debilitating condition that is among the most common reasons for seeking medical attention yet remains challenging to manage. Identifying an underlying respiratory, nasal, or upper gastrointestinal disease triggering cough is the first step in assessment, but once this has been ruled out or adequately treated, many patients remain troubled with chronic cough.

Areas covered: This narrative review discusses the role of existing treatments and describes the current research landscape for the development of new therapies for chronic cough greater than 8 weeks that is refractory (RCC) or unexplained (UCC). The literature search includes published studies found on pubmed and conference abstracts until 2023.

Expert opinion: RCC/UCC can occur due to neuronal dysregulation of the vagus nerve or central nervous system. Hence, novel anti-tussives have targeted ion channels involved in the neuronal signaling which triggers cough. Although some therapies targeting receptors such as TRPV1 have failed to show efficacy, P2X3 antagonists have emerged as the most

promising therapy for patients impacted by chronic cough. Disease-specific therapies such as for idiopathic pulmonary fibrosis are in early development.

Keywords: Chronic cough; P2X3 antagonist; neuromodulator; novel therapy; refractory chronic cough.

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. 2023 Dec;20(1):71-79.

doi: 10.1080/15412555.2022.2141622. Epub 2023 Jan 19.

[Cough Assessment and Management in Pulmonary Rehabilitation- A Canadian Survey](#)

[Ana Maria Illicic](#)¹, [Dina Brooks](#)^{1,2,3}, [Michelle Kho](#)^{1,4,5}, [Roger Goldstein](#)^{2,3}, [Ana Oliveira](#)^{1,2,6,7}

Affiliations expand

- PMID: 36656707
- DOI: [10.1080/15412555.2022.2141622](https://doi.org/10.1080/15412555.2022.2141622)

Abstract

Pulmonary rehabilitation is a cornerstone intervention for controlling respiratory symptoms in people with chronic respiratory diseases. Chronic cough affects up to 90% of people with chronic respiratory diseases, however, it is currently unknown whether chronic cough is assessed and/or managed in pulmonary rehabilitation. This study aimed to determine if and how chronic cough is assessed and managed in pulmonary rehabilitation. This was a cross-sectional study. Pulmonary rehabilitation programs in Canada were identified *via* online websites. A representative from each program was invited to complete an online survey including the following topics: program demographics, assessment and management practices, and barriers and facilitators. Of 133 programs contacted, 31 returned a completed survey (23% response rate). Approximately half (52%) of respondents reported enrolling patients with chronic cough. Of those, 45% reported assessing and 62% reported intervening in chronic cough. Inadequate knowledge of assessment and management techniques was commonly identified to be a barrier and increased education was suggested as a possible facilitator. Based on pulmonary rehabilitation programs that responded to our survey, chronic cough is a prevalent symptom; however, it is scarcely assessed and managed. A need for structured education and the use of standardised strategies were reported as facilitators to the assessment and management of chronic cough in pulmonary rehabilitation.

Keywords: Chronic obstructive pulmonary disease (COPD); lung disease; management; questionnaire; rehabilitation.

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. 2023 Nov 27;75(4):389-394.

doi: 10.3138/ptc-2021-0081. eCollection 2023 Nov.

A Non-Pharmacological Cough Therapy for People with Interstitial Lung Diseases: A Case Report

[Sabrina Dasouki](#)¹, [Shirley Quach](#)^{1,2}, [Renata Mancopes](#)^{3,4}, [Sarah Chamberlain Mitchell](#)⁵, [Roger Goldstein](#)^{2,6}, [Dina Brooks](#)^{1,2,6}, [Ana Oliveira](#)^{1,2,7,8}

Affiliations expand

- PMID: 38037577
- PMCID: PMC10686298 (available on 2024-11-27)
- DOI: [10.3138/ptc-2021-0081](https://doi.org/10.3138/ptc-2021-0081)

Abstract

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

Purpose: To explore the feasibility of a non-pharmacological cough control therapy (CCT) customized for a client with interstitial lung disease (ILD).

Client description: An 83-year-old female with hypersensitivity pneumonitis, and chronic cough for 18 years treated previously with pharmacological treatment for the underlying lung disease and gastroesophageal reflux disease, as well as lozenges and breathing and relaxation strategies.

Intervention: Four cough education and self-management sessions (45-60 minutes each) facilitated by a physiotherapist and speech-language pathologist via videoconference were conducted. Session topics included mechanisms of cough in ILD, breathing and larynx role in cough control, trigger identification, cough suppression and control strategies, and psychosocial support towards behaviour change using motivational interviewing.

Measures and outcome: The following assessments were conducted prior to and one week after the intervention: semi-structured interviews, Leicester Cough Questionnaire, King's Brief Interstitial Lung Disease questionnaire, Functional Assessment of Chronic

Illness Therapy Fatigue Scale, modified Borg Scale for severity and intensity of cough, and the Global Rating of Change Questionnaire.

Implications: Implementing the CCT was feasible. The client reported increased perceived cough control, a reduction in exhaustion from coughing bouts, and a better understanding of the mechanisms behind cough management and suppression. Improvements were also observed in cough-related quality of life, severity, and intensity.

Keywords: cough; education; lung diseases; rehabilitation; self-management.

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Conflict of interest statement

Competing Interests: None declared. This study is funded by the Lung Health Foundation through an Ontario Respiratory Care Society grant.

- [40 references](#)

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

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Editorial

Am J Respir Crit Care Med

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. 2023 Dec 1;208(11):1147-1148.

doi: 10.1164/rccm.202310-1827ED.

Precision Endotyping in Bronchiectasis

[Pamela J McShane](#)¹

Affiliations expand

- PMID: 37917354
- DOI: [10.1164/rccm.202310-1827ED](https://doi.org/10.1164/rccm.202310-1827ED)

No abstract available

Comment on

- [Inflammatory Molecular Endotypes in Bronchiectasis: A European Multicenter Cohort Study.](#)
Choi H, Ryu S, Keir HR, Giam YH, Dicker AJ, Perea L, Richardson H, Huang JTJ, Cant E, Blasi F, Pollock J, Shteinberg M, Finch S, Aliberti S, Sibila O, Shoemark A, Chalmers JD. *Am J Respir Crit Care Med*. 2023 Dec 1;208(11):1166-1176. doi: 10.1164/rccm.202303-0499OC. PMID: 37769155

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Respirol Case Rep

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- . 2023 Oct 31;11(12):e01240.

X-linked inheritance of primary ciliary dyskinesia and retinitis pigmentosa due to *RPGR* variant: A case report and literature review

[Aoi Kuroda](#)¹, [Ho Namkoong](#)², [Eri Iwami](#)¹, [Akihiro Tsutsumi](#)¹, [Takahiro Nakajima](#)¹, [Hajime Shinoda](#)³, [Yusaku Katada](#)³, [Jiro Iimura](#)⁴, [Hisato Suzuki](#)⁵, [Kenjiro Kosaki](#)⁵, [Takeshi Terashima](#)¹

Affiliations expand

- PMID: 37915370
- PMCID: [PMC10616737](#)
- DOI: [10.1002/rcr2.1240](#)

Free PMC article

Abstract

Bronchiectasis is a chronic respiratory condition characterized by irreversible bronchial dilation, often caused by infection or inflammation. It can be associated with primary ciliary dyskinesia (PCD), a hereditary disorder affecting cilia function in various organs and flagella. PCD's genetic heterogeneity leads to varying disease severity. PCD may be more prevalent in Asia, but its diagnosis is often delayed in Japan. This study reviewed a case of PCD and retinitis pigmentosa (RP) with the relevant literature. The patient had a persistent cough, sputum, and diffuse bronchiectasis. He was diagnosed with a combination of PCD and RP, with the presence of an X-linked retinitis pigmentosa GTPase regulator (*RPGR*) variant confirmed through electron microscopy, retinal scan, and genetic testing. Although co-occurrence of bronchiectasis and RP is rare, PCD should be considered in cases of persistent wet cough in childhood or unidentified bronchiectasis aetiology. Ophthalmologists should consider concomitant PCD in RP patients.

Keywords: bronchiectasis; inherited retinal dystrophy; primary ciliary dyskinesia; retinitis pigmentosa; retinitis pigmentosa GTPase regulator.

Conflict of interest statement

None declared.

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

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[Review](#)

Clin Chest Med

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. 2023 Dec;44(4):731-742.

doi: 10.1016/j.ccm.2023.07.005.

[Investigation and Management of Bronchiectasis in Nontuberculous Mycobacterial Pulmonary Disease](#)

[Pamela J McShane](#)¹

Affiliations expand

- PMID: 37890912
- DOI: [10.1016/j.ccm.2023.07.005](https://doi.org/10.1016/j.ccm.2023.07.005)

Abstract

Patients with nontuberculous mycobacterial (NTM) lung infection require life-long attention to their bronchiectasis, whether or not their NTM infection has been cured. The identification of the cause of bronchiectasis and/or coexisting diseases is important because it may affect therapeutic strategies. Airway clearance is the mainstay of bronchiectasis management. It can include multiple breathing techniques, devices, and mucoactive agents. The exact airway clearance regimen should be customized to each individual patient. Chronic pathogenic airway bacteria, such as *Pseudomonas aeruginosa*, may warrant consideration of eradication therapy and/or chronic use of maintenance inhaled antibiotics.

Keywords: Airway clearance; Bronchiectasis; *Pseudomonas aeruginosa*; Pulmonary rehabilitation.

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Am J Respir Crit Care Med

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. 2023 Dec 1;208(11):1166-1176.

doi: 10.1164/rccm.202303-0499OC.

Inflammatory Molecular Endotypes in Bronchiectasis: A European Multicenter Cohort Study

[Hayoung Choi](#)^{1,2}, [Soorack Ryu](#)³, [Holly R Keir](#)¹, [Yan Hui Giam](#)¹, [Alison J Dicker](#)¹, [Lidia Perea](#)¹, [Hollian Richardson](#)¹, [Jeffrey T J Huang](#)⁴, [Erin Cant](#)¹, [Francesco Blasi](#)^{5,6}, [Jennifer Pollock](#)¹, [Michal Shteinberg](#)⁷, [Simon Finch](#)¹, [Stefano Aliberti](#)^{8,9}, [Oriol Sibila](#)¹⁰, [Amelia Shoemark](#)¹, [James D Chalmers](#)¹

Affiliations expand

- PMID: 37769155
- DOI: [10.1164/rccm.202303-0499OC](https://doi.org/10.1164/rccm.202303-0499OC)

Abstract

Rationale: Although inflammation and infection are key disease drivers in bronchiectasis, few studies have integrated host inflammatory and microbiome data to guide precision medicine. **Objectives:** To identify clusters among patients with bronchiectasis on the basis of inflammatory markers and to assess the association between inflammatory endotypes, microbiome characteristics, and exacerbation risk. **Methods:** Patients with stable bronchiectasis were enrolled at three European centers, and cluster analysis was used to stratify the patients according to the levels of 33 sputum and serum inflammatory markers. Clusters were compared in terms of microbiome composition (16S ribosomal RNA sequencing) and exacerbation risk over a 12-month follow-up. **Measurements and Main Results:** A total of 199 patients were enrolled (109 [54.8%] female; median age, 69 yr). Four clusters of patients were defined according to their inflammatory profiles: cluster 1, milder neutrophilic inflammation; cluster 2, mixed-neutrophilic and type 2; cluster 3, most severe neutrophilic; and cluster 4, mixed-epithelial and type 2. Lower microbiome diversity was associated with more severe inflammatory clusters ($P < 0.001$), and β -diversity analysis demonstrated distinct microbiome profiles associated with each inflammatory cluster ($P = 0.001$). Proteobacteria and *Pseudomonas* at phylum and genus levels, respectively, were more enriched in clusters 2 and 3 than in clusters 1 and 4. Furthermore, patients in cluster 2 (rate ratio [RR], 1.49; 95% confidence interval [CI], 1.16-1.92) and cluster 3 (RR, 1.61; 95% CI, 1.12-2.32) were at higher risk of exacerbation over a 12-month follow-up compared with cluster 1, even after adjustment for prior exacerbation history. **Conclusions:** Bronchiectasis inflammatory endotypes are associated with distinct microbiome profiles and future exacerbation risk.

Keywords: biomarkers; bronchiectasis; cluster analysis; inflammation; microbiome.

Comment in

- [Precision Endotyping in Bronchiectasis.](#)

McShane PJ. *Am J Respir Crit Care Med*. 2023 Dec 1;208(11):1147-1148. doi: 10.1164/rccm.202310-1827ED. PMID: 37917354 No abstract available.

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. 2023 Dec;20(1):224-232.

doi: 10.1080/15412555.2023.2228903.

[Development of a Diagnostic Nomogram to Predict CAP in Hospitalized Patients with AECOPD](#)

[Nafeisa Dilixiati](#)¹, [Mengyu Lian](#)¹, [Ziliang Hou](#)¹, [Jie Song](#)¹, [Jingjing Yang](#)¹, [Ruiyan Lin](#)¹, [Jinxiang Wang](#)¹

Affiliations [expand](#)

- PMID: 37403800

- DOI: [10.1080/15412555.2023.2228903](https://doi.org/10.1080/15412555.2023.2228903)

Abstract

The purpose of this study was to establish a nomogram for predicting community-acquired pneumonia (CAP) in hospitalized patients with acute exacerbations of chronic obstructive pulmonary disease (AECOPD). The retrospective cohort study included 1249 hospitalized patients with AECOPD between January 2012 and December 2019. The patients were divided into pneumonia-complicating AECOPD (pAECOPD) and non-pneumonic AECOPD (npAECOPD) groups. The least absolute shrinkage and selection operator (LASSO) regression and multivariate logistic regression were utilized to identify prognostic factors. A prognostic nomogram model was established, and the bootstrap method was used for internal validation. Discrimination and calibration of the nomogram model were evaluated by receiver operating characteristic (ROC) curve, calibration curve, and decision curve analysis (DCA). Logistic and LASSO regression analysis showed that C-reactive protein (CRP) > 10 mg/L, albumin (Alb) <40 g/L, alanine transferase (ALT) >50 U/L, fever, bronchiectasis, asthma, previous hospitalization for pAECOPD in the past year (Pre-H for pAECOPD), and age-adjusted Charlson score (aCCI) ≥ 6 were independent predictors of pAECOPD. The area under the ROC curve (AUC) of the nomogram model was 0.712 (95% CI: 0.682-0.741). The corrected AUC of internal validation was 0.700. The model had well-fitted calibration curves and good clinical usability DCA curve. A nomogram model was developed to assist clinicians in predicting the risk of pAECOPD. **China Clinical Trials Registry:** ChiCTR2000039959.

Keywords: Chronic obstructive pulmonary disease; community-acquired pneumonia; exacerbations; logistic regression; predictive model.

SUPPLEMENTARY INFO

MeSH terms, Associated dataexpand

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Immunol Med

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. 2023 Dec;46(4):153-157.

doi: 10.1080/25785826.2023.2210366. Epub 2023 May 13.

Clinical practice guideline for activated phosphatidyl inositol 3-kinase-delta syndrome in Japan

[Kunihiko Moriya](#)¹, [Kanakano Mitsui-Sekinaka](#)¹, [Yujin Sekinaka](#)¹, [Akifumi Endo](#)², [Hirokazu Kanegane](#)³, [Tomohiro Morio](#)⁴, [Kohsuke Imai](#)¹, [Shigeaki Nonoyama](#)¹

Affiliations expand

- PMID: 37178059
- DOI: [10.1080/25785826.2023.2210366](https://doi.org/10.1080/25785826.2023.2210366)

Abstract

Activated phosphatidyl inositol 3-kinase-delta syndrome (APDS) due to gain-of-function variant in the class IA PI3K catalytic subunit p110 δ (responsible gene: PIK3CD) was described in 2013. The disease is characterized by recurrent airway infections and bronchiectasis. It is associated with hyper-IgM syndrome due to the defect of immunoglobulin class switch recombination and decreased CD27-positive memory B cells. Patients also suffered from immune dysregulations, such as lymphadenopathy, autoimmune cytopenia or enteropathy. T-cell dysfunction due to increased senescence is associated with a decrease in CD4-positive T lymphocytes and CD45RA-positive naive T lymphocytes, along with increased susceptibility to Epstein-Barr virus/cytomegalovirus infections. In 2014, loss-of-function (LOF) mutation of p85 α (responsible gene: PIK3R1), a regulatory subunit of p110 δ , was identified as a causative gene, followed in 2016 by the identification of the LOF mutation of PTEN, which dephosphorylates PIP3, leading to the differentiation of APDS1 (PIK3CD-GOF), APDS2 (PIK3R1-LOF) and APDS-L (PTEN-LOF). Since the pathophysiology of patients with APDS varies with a wide range of severity, it is crucial that patients receive appropriate treatment and management. Our research group

created a disease outline and a diagnostic flow chart and summarized clinical information such as the severity classification of APDS and treatment options.

Keywords: APDS; diagnostic flow chart; hyper-IgM syndrome; immune dysregulations.

- [Cited by 1 article](#)

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. 2023 Dec;55(1):2204449.

doi: 10.1080/07853890.2023.2204449.

[Clinical significance of microscopic polyangiitis with interstitial lung disease and bronchiectasis: probability of preexisting comorbidities](#)

[Yun Zhang](#)¹, [Qunli Ding](#)¹, [Chengna Lv](#)¹, [Yanan Ying](#)¹, [Zekai Cen](#)¹, [Haijun Zhou](#)², [Tingting Wu](#)¹

Affiliations expand

- PMID: 37126372

- PMCID: [PMC10134949](#)
- DOI: [10.1080/07853890.2023.2204449](#)

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Abstract

Background: The association between pulmonary involvement and microscopic polyangiitis (MPA) has been increasingly recognized in recent years. Whether interstitial lung disease (ILD) and bronchiectasis (BE) are disease manifestations of MPA, preexisting comorbidities or important complications remains unclear. The purpose of this study was to determine the clinical characteristics and prognosis of MPA with pulmonary involvement to further guide clinical management.

Methods: The data for 97 patients with a definitive diagnosis of MPA were retrospectively reviewed. The MPA diagnosis was based on the 2012 revised Chapel Hill Consensus Conference (CHCC) criteria. The baseline clinical information and laboratory parameters were collected and analysed at each patient's initial diagnosis.

Results: Forty-seven out of the 97 (48.5%) patients who were diagnosed with MPA presented with pulmonary involvement, including 37 patients with ILD, 12 patients with BE and two patients with diffuse alveolar haemorrhage (DAH). ILD and BE antedated MPA in 56.76% and 75.00% of the patients, respectively. Compared with that in the MPA-BE group, the serum LDH level (222.86 ± 68.19 vs. 171.58 ± 31.43 , $p = .016$) in the MPA-ILD group was significantly higher. In the multivariate Cox analysis, elevated serum creatinine (HR 4.08, confidence interval (CI) 1.38-12.05, $p = .011$) was an independent risk factor for shorter survival in MPA patients with pulmonary involvement, and treatment with glucocorticoid pulse cyclophosphamide therapy (HR 0.095, 95% CI 0.019-0.47, $p = .004$) was independently associated with prolonged survival. Among the patients in the MPA-ILD group, acute exacerbations of ILD (HR 4.55 CI 1.16-17.86, $p = .029$) and elevated serum creatinine (HR 4.95, CI 1.39-17.54, $p = .014$) were independently associated with a poor prognosis, and treatment with glucocorticoids (HR 0.057, 95% CI 0.012-0.28, $p < .001$) was independently associated with significant prolongation of survival.

Conclusions: Patients with MPA have a high prevalence of pulmonary involvement, and ILD is the most common subtype of MPA. ILD and BE can be considered preexisting comorbidities of MPA. Elevated serum creatinine was associated with shorter survival. However, remission induction regimens with glucocorticoids and/or immunosuppressants may improve this outcome.

Keywords: Vasculitis; bronchiectasis; interstitial lung disease; microscopic polyangiitis.

Conflict of interest statement

No potential conflict of interest was reported by the author(s).

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

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. 2023 Dec;12(1):2202277.

doi: 10.1080/22221751.2023.2202277.

[Sputum pathogen spectrum and clinical outcomes of upper respiratory tract infection in bronchiectasis exacerbation: a prospective cohort study](#)

[Yan Huang](#)^{1,2}, [Chun-Lan Chen](#)³, [Lai-Jian Cen](#)¹, [Hui-Min Li](#)¹, [Zhen-Hong Lin](#)¹, [Si-Yu Zhu](#)⁴, [Chong-Yang Duan](#)⁴, [Ri-Lan Zhang](#)¹, [Cui-Xia Pan](#)¹, [Xiao-Fen Zhang](#)¹, [Xiao-Xian Zhang](#)¹, [Zhen-Feng He](#)¹, [Ming-Xin Shi](#)¹, [Nan-Shan Zhong](#)¹, [Wei-Jie Guan](#)^{1,5,6}

Affiliations expand

- PMID: 37038356
- PMCID: [PMC10167879](#)
- DOI: [10.1080/22221751.2023.2202277](#)

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Abstract

Upper respiratory tract infection (URTI) is common in humans. We sought to profile sputum pathogen spectrum and impact of URTI on acute exacerbation of bronchiectasis (AE). Between March 2017 and December 2021, we prospectively collected sputum from adults with bronchiectasis. We stratified AEs into events related (URTI-AE) and unrelated to URTI (non-URTI-AE). We captured URTI without onset of AE (URTI-non-AE). We did bacterial culture and viral detection with polymerase chain reaction, and explored the pathogen spectrum and clinical impacts of URTI-AE via longitudinal follow-up. Finally, we collected 479 non-AE samples (113 collected at URTI-non-AE and 225 collected at clinically stable) and 170 AE samples (89 collected at URTI-AE and 81 collected at non-URTI-AE). The viral detection rate was significantly higher in URTI-AE (46.1%) than in non-URTI-AE (4.9%) and URTI-non-AE (11.5%) (both $P < 0.01$). Rhinovirus [odds ratio (OR): 5.00, 95% confidence interval (95%CI): 1.06-23.56, $P = 0.03$] detection was independently associated with URTI-AE compared with non-URTI-AE. URTI-AE tended to yield higher viral load and detection rate of rhinovirus, metapneumovirus and bacterial shifting compared with URTI-non-AE. URTI-AE was associated with higher initial viral loads (esp. rhinovirus, metapneumovirus), greater symptom burden (higher scores of three validated questionnaires) and prolonged recovery compared to those without. Having experienced URTI-AE predicted a greater risk of future URTI-AE (OR: 10.90, 95%CI: 3.60-33.05). In summary, URTI is associated with a distinct pathogen spectrum and aggravates bronchiectasis exacerbation, providing the scientific rationale for the prevention of URTI to hinder bronchiectasis progression.

Keywords: Upper respiratory tract infections; bronchiectasis; exacerbation; symptom burden; virus.

Conflict of interest statement

No potential conflict of interest was reported by the author(s).

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

SUPPLEMENTARY INFO

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J Child Health Care

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. 2023 Dec;27(4):587-598.

doi: 10.1177/13674935221082437. Epub 2022 Apr 4.

Sore and tired. A qualitative study exploring the symptom experience of youth with bronchiectasis

[Julie Blamires](#)¹, [Annette Dickinson](#)¹, [Catherine A Byrnes](#)², [El Shadan Tautolo](#)³

Affiliations [expand](#)

- PMID: 35379016
- DOI: [10.1177/13674935221082437](https://doi.org/10.1177/13674935221082437)

Abstract

This qualitative study was conducted to explore the experiences of youth living with bronchiectasis in New Zealand (NZ). Semi-structured interviews were conducted with youth with bronchiectasis. Key themes were identified using an inductive approach through constant comparative analysis and guided by Thorne's interpretive description (ID). Fifteen young people of mixed ethnicity (nine females and six males) aged between 13 and 23 years participated. Three key themes 'sore and tired', 'life interrupted and 'looking after self' were identified. This paper will focus on 'sore and tired' and its three subthemes which describe the participants symptom experience. While there was variability in physical symptom patterns, cough, soreness and fatigue were prominent features impacting physical, emotional and social aspects of day-to-day life. All identified pervasive and profound fatigue as significant. The identification of prodromal symptoms provides opportunity for greater appreciation of the varied and personal symptom experience of young people with bronchiectasis. Early identification of these symptoms and inclusion within management plans for escalating treatment has the potential to improve outcomes, reducing delays in seeking additional medical management and preventing further exacerbation.

Keywords: Adolescent; New Zealand; bronchiectasis; qualitative research.

Conflict of interest statement

Declaration of conflicting interestsThe author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

SUPPLEMENTARY INFO

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Review

Nijmegen Breakage Syndrome

[Raymonda Varon](#)¹, [Ilja Demuth](#)², [Krystyna H Chrzanowska](#)³

[Margaret P Adam](#), [Jerry Feldman](#), [Ghayda M Mirzaa](#), [Roberta A Pagon](#), [Stephanie E Wallace](#), [Lora JH Bean](#), [Karen W Gripp](#), [Anne Amemiya](#)

, editors.

In: GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993.

1999 May 17 [updated 2023 Nov 30].

Affiliations expand

- PMID: 20301355
- Bookshelf ID: [NBK1176](#)

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Excerpt

Clinical characteristics: Nijmegen breakage syndrome (NBS) is characterized by progressive microcephaly, early growth deficiency that improves with age, recurrent respiratory infections, an increased risk for malignancy (primarily lymphoma), and premature ovarian failure in females. Developmental milestones are attained at the usual time during the first year; however, borderline delays in development and hyperactivity may be observed in early childhood. Intellectual abilities tend to decline over time. Recurrent pneumonia and bronchitis may result in respiratory failure and early death. Other reported malignancies include solid tumors (e.g., medulloblastoma, glioma, rhabdomyosarcoma).

Diagnosis/testing: The diagnosis of NBS is established in a proband with characteristic clinical features and biallelic pathogenic variants in *NBN* on molecular genetic testing and/or absent nibrin protein on immunoblotting assay.

Management: *Treatment of manifestations:* Standard antimicrobial therapies for infections; immunoglobulin replacement therapy in individuals with severe hypogammaglobulinemia and frequent infections; acellular vaccines; standard treatment of bronchiectasis and pulmonary infections; chemotherapy protocols for lymphoid malignancies adapted to individual tolerance; treatment of solid tumors adapted to individual tolerance; consideration of hematopoietic stem cell transplantation; hormone replacement therapy for females who have hypergonadotropic hypogonadism.

Surveillance:

- **For affected individuals.** Periodic follow up to monitor physical growth, infection frequency, and developmental progress; lifelong monitoring of immune biomarkers; monitor for malignancy and particularly in those with weight loss, fever, weakness, enlargement of peripheral lymph nodes, dyspnea, cough, and hepatosplenomegaly (assessment should be considered using ultrasonography, MRI, biopsy); monitor pubertal progression in both sexes and for premature ovarian insufficiency in females; monthly breast self-examination when hormone replacement therapy is administered; assess cognitive developmental and intellectual abilities before starting school and follow up periodically.
- **For heterozygous adults.** Monitor for malignancy, particularly breast cancer in women and prostate cancer in men.

Agents/circumstances to avoid: Because the cells from individuals with NBS are radiosensitive in vitro, doses of radiation used in radiotherapy need to be reduced. Unnecessary exposure to imaging studies that use ionizing radiation (plain radiograph, CT scan) should be avoided and use of MRI and/or ultrasound considered. Live vaccines (e.g., live vaccines for tuberculosis, measles, mumps, rubella, and varicella) should not be given.

Evaluation of relatives at risk: It is appropriate to offer molecular genetic testing for the familial *NBN* pathogenic variants to apparently asymptomatic adult relatives of an affected individual in order to identify family members who are heterozygous for an *NBN* pathogenic variant and would benefit from monitoring for malignancy.

Genetic counseling: NBS is inherited in an autosomal recessive manner. At conception, each sib of an affected individual has a 25% chance of inheriting both pathogenic variants and being affected, a 50% chance of inheriting one pathogenic variant and being a heterozygote, and a 25% chance of inheriting neither of the familial *NBN* pathogenic variants. Heterozygotes are not at risk for NBS. However, heterozygous *NBN* pathogenic variants may be associated with an increased risk for breast cancer in women and prostate cancer in men. Carrier testing for at-risk family members and prenatal and preimplantation genetic testing are possible if the pathogenic variants in the family are known.

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. 2023 Nov 28:1-9.

doi: 10.1080/09593985.2023.2286526. Online ahead of print.

[Comparison of respiratory functions, muscle strength, and physical activity among children with primary ciliary dyskinesia with and without Kartagener's syndrome and healthy controls](#)

[Merve Fırat](#)¹, [Şeyma Mutlu](#)², [Betül Yoleri](#)³, [Meral Boşnak Güçlü](#)³

Affiliations [expand](#)

- PMID: 38018157
- DOI: [10.1080/09593985.2023.2286526](https://doi.org/10.1080/09593985.2023.2286526)

Abstract

Introduction: Kartagener's syndrome (KS), consisting of bronchiectasis, situs inversus totalis, and sinusitis, is a subtype of primary ciliary dyskinesia (PCD). The presence of KS may affect respiratory and physical functions.

Purpose: This study aimed to compare respiratory functions, exercise capacity, muscle strength, and physical activity levels among children with PCD with/without KS and healthy peers.

Methods: Fifteen patients with KS, 23 with PCD without KS, and 27 controls were compared. Pulmonary function, functional exercise capacity (6-minute walk test - 6MWT), maximal inspiratory, expiratory (MIP, MEP), and skeletal muscle strength, inspiratory muscle endurance (IME), and physical activity level were evaluated.

Results: The forced expiratory volume in one second (FEV₁) % ($p = .009$), forced expiratory flow from 25%-75% (FEF_{25-75%}) % ($p = .001$), MIP ($p = .034$), MEP ($p = .003$), 6MWT distance ($p = .001$), and daily steps ($p = .034$) were significantly different among the groups. Quadriceps femoris (QF) muscle strength and IME were similar in groups ($p > .05$). FEV₁% ($p = .002$), FEF_{25-75%} % ($p = .001$), MIP ($p = .027$), MEP ($p = .001$), and 6MWT distance ($p = .003$) in patients with KS; 6MWT distance ($p = .003$) in patients with PCD without KS was significantly lower than controls.

Conclusion: The presence of KS affects pulmonary function, respiratory muscle strength, and physical activity more. Exercise capacity and physical activity levels are decreased, inspiratory muscle endurance and QF muscle strength are preserved in patients with KS and PCD without KS. Kartagener's syndrome further impairs pulmonary and extrapulmonary outcomes; the reasons should be investigated, and the necessity of rehabilitation approaches that will prevent deterioration come to the fore.

Keywords: Exercise tolerance; physical activity; primary ciliary dyskinesia.

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. 2023 Nov 28;13(1):20886.

doi: 10.1038/s41598-023-48276-1.

The prevalence of anxiety and depression in bronchiectasis patients and their association with disease severity: a cross-sectional study

[Khaled Al Oweidat](#)¹, [Dana Marie](#)², [Ahmad A Toubasi](#)³, [Dunia Z Jaber](#)², [Khalid E Ahmed](#)², [Bayan O Abu Alragheb](#)², [Asma S Albtoosh](#)¹

Affiliations expand

- PMID: 38017245
- PMCID: [PMC10684858](#)
- DOI: [10.1038/s41598-023-48276-1](#)

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Abstract

Bronchiectasis is a chronic lung disease characterized by recurrent respiratory symptoms. Several studies demonstrated that psychological comorbidities are common in patients with bronchiectasis. The aim of this study is to investigate the prevalence of anxiety and depression in bronchiectasis patients and assess their association with disease severity. In this cross-sectional study, we included patients diagnosed with bronchiectasis. The study was conducted using an interviewer-administered questionnaire via phone calls and data collected from the electronic medical records at JUH. The questionnaire included patients' demographics and disease characteristics. Anxiety and depression were assessed using GAD7 and PHQ9 respectively. Bronchiectasis disease severity was assessed using BSI and FACED score. The total number of included patients was 133. Moreover, 53.4% of the participants were females while the rest were males (46.6%). PHQ9 demonstrated that 65.4% of the patients had depression. Regarding anxiety, GAD7 scale showed that 54.1% of the patients had anxiety. Pearson correlation showed that bronchiectasis severity index was significantly associated only with PHQ9 depression scores ($r = 0.212$, $P \text{ value} = 0.014$). The

prevalence of depression and anxiety is high among patients with bronchiectasis. We believe that patients affected with bronchiectasis should be screened for depression to improve their quality of life.

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Conflict of interest statement

The authors declare no competing interests.

- [20 references](#)
- [6 figures](#)

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Am J Respir Crit Care Med

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. 2023 Nov 28.

doi: 10.1164/rccm.202306-1093OC. Online ahead of print.

Proximal and Distal Bronchioles Contribute to the Pathogenesis of Non- Cystic Fibrosis Bronchiectasis (NCFB)

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[Margarita Barbosa Cardenas](#)¹¹, [Minako Saito](#)¹, [Anne Marie Cawley](#)⁵, [Gabriela De la Cruz](#)¹², [Michael Chua](#)⁷, [Neil E Alexis](#)¹³, [Yohei Masugi](#)¹⁴, [Peadar G Noone](#)¹⁵, [Carla M P Ribeiro](#)^{16 17}, [Mehmet Kesimer](#)¹, [Kenneth N Olivier](#)¹⁸, [Naoki Hasegawa](#)¹⁹, [Scott H Randell](#)²⁰, [Wanda K O'Neal](#)¹¹, [Richard C Boucher](#)²¹

Affiliations expand

- PMID: 38016030
- DOI: [10.1164/rccm.202306-1093OC](https://doi.org/10.1164/rccm.202306-1093OC)

Abstract

Rationale: Non-cystic fibrosis bronchiectasis (NCFB) may originate in bronchiolar regions of the lung. Accordingly, there is a need to characterize the morphology and molecular characteristics of NCFB bronchioles. **Objective:** Test the hypothesis that NCFB exhibits a major component of bronchiolar disease manifest by mucus plugging and ectasia. **Methods:** Morphologic criteria and region-specific epithelial gene expression, measured histologically and by RNA *in situ* hybridization (RNA-ISH) and immunohistochemistry (IHC), identified proximal and distal bronchioles in excised NCFB lungs. RNA-ISH and IHC assessed bronchiolar mucus accumulation and mucin gene expression. CRISPR-Cas9-mediated IL-1R1 knockout in human bronchial epithelial (HBE) cultures tested IL-1 α/β contributions to mucin production. Spatial transcriptional profiling characterized NCFB distal bronchiolar gene expression. **Measurements and Main Results:** Bronchiolar perimeters and lumen areas/section area were increased in proximal, but not distal, bronchioles in NCFB vs control lungs, suggesting proximal bronchiolectasis. In NCFB, mucus plugging was observed in ectatic proximal bronchioles and associated non-ectatic distal bronchioles in sections with disease. MUC5AC and MUC5B mucins were upregulated in NCFB proximal bronchioles, whereas MUC5B was selectively upregulated in distal bronchioles. Bronchiolar mucus plugs were populated by IL-1 β -expressing macrophages. NCFB sterile sputum supernatants induced HBE MUC5B/MUC5AC expression that was >80% blocked by IL-1R1 ablation. Spatial transcriptional profiling identified upregulation of genes associated with secretory cells, hypoxia, interleukin pathways, IL-1 β -producing macrophages in mucus plugs, and downregulation of epithelial ciliogenesis genes. **Conclusions:** NCFB exhibits distinctive proximal and distal bronchiolar disease. Both bronchiolar regions exhibit bronchiolar secretory cell features and mucus plugging but differ in mucin gene regulation and ectasia.

Keywords: alveolar type (AT0) cells; mucus; nontuberculous mycobacteria (NTM); secretoglobin family 3A member 2 (SCGB3A2); surfactant protein B (SFTPB).

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BMJ Open Respir Res

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. 2023 Nov 27;10(1):e001517.

doi: 10.1136/bmjresp-2022-001517.

Incidence of community-acquired pneumonia hospitalisation in persons with bronchiectasis during the COVID-19 lockdown in Denmark: a retrospective cohort study

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Affiliations expand

- PMID: 38016706
- PMCID: [PMC10685970](#)
- DOI: [10.1136/bmjresp-2022-001517](#)

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Abstract

Background: Persons with bronchiectasis have a high risk of community-acquired pneumonia. Social distancing measures, implemented to prevent the spreading of SARS-CoV-2, could potentially reduce the incidence of other infectious diseases.

Research question: Was the COVID-19 lockdown period, along with accompanying social distancing measures, associated with reduced hospital admissions for community-acquired pneumonia and decreased overall mortality rates among individuals with bronchiectasis?

Methods: Social distancing measures were introduced in Denmark by 12 March 2020 and were preserved until 20 May 2020 (social distancing period), after which the measures were gradually dismissed. The study included all adults (≥ 18 years) with bronchiectasis residing in Denmark. Confirmed cases of SARS-CoV-2 infection were excluded. We retrospectively investigated the incidence of community-acquired pneumonia hospital admission, death of all causes and respiratory antibiotic treatment in the 10-week social distancing period in 2020, compared with the same dates in 2019. 9344 persons were included in the study.

Results: In the social distancing period, the incidence rate of pneumonia-hospitalisation per 10 000 person-weeks was 9.2 compared with 13.8 in the reference period. This reduction corresponds to an incidence rate ratio (IRR) of 0.67 (95% CI 0.51 to 0.88, $p < 0.01$). Mortality was unchanged (IRR 0.90, 95% CI 0.61 to 1.32, $p = 0.58$). Fewer persons received respiratory antibiotics (IRR 0.85, 95% CI 0.78 to 0.94, $p < 0.001$).

Conclusion: The social distancing period was associated with a lower incidence of community-acquired pneumonia hospitalisations and respiratory antibiotic treatments in persons with bronchiectasis while all-cause mortality remained unchanged.

Keywords: Bronchiectasis; COVID-19; Pneumonia.

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Conflict of interest statement

Competing interests: None declared.

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