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Considerato il crescente interesse sull'argomento, abbiamo aggiunto una sezione su (premature birth)

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

1

Respir Res

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. 2023 Nov 4;24(1):265.

doi: 10.1186/s12931-023-02576-2.

Plasma metabolomics and quantitative interstitial abnormalities in ever-smokers

[Bina Choi](#)^{1,2}, [Raúl San José Estépar](#)^{3,4}, [Suneeta Godbole](#)⁵, [Jeffrey L Curtis](#)^{6,7}, [Jennifer M Wang](#)⁶, [Rubén San José Estépar](#)^{3,4}, [Ivan O Rosas](#)⁸, [Jared R Mayers](#)⁹, [Brian D Hobbs](#)^{9,10}, [Craig P Hersh](#)^{9,10}, [Samuel Y Ash](#)^{3,11}, [MeiLan K Han](#)⁶, [Russell P Bowler](#)¹², [Kathleen A Stringer](#)^{6,13}, [George R Washko](#)^{9,3}, [Wassim W Labaki](#)⁶

Affiliations expand

- PMID: 37925418
- DOI: [10.1186/s12931-023-02576-2](https://doi.org/10.1186/s12931-023-02576-2)

Abstract

Background: Quantitative interstitial abnormalities (QIA) are an automated computed tomography (CT) finding of early parenchymal lung disease, associated with worse lung function, reduced exercise capacity, increased respiratory symptoms, and death. The metabolomic perturbations associated with QIA are not well known. We sought to identify plasma metabolites associated with QIA in smokers. We also sought to identify shared and differentiating metabolomics features between QIA and emphysema, another smoking-related advanced radiographic abnormality.

Methods: In 928 former and current smokers in the Genetic Epidemiology of COPD cohort, we measured QIA and emphysema using an automated local density histogram method and generated metabolite profiles from plasma samples using liquid chromatography-mass spectrometry (Metabolon). We assessed the associations between metabolite levels and QIA using multivariable linear regression models adjusted for age, sex, body mass index, smoking status, pack-years, and inhaled corticosteroid use, at a Benjamini-Hochberg False Discovery Rate p-value of ≤ 0.05 . Using multinomial regression models adjusted for these covariates, we assessed the associations between metabolite levels and the following CT phenotypes: QIA-predominant, emphysema-predominant, combined-predominant, and neither-predominant. Pathway enrichment analyses were performed using MetaboAnalyst.

Results: We found 85 metabolites significantly associated with QIA, with overrepresentation of the nicotinate and nicotinamide, histidine, starch and sucrose, pyrimidine, phosphatidylcholine, lysophospholipid, and sphingomyelin pathways. These included metabolites involved in inflammation and immune response, extracellular matrix remodeling, surfactant, and muscle cachexia. There were 75 metabolites significantly different between QIA-predominant and emphysema-predominant phenotypes, with overrepresentation of the phosphatidylethanolamine, nicotinate and nicotinamide, aminoacyl-tRNA, arginine, proline, alanine, aspartate, and glutamate pathways.

Conclusions: Metabolomic correlates may lend insight to the biologic perturbations and pathways that underlie clinically meaningful quantitative CT measurements like QIA in smokers.

Keywords: Cross-Sectional Studies; Lung Diseases, Interstitial; Metabolomics; Pulmonary Emphysema; Tomography, X-Ray Computed.

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Lancet Respir Med



. 2023 Nov 1:S2213-2600(23)00298-9.

doi: 10.1016/S2213-2600(23)00298-9. Online ahead of print.

[Blood eosinophil-guided oral prednisolone for COPD exacerbations in primary care in the UK \(STARR2\): a non-inferiority, multicentre, double-blind, placebo-controlled, randomised controlled trial](#)

[Sanjay Ramakrishnan](#)¹, [Helen Jeffers](#)², [Beverly Langford-Wiley](#)³, [Joanne Davies](#)², [Samantha J Thulborn](#)³, [Mahdi Mahdi](#)³, [Christine A'Court](#)⁴, [Ian Binnian](#)⁵, [Stephen Bright](#)⁶, [Simon Cartwright](#)⁷, [Victoria Glover](#)⁷, [Alison Law](#)⁸, [Robin Fox](#)⁹, [Adam Jones](#)¹⁰, [Christopher Davies](#)¹¹, [David Copping](#)¹², [Richard Ek Russell](#)¹³, [Mona Bafadhel](#)¹⁴

Affiliations expand

- PMID: 37924830
- DOI: [10.1016/S2213-2600\(23\)00298-9](https://doi.org/10.1016/S2213-2600(23)00298-9)

Abstract

Background: Systemic glucocorticoids are recommended for use in chronic obstructive pulmonary disease (COPD) exacerbations; however, there is increased harm associated with their use. We hypothesised that the use of eosinophil biomarker-directed oral

prednisolone therapy at the time of an exacerbation of COPD was effective at reducing prednisolone use without affecting adverse outcomes.

Methods: The studying acute exacerbations and response (STARR2) study was a multicentre, randomised, double-blind, placebo-controlled trial conducted in 14 primary care practices in the UK. We included adults (aged ≥ 40 years), who were current or former smokers (with at least a 10 pack year smoking history) with a diagnosis of COPD, defined as a post-bronchodilator FEV₁/forced vital capacity ratio of less than 0.7 previously recorded by the primary care physician, and a history of at least one exacerbation in the previous 12 months requiring systemic corticosteroids with or without antibiotics. All study staff and participants were masked to study group allocation and to treatment allocation. Participants were randomly assigned (1:1) to blood eosinophil-directed treatment (BET; to receive oral prednisolone 30 mg once daily if eosinophil count was high [$\geq 2\%$] or placebo if eosinophil count was low [$< 2\%$]) or to standard care treatment (ST; to receive prednisolone 30 mg once daily irrespective of the point-of-care eosinophil result). Treatment was prescribed for 14 days and all patients also received antibiotics. The primary outcome was the rate of treatment failure, defined as any need for re-treatment with antibiotics or steroids, hospitalisation for any cause, or death, assessed at 30 days after exacerbation in the modified intention-to-treat population. Participants were eligible for re-randomisation at further exacerbations (with a maximum of four exacerbations per participant). A safety analysis was conducted on all randomly assigned participants. Although designed as a superiority trial, after identification of an error in the randomisation code before data lock the study converted to show non-inferiority. An upper margin of 1.105 for the 95% CI was defined as the non-inferiority margin. This study was registered with EudraCT, 2017-001586-24, and is complete.

Findings: Between Nov 6, 2017, and April 30, 2020, 308 participants were recruited from 14 general practices. 144 exacerbations (73 in the BET group and 71 in the ST group) from 93 participants (mean age 70 years [range 46-84] and mean percent predicted FEV₁ 60.9% [SD 19.4]; 52 [56%] male and 41 [44%] female; ethnicity data was not collected) were included in the modified intention-to-treat analysis. There were 14 (19%) treatment failures at 30 days post-exacerbation in the BET group and 23 (32%) in the ST group; we found a large non-significant estimated effect between BET and ST (RR 0.60 [95% CI 0.33-1.04]; $p=0.070$) in reducing treatment failures after a COPD exacerbation. The non-inferiority analysis supported that BET was non-inferior to ST. Frequency of adverse events were similar between the study groups; glycosuria (2/102 [2%] in BET group and 1/101 [1%] in the ST group) and hospital admission for COPD exacerbation (2/102 [2%] in BET group and 1/101 [1%] in the ST group) were the two most common adverse events in both groups. No deaths occurred in the study.

Interpretation: Blood eosinophil-directed prednisolone therapy at the time of an acute exacerbation of COPD is non-inferior to standard care and can be used to safely reduce systemic glucocorticoid use in clinical practice.

Funding: National Institute for Health and Care Research.

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Conflict of interest statement

Declaration of interests SR reports personal salary support from the National Institute for Health and Care Research, an unrestricted research grant from AstraZeneca to his institution, and speaker fees and conference travel support from AstraZeneca, all outside of the submitted work. MB reports salary support and direct funding for the study from the National Institute for Health and Care Research through a named fellowship. Outside of the submitted work, MB reports research grant funding paid to her institution from AstraZeneca, Roche, the European Respiratory Society, and Asthma + Lung UK. Outside of the submitted work, she also reports consulting fees from AstraZeneca, Sanofi, GSK, and Areteia, paid to her and her institution. She has received conference travel support from Chiesi. She has a leadership and board roles at the British Thoracic Society, AlbusHealth, and ProAxis. All other authors declare no competing interests.

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Lancet Respir Med



. 2023 Nov 1:S2213-2600(23)00339-9.

doi: 10.1016/S2213-2600(23)00339-9. Online ahead of print.

[Blood eosinophil-guided therapy for COPD exacerbations](#)

[Alejandro P Comellas](#)¹, [Spyridon Fortis](#)²

Affiliations expand

- PMID: 37924828

- DOI: [10.1016/S2213-2600\(23\)00339-9](https://doi.org/10.1016/S2213-2600(23)00339-9)

No abstract available

Conflict of interest statement

APC received grants from the National Institutes of Health and consultation fees from GlaxoSmithKline and AstraZeneca. APC is a non-paid consultant for VIDA. SF received grants from the American Thoracic Society and Fisher & Paykel Healthcare and fees from the Society of Hospital Medicine.

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BMC Pulm Med

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. 2023 Nov 3;23(1):424.

doi: 10.1186/s12890-023-02728-6.

[Screening and early diagnosis of chronic obstructive pulmonary disease: a population study](#)

[Wenhui Tang](#)¹, [Yan Rong](#)², [Hongmei Zhang](#)², [Wenji Lin](#)², [Wenmei Zeng](#)², [Wenhong Wu](#)²

Affiliations expand

- PMID: 37924038

- DOI: [10.1186/s12890-023-02728-6](https://doi.org/10.1186/s12890-023-02728-6)

Abstract

Background and objective: Although chronic obstructive pulmonary disease (COPD) is a common disease leading to further morbidity and significant mortality, there is still limited data on screening for COPD. The purpose of this study was to establish an early chronic obstructive pulmonary disease (COPD) screening system for the community and hospitals in Nanshan District in Shenzhen City, to improve the rate of early diagnosis and treatment of patients with COPD.

Methods: We identified individuals at high risk of COPD using a questionnaire survey and analyzed the relevant influencing factors in the early stages of COPD in high-risk groups.

Results: We collected a total of 5,000 COPD screening questionnaires, and a total of 449 patients were diagnosed with COPD by pulmonary function examination. The prevalence of COPD in people aged 20 and above in Nanshan District of Shenzhen City was estimated to be 8.98%, with a base of 5000. The severity classification as per the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria was as follows: GOLD I accounted for 34.74%; GOLD II accounted for 37.64%; GOLD III accounted for 16.04%; and GOLD IV accounted for 11.58%. Common features of early COPD that we identified were: (1) patients were mainly males, accounting for 68.0%; (2) COPD was common among people aged 50-59 years, comprising 31%; (3) 96.0% of patients often had severe respiratory symptoms and had frequent coughs when they did not have a cold; (4) 57.2% of patients experienced shortness of breath when walking quickly on level ground or climbing gentle slopes; (5) 72.6% of patients had a family history of bronchial asthma and COPD. Multivariate ordinal multi-classification logistic regression showed that gender, age, shortness of breath, and the use of firewood, grass, and coal stoves were all influencing factors in pulmonary function grading.

Conclusion: A screening questionnaire combined with a pulmonary function test should be adopted as a COPD screening strategy to be implemented at the primary level as a public health priority in China to reduce the incidence, disability, and mortality from COPD.

Keywords: Chronic obstructive pulmonary disease; Early diagnosis; Screening.

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. 2023 Nov-Dec;41(6):330-337.

doi: 10.1097/NHH.0000000000001206.

[Acceptability, Appropriateness, and Feasibility of an Educational Program to Promote Treatment Adherence in Patients with Chronic Obstructive Pulmonary Disease](#)

[Nguyen Thi Thu Trieu](#), [Michele Upval](#), [Nguyen Thi Yen Hoai](#), [Tran Van Long](#), [Nguyen Thi Anh Phuong](#)

- PMID: 37922136
- DOI: [10.1097/NHH.0000000000001206](https://doi.org/10.1097/NHH.0000000000001206)

Abstract

The mortality rate due to chronic obstructive pulmonary disease (COPD) has increased annually, and non-adherence to treatment is one reason for this rise. Developing intervention programs to enhance treatment adherence for people with COPD is essential. The purpose of this mixed-methods study was to determine the acceptability,

appropriateness, and feasibility of such a program. We sought the opinions of 15 healthcare managers and 15 practicing nurses from three hospitals across Vietnam and conducted group discussions and interviews with 30 patients with COPD. We then formulated integrated conclusions on the acceptability, appropriateness, and feasibility of the program. The overall average score of 12 items to test the acceptability, appropriateness, and feasibility of the program from both healthcare managers and practicing nurses was high (M = 4.31; SD = 0.11) and (M = 4.37; SD = 0.12), respectively. Thirty COPD outpatients agreed the content and plan of the program were necessary for them to enhance their treatment adherence at home. The document content was appropriate, easy to understand, and the support and education provided by nurses was helpful. The educational intervention program to promote treatment adherence for patients with COPD was acceptable, appropriate, and feasible from the views of healthcare managers, nurses, and patients with COPD.

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Pharmacol Rep

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. 2023 Nov 3.

doi: 10.1007/s43440-023-00548-3. Online ahead of print.

[Serum levels of biomarkers that may link chronic obstructive pulmonary disease and depressive disorder](#)

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

Affiliations expand

- PMID: 37921965
- DOI: [10.1007/s43440-023-00548-3](https://doi.org/10.1007/s43440-023-00548-3)

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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BMJ Open

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. 2023 Nov 2;13(11):e076746.

doi: 10.1136/bmjopen-2023-076746.

[Relationship between an ageing measure and chronic obstructive pulmonary disease, lung function: a cross-sectional study of NHANES, 2007–2010](#)

[Zhishen Ruan](#)¹, [Dan Li](#)¹, [Di Huang](#)¹, [Minghao Liang](#)¹, [Yifei Xu](#)¹, [Zhanjun Qiu](#)², [Xianhai Chen](#)²

Affiliations expand

- PMID: 37918922
- DOI: [10.1136/bmjopen-2023-076746](https://doi.org/10.1136/bmjopen-2023-076746)

Free article

Abstract

Objectives: Chronic obstructive pulmonary disease (COPD) is a disease associated with ageing. However, actual age does not accurately reflect the degree of biological ageing.

Phenotypic age (PhenoAge) is a new indicator of biological ageing, and phenotypic age minus actual age is known as phenotypic age acceleration (PhenoAgeAccel). This research aimed to analyse the relationship between PhenoAgeAccel and lung function and COPD.

Design: A cross-sectional study.

Participants: Data for the study were obtained from the National Health and Nutrition Examination Survey (NHANES) 2007-2010. We defined people with forced expiratory volume in 1 s/forced vital capacity <0.70 after inhaled bronchodilators as COPD and the rest of the population as non-COPD. Adults aged 40 years or older were enrolled in the study.

Primary and secondary outcome measures: Linear and logistic regression were used to investigate the relationship between PhenoAgeAccel, lung function and COPD. Subgroup analysis was performed by gender, age, ethnicity and smoking index COPD. In addition, we analysed the relationship between the smoking index, respiratory symptoms and PhenoAgeAccel. Multiple models were used to reduce confounding bias.

Results: 5397 participants were included in our study, of which 1042 had COPD. Compared with PhenoAgeAccel Quartile1, Quartile 4 had a 52% higher probability of COPD; elevated PhenoAgeAccel was also significantly associated with reduced lung function. Further subgroup analysis showed that high levels of PhenoAgeAccel had a more significant effect on lung function in COPD, older adults and whites (P for interaction <0.05). Respiratory symptoms and a high smoking index were related to higher indicators of ageing.

Conclusions: Our study found that accelerated ageing is associated with the development of COPD and impaired lung function. Smoking cessation and anti-ageing therapy have potential significance in COPD.

Keywords: aging; respiratory medicine (see thoracic medicine); thoracic medicine.

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Conflict of interest statement

Competing interests: None declared.

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Editorial

Eur Respir J

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. 2023 Nov 2;62(5):2301538.

doi: 10.1183/13993003.01538-2023. Print 2023 Nov.

Can the curse of mood disorders in COPD be lifted and enable pulmonary rehabilitation?

[Rachael Evans](#)¹, [Gillian Doe](#)²

Affiliations expand

- PMID: 37918881
- DOI: [10.1183/13993003.01538-2023](https://doi.org/10.1183/13993003.01538-2023)

No abstract available

Conflict of interest statement

Conflict of interest: R. Evans reports grants from NIHR/UKRI/Wolfson Foundation and Genentec/Roche, consulting fees from AstraZeneca/Evidera, lecture honoraria from Boehringer and Moderna, travel support from Chiesi, and leadership roles as ERS Group 01.02 Pulmonary Rehabilitation and Chronic Care Secretary, and ATS Pulmonary Rehabilitation Assembly Chair, outside the submitted work. G. Doe is funded by the National Institute for Health Research (NIHR) through an AI Award in Health and Care (phase 3 application: grant number AI_AWARD02204).

Comment on

- [Tailored psychological intervention for anxiety or depression in COPD \(TANDEM\): a randomised controlled trial.](#)

Taylor SJC, Sohanpal R, Steed L, Marshall K, Chan C, Yaziji N, Barradell AC, Font-Gilabert P, Healey A, Hooper R, Kelly MJ, Mammoliti KM, Priebe S, Rajasekaran A, Roberts CM, Rowland V, Singh SJ, Smuk M, Underwood M, Waseem S, White P, Wileman V, Pinnock H. *Eur Respir J*. 2023 Nov 2;62(5):2300432. doi:

10.1183/13993003.00432-2023. Print 2023 Nov. PMID: 37620042 **Free PMC article.**

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Respir Med

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. 2023 Oct 31:107437.

doi: 10.1016/j.rmed.2023.107437. Online ahead of print.

[Physical status, symptoms and health-related quality of life during a severe exacerbation of COPD: Recovery and discriminative capacity for future events](#)

[Kirsten Quadflieg](#)¹, [Ana Machado](#)², [Fabiano Francisco de Lima](#)³, [Anand Dederen](#)⁴, [Marc Daenen](#)⁴, [David Ruttens](#)⁵, [Michiel Thomeer](#)⁵, [Martijn A Spruit](#)⁶, [Chris Burtin](#)⁷

Affiliations expand

- PMID: 37918543
- DOI: [10.1016/j.rmed.2023.107437](https://doi.org/10.1016/j.rmed.2023.107437)

Abstract

Objective: Severe acute exacerbations of chronic obstructive pulmonary disease (AECOPD) can have a negative impact on functional capacity, symptoms and health-related quality of life (HRQOL). This study aimed to i) investigate the recovery of muscle strength, functional capacity, symptoms, and HRQOL in patients after a severe AECOPD; ii) compare with matched patients with stable COPD (SCOPD); and iii) assess whether these assessments at hospital discharge could discriminate patients' risk for future events.

Methods: This observational study assessed patients with AECOPD during hospital discharge (T1) and one month after discharge (T2). Patients with SCOPD were assessed once. Quadriceps force, handgrip strength, short physical performance battery (SPPB), 6-min walk distance (6 MWD), COPD assessment test (CAT), London chest activity of daily living (LCADL), modified medical research council, checklist individual strength-fatigue, patient health questionnaire, and physical activity (Actigraph) were measured. Exacerbation-related readmission and mortality within six months and 1-year were collected.

Results: Forty-four patients with AECOPD were matched with 44 patients with SCOPD. At T2, a significant improvement was found for the SPPB total score, 6 MWD, CAT score, and LCADL score. Compared to patients with SCOPD, a worse LCADL score was found at T2 in patients with AECOPD. Patients with AECOPD that were readmitted or died had a worse SPPB classification and five-repetition sit-to-stand test at T1.

Conclusion: Patients after severe AECOPD improved in functional capacity and HRQOL one month after hospital discharge, but ADL performance was still worse compared to SCOPD. Patients who were readmitted or died had significantly worse scores on functional tests at hospital discharge.

Keywords: COPD; Exacerbation; Hospitalization; Mortality; Readmission.

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Conflict of interest statement

Declaration of competing interest There is no conflict of interest.

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Respir Med

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. 2023 Oct 31:107436.

doi: 10.1016/j.rmed.2023.107436. Online ahead of print.

[Effect of chest wall mobilization on respiratory muscle function in patients with severe chronic obstructive pulmonary disease \(COPD\): A randomized controlled trial](#)

[Amy Y Y Tsui](#)¹, [Rosanna M W Chau](#)¹, [Gladys L Y Cheing](#)², [Thomas Y W Mok](#)³, [S O Ling](#)³, [Candy H Y Kwan](#)³, [Sharon M H Tsang](#)²

Affiliations [expand](#)

- PMID: 37918542
- DOI: [10.1016/j.rmed.2023.107436](https://doi.org/10.1016/j.rmed.2023.107436)

Abstract

Background: Clinical trials have demonstrated positive correlation between pulmonary function and chest wall expansion in COPD. Decrease in chest wall expansion in patients

with COPD compromises rib cage mobility and functional length of respiratory muscles that ultimately jeopardize the efficacy and function of respiratory system.

Method: Thirty male adults (mean age: 74.97 ± 6.29) suffered with severe COPD were randomly allocated to either experimental group (chest wall mobilizations) or control group. Both groups received standardized education and walking exercise (twice/week) for 6 weeks. Patients in experimental group received additional chest wall mobilizations that include stretching and joints mobilization. Pulmonary function, respiratory muscle strength, thoracic excursion, cervical and thoracic range of movement were evaluated at baseline, post-program and at 3-month follow-up.

Results: There were significantly greater improvements in respiratory muscle strength, thoracic excursion and thoracic range of movement ($p < 0.01$) except thoracic flexion. Lower thoracic excursion is strongly associated with increase in maximum inspiratory pressure ($\beta = 13.64$, $p < 0.001$) and maximum expiratory pressure ($\beta = 16.23$, $p < 0.001$). Thoracic range of movement especially extension ($p < 0.001$) and bilateral rotation ($p < 0.01$) exhibit a strong relationship with increase in lower thoracic excursion (adjusted $R^2 = 0.876$) as shown in multiple regression analysis.

Conclusion: Additional chest wall mobilization in the rehabilitation of patients with COPD is likely to enhance thoracic extension and rotation which increase lower thoracic excursion. This significant improvement in chest expansion capacity allows respiratory muscles to work at an optimal functional length which result in greater respiratory muscle strength in patients with severe COPD.

Keywords: Chest wall mobilization; Chronic obstructive respiratory diseases (COPD); Respiratory muscle strength.

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Conflict of interest statement

Declaration of competing interest The authors report no declarations of interest. This research had received the Kowloon Central Cluster Research Grant from The Hong Kong Hospital Authority.

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Am J Respir Crit Care Med



. 2023 Nov 2.

doi: 10.1164/rccm.202301-0067OC. Online ahead of print.

Blood-based Transcriptomic and Proteomic Biomarkers of Emphysema

[Rahul Suryadevara](#)¹, [Andrew Gregory](#)¹, [Robin Lu](#)¹, [Zhonghui Xu](#)², [Aria Masoomi](#)³, [Sharon M Lutz](#)⁴, [Seth Berman](#)², [Jeong H Yun](#)², [Aabida Saferali](#)², [Min Hyung Ryu](#)⁵, [Matthew Moll](#)^{1,6}, [Don D Sin](#)⁷, [Craig P Hersh](#)⁸, [Edwin K Silverman](#)⁹, [Jennifer Dy](#)¹⁰, [Katherine A Pratte](#)¹¹, [Russell P Bowler](#)¹², [Peter J Castaldi](#)¹³, [Adel Boueiz](#)¹⁴; COPDGene investigators

Affiliations expand

- PMID: 37917913
- DOI: [10.1164/rccm.202301-0067OC](https://doi.org/10.1164/rccm.202301-0067OC)

Abstract

Rationale: Emphysema is a COPD phenotype with important prognostic implications. Identifying blood-based biomarkers of emphysema will facilitate early diagnosis and development of targeted therapies.

Objectives: Discover blood omics biomarkers for chest CT-quantified emphysema and develop predictive biomarker panels.

Methods: Emphysema blood biomarker discovery was performed using differential gene expression, alternative splicing, and protein association analyses in a training sample of 2,370 COPDGene participants with available blood RNA sequencing (RNA-seq), plasma proteomics, and clinical data. Internal validation was conducted in a COPDGene testing sample (n=1,016) and external validation was done in the ECLIPSE study (n=526). Since low BMI and emphysema often co-occur, we performed a mediation analysis to quantify the effect of BMI on gene and protein associations with emphysema. Elastic net models with bootstrapping were also developed in the training sample sequentially using clinical, blood

cell proportions, RNA-seq, and proteomic biomarkers to predict quantitative emphysema. Model accuracy was assessed by the area under the receiver-operator-characteristic-curves (AUROC) for subjects stratified into tertiles of emphysema severity.

Measurements and main results: 3,829 genes, 942 isoforms, 260 exons, and 714 proteins were significantly associated with emphysema (*FDR* 5%) and yielded 11 biological pathways. 74% of these genes and 62% of these proteins showed mediation by BMI. Our prediction models demonstrated reasonable predictive performance in both COPDGene and ECLIPSE. The highest-performing model used clinical, blood cell, and protein data (AUROC in COPDGene testing: 0.90, 95% CI: 0.85-0.90).

Conclusions: Blood transcriptome and proteome-wide analyses reveal key biological pathways of emphysema and enhance the prediction of emphysema.

Keywords: Biomarkers; Emphysema; Prediction; Proteomics; Transcriptomics.

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JMIR Aging

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. 2023 Nov 2:6:e41539.

doi: 10.2196/41539.

[Experiences of Patients With Chronic Obstructive Pulmonary Disease Using the Apple Watch Series 6 Versus the Traditional Finger Pulse Oximeter for](#)

Home SpO₂ Self-Monitoring: Qualitative Study Part 2

[Yuxin Liu](#)¹, [Antonia Arnaert](#)^{#1}, [Daniel da Costa](#)¹, [Pia Sumbly](#)¹, [Zoumanan Debe](#)¹, [Sylvain Charbonneau](#)^{#2}

Affiliations expand

- PMID: 37917147
- DOI: [10.2196/41539](https://doi.org/10.2196/41539)

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Abstract

Background: Amid the rise in mobile health, the Apple Watch now has the capability to measure peripheral blood oxygen saturation (SpO₂). Although the company indicated that the Watch is not a medical device, evidence suggests that SpO₂ measurements among patients with chronic obstructive pulmonary disease (COPD) are accurate in controlled settings. Yet, to our knowledge, the SpO₂ function has not been validated for patients with COPD in naturalistic settings.

Objective: This qualitative study explored the experiences of patients with COPD using the Apple Watch Series 6 versus a traditional finger pulse oximeter for home SpO₂ self-monitoring.

Methods: We conducted individual semistructured interviews with 8 female and 2 male participants with moderate to severe COPD, and transcripts were qualitatively analyzed. All received a watch to monitor their SpO₂ for 5 months.

Results: Due to respiratory distress, the watch was unable to collect reliable SpO₂ measurements, as it requires the patient to remain in a stable position. However, despite the physical limitations and lack of reliable SpO₂ values, participants expressed a preference toward the watch. Moreover, participants' health needs and their unique accessibility experiences influenced which device was more appropriate for self-monitoring purposes. Overall, all shared the perceived importance of prioritizing their physical COPD symptoms over device selection to manage their disease.

Conclusions: Differing results between participant preferences and smartwatch limitations warrant further investigation into the reliability and accuracy of the SpO₂ function of the

watch and the balance among self-management, medical judgment, and dependence on self-monitoring technology.

Keywords: Apple Watch; chronic obstructive pulmonary disease; pulse oximeter; qualitative descriptive; self-monitoring; smartwatch.

©Yuxin Liu, Antonia Arnaert, Daniel da Costa, Pia Sumbly, Zoumanan Debe, Sylvain Charbonneau. Originally published in JMIR Aging (<https://aging.jmir.org>), 02.11.2023.

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Ann Am Thorac Soc

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. 2023 Nov 2.

doi: 10.1513/AnnalsATS.202307-654OC. Online ahead of print.

[Risks of Zolpidem among Patients with Chronic Obstructive Pulmonary Disease](#)

[Jason M Castaneda](#)¹, [Travis Hee Wai](#)², [Laura J Spece](#)³, [Kevin I Duan](#)⁴, [Aristotle Leonhard](#)¹, [Matthew F Griffith](#)⁵, [Robert Plumley](#)⁶, [Brian N Palen](#)^{7,8}, [Laura C Feemster](#)^{9,1}, [David H Au](#)⁸, [Lucas M Donovan](#)^{1,10}

Affiliations expand

- PMID: 37916873
- DOI: [10.1513/AnnalsATS.202307-654OC](https://doi.org/10.1513/AnnalsATS.202307-654OC)

Abstract

Rationale: Non-benzodiazepine benzodiazepine receptor agonists (NBZRA, e.g., zolpidem) are frequently used to treat insomnia among patients with chronic obstructive pulmonary disease (COPD). However, multiple observational studies find that patients with COPD who are prescribed NBZRAs have greater risks for mortality and respiratory complications than patients without such prescriptions. Without an active comparator, these studies are susceptible to confounding by indication.

Objectives: Compare the risk of death or inpatient COPD exacerbation among patients receiving zolpidem relative to patients receiving other hypnotics.

Methods: Using nationwide Veterans Health Administration (VA) data, we identified patients with clinically diagnosed COPD and new receipt of zolpidem or another hypnotic available on VA formulary without prior authorization (melatonin, trazodone, doxepin). We excluded those receiving traditional benzodiazepines or multiple concurrent hypnotics. We propensity-matched patients receiving zolpidem to other hypnotics on 32 variables, including demographics, comorbidities, and markers of COPD severity. We compared risk of the primary composite outcome of death or inpatient COPD exacerbation over one year. In secondary analyses, we propensity-matched patients receiving zolpidem to those without hypnotic receipt.

Results: Among 283,740 patients meeting inclusion criteria, 1,126 (0.4%) received zolpidem and 3,057 (1.1%) received other hypnotics. We propensity matched patients receiving zolpidem 1:1 to peers receiving other hypnotics. We did not find a difference in the primary composite outcome of death or inpatient exacerbation (HR 0.97, 95%CI 0.0.77-1.23). In secondary analyses comparing patients receiving zolpidem to matched peers without hypnotic receipt, we observed greater risk of death or inpatient exacerbation with zolpidem (HR 1.40, 95%CI 1.09-1.81).

Conclusions: Among patients with COPD, we did not observe greater risks following new receipt of zolpidem relative to other hypnotics. However, we did observe greater risks relative to those without hypnotic receipt. This latter finding may reflect: 1) residual, unmeasured confounding related to insomnia, or, 2) true adverse effects of hypnotics across classes. Future work is needed to better understand the risks of hypnotics in COPD.

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Bronchoscopic lung volume reduction in emphysema: a review

[Nakul Ravikumar](#)¹, [Ajay Wagh](#)², [Van K Holden](#)³, [D Kyle Hogarth](#)²

Affiliations expand

- PMID: 37916600
- DOI: [10.1097/MCP.0000000000001031](https://doi.org/10.1097/MCP.0000000000001031)

Abstract

Purpose of review: Chronic obstructive pulmonary disease (COPD) poses a substantial burden on the healthcare system and is currently considered the sixth leading cause of death in the United States. Emphysema, as evidenced by severe air-trapping in patients with COPD, leads to significant dyspnea and morbidity. Lung volume reduction via surgery or minimally invasive endobronchial interventions are currently available, which improve lung function and quality of life.

Recent findings: Newer studies have noted a survival benefit in patients post bronchoscopic lung volume reduction vs. those subjected to standard of care. The presence of collateral ventilation is one of the most common impeding factors to placing endobronchial valves, and if placed, these patients might not achieve lobar atelectasis; however, there are newer modalities that are now available for patients with collateral ventilation which we have described.

Summary: Combining standard of care treatment that includes smoking cessation, bronchodilators, preventive care including vaccinations, pulmonary rehabilitation, and endobronchial treatment using various interventions in decreasing hyperinflation improves quality of life and may improve survival and hence significantly reduce the burden of COPD on healthcare.

- [63 references](#)

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Am J Physiol Renal Physiol

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. 2023 Nov 2.

doi: 10.1152/ajprenal.00254.2023. Online ahead of print.

[Beta 2 adrenergic receptor agonists as a treatment for diabetic kidney disease](#)

[Ehtesham Arif](#)¹, [Danira Medunjanin](#)², [Ashish Solanki](#)³, [Xiaofeng Zuo](#)³, [Yanhui Su](#)⁴, [Yujing Dang](#)³, [Brennan Winkler](#)³, [Kasey Lerner](#)³, [Ahmed I Kamal](#)³, [Oleg Palygin](#)⁵, [Marc-Andre Cornier](#)⁶, [Bethany J Wolf](#)⁷, [Kelly J Hunt](#)⁷, [Joshua H Lipschutz](#)¹

Affiliations expand

- PMID: 37916289
- DOI: [10.1152/ajprenal.00254.2023](https://doi.org/10.1152/ajprenal.00254.2023)

Abstract

We previously showed that the long-acting β_2 -AR agonist formoterol induced recovery from AKI in mice. To determine if formoterol protected against diabetic nephropathy, the most common cause of ESKD, we used a high fat diet (HFD), a murine type 2 diabetes model, and streptozotocin, a murine type 1 diabetes model. Following formoterol treatment there was a marked recovery from and reversal of diabetic nephropathy in HFD

mice compared to those treated with vehicle alone at the ultrastructural, histological, and functional levels. Similar results were seen after formoterol treatment in mice receiving streptozotocin. To investigate effects in humans we performed a competing risk regression analysis with death as a competing risk to examine the association between patients with COPD, who use β_2 -AR agonists, and patients without COPD and progression to ESKD in a large national cohort of Veterans with stage 4 CKD between 2011-2013. Veterans were followed until 2016 or death. ESKD was defined as initiation of dialysis and/or receipt of kidney transplant. We found that COPD was associated with a 25.6% reduction in progression from stage 4 CKD to ESKD compared to no COPD after adjusting for age, diabetes, sex, race-ethnicity, comorbidities, and medication use. Sensitivity analysis showed a 33.2% reduction in ESKD in Veterans with COPD taking long-acting formoterol and a 20.8% reduction in ESKD in Veterans taking other β_2 -AR agonists when compared to those with no COPD. These data indicate that β_2 -AR agonists, especially formoterol, may be a treatment for diabetic nephropathy and perhaps other forms of CKD.

Keywords: beta agonist; diabetes; nephropathy.

SUPPLEMENTARY INFO

Grants and fundingexpand

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BMC Infect Dis

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. 2023 Nov 1;23(1):749.

doi: 10.1186/s12879-023-08689-9.

[Incremental mortality associated with nontuberculous mycobacterial lung](#)

disease among US Medicare beneficiaries with chronic obstructive pulmonary disease

[Ping Wang](#)¹, [Theodore K Marras](#)², [Mariam Hassan](#)³, [Anjan Chatterjee](#)³

Affiliations expand

- PMID: 37914999
- PMCID: [PMC10619258](#)
- DOI: [10.1186/s12879-023-08689-9](#)

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a common comorbidity in patients with nontuberculous mycobacterial lung disease (NTMLD). Both conditions are associated with increased morbidity and mortality, but data are lacking on the additional burden associated with NTMLD among patients with COPD. Thus, the goal of this study was to assess the incremental mortality risk associated with NTMLD among older adults with COPD.

Methods: A retrospective cohort study was conducted using the US Medicare claims database (2010-2017). Patients with preexisting COPD and NTMLD (cases) were matched 1:3 by age and sex with patients with COPD without NTMLD (control patients). Patients were followed up until death or data cutoff (December 31, 2017). Incremental risk of mortality was evaluated by comparing the proportions of death, annualized mortality rate, and mortality hazard rate between cases and control patients using both univariate and multivariate analyses adjusting for age, sex, comorbidities, and COPD severity.

Results: A total of 4,926 cases were matched with 14,778 control patients. In univariate analyses, a higher proportion of cases (vs. control patients) died (41.5% vs. 26.7%; $P < 0.0001$), unadjusted annual mortality rates were higher among cases (158.5 vs. 86.0 deaths/1000 person-years; $P < 0.0001$), and time to death was shorter for cases. This increased mortality risk was also reflected in subsequent multivariate analyses. Patients with COPD and NTMLD were more likely to die (odds ratio [95% CI], 1.39 [1.27-1.51]), had

higher mortality rates (rate ratio [95% CI], 1.36 [1.28-1.45]), and had higher hazard of death (hazard ratio [95% CI], 1.37 [1.28-1.46]) than control patients.

Conclusions: The substantial incremental mortality burden associated with NTMLD in patients with COPD highlights the importance of developing interventions targeting this high-risk group and may indicate an unmet need for timely and appropriate management of NTMLD.

Keywords: Chronic obstructive pulmonary disease; Incremental mortality; Nontuberculous mycobacterial lung disease; US Medicare.

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Conflict of interest statement

TKM received financial and nonfinancial research support for this manuscript from Insmmed Incorporated (Bridgewater, NJ), grants and consulting fees from Insmmed Incorporated, speaking and lecture fees from AstraZeneca and Novartis, and consultation or advisory fees from Spero and RedHill Biopharma; PW, MH, and AC are employees and shareholders of Insmmed Incorporated.

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

SUPPLEMENTARY INFO

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Tuberc Respir Dis (Seoul)

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. 2023 Nov 1.

doi: 10.4046/trd.2023.0146. Online ahead of print.

Sarcopenia in Outcome in COPD: is the tip of the iceberg?

[Hulya Sungurtekin](#)¹, [Ugur Sungurtekin](#)², [Antonio M Esquinas](#)³

Affiliations expand

- PMID: 37913749
- DOI: [10.4046/trd.2023.0146](https://doi.org/10.4046/trd.2023.0146)

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No abstract available

Keywords: Chronic obstructive pulmonary disease; Exacerbation; Mortality; Sarcopenia.

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PLoS One

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. 2023 Nov 1;18(11):e0292876.

doi: 10.1371/journal.pone.0292876. eCollection 2023.

Exploring the impact of varying definitions of exacerbations of chronic

obstructive pulmonary disease in routinely collected electronic medical records

[Hannah Whittaker](#)¹, [Kieran J Rothnie](#)², [Jennifer K Quint](#)¹

Affiliations expand

- PMID: 37910484
- PMCID: [PMC10619826](#)
- DOI: [10.1371/journal.pone.0292876](#)

Free PMC article

Abstract

Background: Validity of exposure and outcome measures in electronic medical records is vital to ensure robust, comparable study findings however, despite validation studies, definitions of variables used often differ. Using exacerbations of chronic obstructive pulmonary disease (COPD) as an example, we investigated the impact of potential misclassification of different definitions commonly used in publications on study findings.

Methods: A retrospective cohort study was performed. English primary care data from the Clinical Practice Research Datalink Aurum database with linked secondary care data were used to define a population of COPD patients ≥ 40 years old registered at a general practice. Index date was the date eligibility criteria were met and end of follow-up was 30/12/19, death or end of data collection. Exacerbations were defined using 6 algorithms based on definitions commonly used in the literature, including one validated definition. For each algorithm, the proportion of frequent exacerbators (≥ 2 exacerbations/year) and exacerbation rates were described. Cox proportional hazard regression was used to investigate each algorithm on the association between heart failure and risk of COPD exacerbation.

Findings: A total of 315,184 patients were included. Baseline proportion of frequent exacerbators varied from 2.7% to 15.3% depending on the algorithm. Rates of exacerbations over follow-up varied from 19.3 to 66.6 events/100 person-years. The adjusted hazard ratio for the association between heart failure and exacerbation varied from 1.45, 95% confidence intervals 1.42-1.49, to 1.01, 0.98-1.04.

Interpretation: The use of high validity definitions and standardisation of definitions in electronic medical records is crucial to generating high quality, robust evidence.

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Conflict of interest statement

HW and JKQ report grants from GSK, during the conduct of this study. KJR is an employee of and holds shares in GSK plc. This does not alter our adherence to PLOS ONE policies on sharing data and materials.

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

SUPPLEMENTARY INFO

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

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Anticancer Res

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. 2023 Nov;43(11):5215-5222.

doi: 10.21873/anticancerres.16723.

[Impact of Chronic Obstructive Pulmonary Disease on the Long-term](#)

Prognosis of Patients Undergoing Lobectomy for Non-small-cell Lung Cancer: A Propensity Score-matched Analysis

[Kyoto Matsudo](#)¹, [Tomoyoshi Takenaka](#)², [Asato Hashinokuchi](#)¹, [Taichi Nagano](#)¹, [Fumihiko Kinoshita](#)¹, [Shinkichi Takamori](#)¹, [Takaki Akamine](#)¹, [Mikihiro Kohno](#)¹, [Naoko Miura](#)¹, [Tomoharu Yoshizumi](#)¹

Affiliations expand

- PMID: 37909968
- DOI: [10.21873/anticancerres.16723](https://doi.org/10.21873/anticancerres.16723)

Abstract

Background/aim: Recent advances in surgery, such as thoracoscopic surgery, have made it possible to treat patients with chronic obstructive pulmonary disease (COPD) more safely than before. This study evaluated the short- and long-term prognosis of lobectomy in non-small cell lung cancer (NSCLC) patients with COPD.

Patients and methods: This retrospective, propensity-matched, cohort analysis was conducted from January 2014 to December 2018. Among 441 patients who underwent lobectomy for NSCLC, 158 (35.8%) had a preoperative diagnosis of COPD. Propensity-matched analysis, incorporating preoperative variables, was used to compare postoperative hospital stay and complications, and long-term prognosis between the groups.

Results: Propensity matching estimated 145 patients in each group. There was no difference between the two groups for length of postoperative hospital stay (12 vs. 11 days, $p=0.306$). Postoperative complications were more frequent in the COPD group (24.1%) than in the non-COPD group (16.6%), but the difference was not significant ($p=0.108$). The 5-year overall survival rate was 86.2% in the COPD group and 82.1% in the non-COPD group after matching ($p=0.580$). The corresponding 5-year recurrence-free survival rate was 72.8% in the COPD group and 67.2% in the non-COPD group after matching ($p=0.601$).

Conclusion: In case of Global Initiative for Chronic Obstructive Lung Disease (GOLD) I/II classification, COPD did not significantly worsen the prognosis of patients with NSCLC after lobectomy.

Keywords: COPD; non-small cell lung cancer; thoracoscopic surgery.

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SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS



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Int J Chron Obstruct Pulmon Dis

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. 2023 Oct 26;18:2341-2352.

doi: 10.2147/COPD.S429104. eCollection 2023.

[Prediction of Hospitalization and Mortality in Patients with Chronic Obstructive Pulmonary Disease with the New Global Initiative for Chronic Obstructive Lung Disease 2023 Group](#)

Classification: A Prospective Cohort and a Retrospective Analysis

[Wei Cheng](#)¹, [Aiyuan Zhou](#)², [Yuqin Zeng](#)¹, [Ling Lin](#)¹, [Qing Song](#)¹, [Cong Liu](#)¹, [Zijing Zhou](#)¹, [Yating Peng](#)¹, [Min Yang](#)¹, [Lizhen Yang](#)¹, [Yan Chen](#)¹, [Shan Cai](#)¹, [Ping Chen](#)¹

Affiliations expand

- PMID: 37908629
- PMCID: [PMC10615105](#)
- DOI: [10.2147/COPD.S429104](#)

Free PMC article

Abstract

Background: The revised Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2023 group ABE classification has undergone major modifications, which can simplify clinical assessment and optimize treatment recommendations for Chronic Obstructive Pulmonary Disease (COPD). However, the predictive value of the new grouping classification for prognosis is worth further exploration. We aimed to compare the prediction of hospitalization and mortality between this new GOLD group 2023 ABE classification and the earlier 2017 ABCD classification in a Chinese COPD cohort.

Methods: Data from 2,499 outpatients with COPD, who first registered in the RealDTC study of Second Xiangya Hospital from December 2016 to December 2019, were collected prospectively and assessed retrospectively. Patients were followed up on all-cause mortality until October 2022 or death.

Results : Of the 2,499 patients with COPD, the risk of hospitalization during the first-year follow-up was higher in group E than in groups A and B. The mortality was higher in group E than in groups A and B, and group B was higher than group A. No differences were seen in the area under the curve (AUC) of 2017 vs 2023 GOLD grouping to predict hospitalization. The time-dependent AUC and concordance index for predicting mortality is slightly higher in the GOLD 2017 ABCD than in the 2023 ABE groups. The new GOLD 12-subgroup (1A-4E) classification combining the GOLD 1-4 staging and grouping performed similarly discriminate predictive power for mortality to the GOLD 2017 16-subgroup (A1-4D) classification.

Conclusion: The risk of hospitalization during the first-year follow-up was higher in group E than in groups A and B. The all-cause mortality increased gradually from GOLD group A to E. The GOLD 2023 classification based on ABE groups did not predict mortality better than the earlier 2017 ABCD classifications.

Keywords: COPD; GOLD 2023; hospitalization; mortality.

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Conflict of interest statement

The authors report no conflicts of interest in this work.

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

SUPPLEMENTARY INFO

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

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[Review](#)

ERJ Open Res

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. 2023 Oct 30;9(5):00180-2023.

doi: 10.1183/23120541.00180-2023. eCollection 2023 Sep.

Update on metabolomic findings in COPD patients

[Joaquim Gea](#)^{1,2,3}, [César J Enríquez-Rodríguez](#)^{1,2}, [Bella Agranovich](#)⁴, [Sergi Pascual-Guardia](#)^{1,2,3}

Affiliations expand

- PMID: 37908399
- PMCID: [PMC10613990](#)
- DOI: [10.1183/23120541.00180-2023](#)

Free PMC article

Abstract

COPD is a heterogeneous disorder that shows diverse clinical presentations (phenotypes and "treatable traits") and biological mechanisms (endotypes). This heterogeneity implies that to carry out a more personalised clinical management, it is necessary to classify each patient accurately. With this objective, and in addition to clinical features, it would be very useful to have well-defined biological markers. The search for these markers may either be done through more conventional laboratory and hypothesis-driven techniques or relatively blind high-throughput methods, with the omics approaches being suitable for the latter. Metabolomics is the science that studies biological processes through their metabolites, using various techniques such as gas and liquid chromatography, mass spectrometry and nuclear magnetic resonance. The most relevant metabolomics studies carried out in COPD highlight the importance of metabolites involved in pathways directly related to proteins (peptides and amino acids), nucleic acids (nitrogenous bases and nucleosides), and lipids and their derivatives (especially fatty acids, phospholipids, ceramides and eicosanoids). These findings indicate the relevance of inflammatory-immune processes, oxidative stress, increased catabolism and alterations in the energy production. However, some specific findings have also been reported for different COPD phenotypes, demographic characteristics of the patients, disease progression profiles, exacerbations, systemic manifestations and even diverse treatments. Unfortunately, the studies carried out to date have some limitations and shortcomings and there is still a need to define clear metabolomic profiles with clinical utility for the management of COPD and its implicit heterogeneity.

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Conflict of interest statement

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

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COPD

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. 2023 Dec;20(1):338-347.

doi: 10.1080/15412555.2023.2270729. Epub 2023 Oct 31.

The Study of the Influence of *IL5RA* Variants on Chronic Obstructive Pulmonary Disease

[Siguang Li](#)¹, [Lingsang Lin](#)¹, [Jie Zhao](#)², [Zehua Yang](#)², [Yi Zhong](#)¹, [Linhui Huang](#)², [Jie Chen](#)¹, [Lei Zhang](#)², [Yipeng Ding](#)^{1,2}, [Tian Xie](#)²

Affiliations expand

- PMID: 37905709
- DOI: [10.1080/15412555.2023.2270729](https://doi.org/10.1080/15412555.2023.2270729)

Abstract

Chronic obstructive pulmonary disease (COPD) is a complex disease, and its pathogenesis is influenced by genetic factors. This study aimed to evaluate the role of *IL5RA* genetic variation in the risk of COPD. In this study, 498 patients with COPD and 498 normal controls were recruited. Subsequently, five SNPs (rs3804795, rs2290610, rs13097407, rs334782, and rs3856850) in the *IL5RA* gene were genotyped. Logistic analysis examined the association of five single nucleotide polymorphisms (SNPs) in *IL5RA* with the risk of COPD under various genetic models. Furthermore, the association between *IL5RA* and susceptibility to COPD was comprehensively analyzed with stratification based on age, sex, smoking, and alcohol consumption. Our study showed that *IL5RA* rs13097407 reduced susceptibility to COPD (OR = 0.43, $p < 0.001$, p (FDR) < 0.001). On the other hand, rs3856850 was associated with an increased risk of COPD (OR = 1.71, $p = 0.002$, p (FDR) = 0.002). Interestingly, the effect of *IL5RA* SNPs on susceptibility to COPD was found to be influenced by factors such as sex and smoking. *IL5RA* gene variants were significantly associated with susceptibility to COPD.

Keywords: A case-control study; *IL5RA*; chronic obstructive pulmonary disease (COPD); genetic variation; single nucleotide polymorphism (SNP); susceptibility.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances expand

FULL TEXT LINKS



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23

J Korean Med Sci



. 2023 Oct 30;38(42):e344.

doi: 10.3346/jkms.2023.38.e344.

[Risk of Ischemic Heart Disease in Chronic Obstructive Pulmonary Disease: A Nationwide Cohort Study](#)

[Bo-Guen Kim](#)^{#1}, [Hyun Lee](#)^{#1}, [Min Gu Kang](#)^{#2,3}, [Jong Seung Kim](#)^{2,3,4}, [Ji-Yong Moon](#)⁵

Affiliations [expand](#)

- PMID: 37904657
- PMCID: [PMC10615639](#)
- DOI: [10.3346/jkms.2023.38.e344](#)

Free PMC article

Abstract

Background: Subjects with chronic obstructive pulmonary disease (COPD) have a higher risk of ischemic heart disease (IHD) than individuals without COPD; however, longitudinal evidence is lacking. Therefore, we aimed to estimate the risk of IHD between COPD and control cohorts using a longitudinal nationwide database.

Methods: We used 2009-2017 data from the Korean National Health Insurance Service National Sample Cohort (NHIS-NSC). Adult participants at least 20 years of age who underwent health examinations and without a history of COPD or IHD were included (n = 540,976). Participants were followed from January 1, 2009, until death, development of IHD, or December 31, 2019, whichever came first.

Results: At baseline, there were 3,421 participants with incident COPD and 537,555 participants without COPD. During a median of 8.0 years (5.3-9.1 years) of follow-up, 2.51% of the participants with COPD (n = 86) and 0.77% of the participants without COPD (n = 4,128) developed IHD, with an incidence of 52.24 and 10.91 per 10,000 person-years, respectively. Participants with COPD had a higher risk of IHD (adjusted hazard ratio, 1.55; 95% confidence interval, 1.25-1.93) than subjects without COPD. Demographics such as age, sex, body mass index, and personal health behaviors including smoking status and physical activity did not show significant interaction with the relationship between COPD and IHD (*P* for interaction > 0.05 for all).

Conclusion: The results indicate that COPD is associated with the development of IHD independent of demographic characteristics and health-related behaviors. Based on these results, clinicians should closely monitor the onset of IHD in subjects with COPD.

Keywords: Chronic Obstructive Pulmonary Disease; Ischemic Heart Disease.

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Conflict of interest statement

The authors have no potential conflicts of interest to disclose.

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

SUPPLEMENTARY INFO

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

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. 2023 Oct 30;13(10):e075209.

doi: 10.1136/bmjopen-2023-075209.

Associations between spirometric impairments and microvascular complications in type 2 diabetes: a cross-sectional study

[Charles F Hayfron-Benjamin](#)^{1,2}, [Charles Agyemang](#)^{3,4}, [Bert-Jan H van den Born](#)^{5,6}, [Albert G B Amoah](#)⁷, [Kwesi Nyan Amisah-Arthur](#)⁸, [Latif Musah](#)², [Benjamin Abaidoo](#)⁸, [Pelagia Awula](#)², [Henry Wedoi Awuviri](#)², [Joseph Agyapong Abbey](#)², [Deladem A Fummey](#)², [Joana N Ackam](#)⁹, [Gloria Odom Asante](#)¹⁰, [Simone Hashimoto](#)^{11,12}, [Anke H Maitland-van der Zee](#)^{11,12}

Affiliations expand

- PMID: 37903605
- PMCID: [PMC10619106](#)
- DOI: [10.1136/bmjopen-2023-075209](#)

Free PMC article

Abstract

Objective: Evidence shows that the conventional cardiometabolic risk factors do not fully explain the burden of microvascular complications in type 2 diabetes (T2D). One potential factor is the impact of pulmonary dysfunction on systemic microvascular injury. We assessed the associations between spirometric impairments and systemic microvascular complications in T2D.

Design: Cross-sectional study.

Setting: National Diabetes Management and Research Centre in Ghana.

Participants: The study included 464 Ghanaians aged ≥ 35 years with established diagnosis of T2D without primary myocardial disease or previous/current heart failure. Participants were excluded if they had primary lung disease including asthma or chronic obstructive pulmonary disease.

Primary and secondary outcome measures: The associations of spirometric measures (forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC) and FEV_1/FVC ratio) with microvascular complications (nephropathy (albumin-creatinine ratio ≥ 3 mg/g), neuropathy (vibration perception threshold ≥ 25 V and/or Diabetic Neuropathy Symptom score > 1) and retinopathy (based on retinal photography)) were assessed using multivariable logistic regression models with adjustments for age, sex, diabetes duration, glycated haemoglobin concentration, suboptimal blood pressure control, smoking pack years and body mass index.

Results: In age and sex-adjusted models, lower Z-score FEV_1 was associated with higher odds of nephropathy (OR 1.55, 95% CI 1.19-2.02, $p=0.001$) and neuropathy (1.27 (1.01-1.65), 0.038) but not retinopathy (1.22 (0.87-1.70), 0.246). Similar observations were made for the associations of lower Z-score FVC with nephropathy (1.54 (1.19-2.01), 0.001), neuropathy (1.25 (1.01-1.54), 0.037) and retinopathy (1.19 (0.85-1.68), 0.318). In the fully adjusted model, the associations remained significant for only lower Z-score FEV_1 with nephropathy (1.43 (1.09-1.87), 0.011) and neuropathy (1.34 (1.04-1.73), 0.024) and for lower Z-score FVC with nephropathy (1.45 (1.11-1.91), 0.007) and neuropathy (1.32 (1.03-1.69), 0.029). Lower Z-score FEV_1/FVC ratio was not significantly associated with microvascular complications in age and sex and fully adjusted models.

Conclusion: Our study shows positive but varying strengths of associations between pulmonary dysfunction and microvascular complications in different circulations. Future studies could explore the mechanisms linking pulmonary dysfunction to microvascular complications in T2D.

Keywords: diabetic nephropathy & vascular disease; diabetic neuropathy; diabetic retinopathy; pulmonary disease, chronic obstructive.

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Conflict of interest statement

Competing interests: None declared.

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

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Publication types, MeSH termsexpand

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Curr Opin Pulm Med

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. 2023 Oct 31.

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[Burden, clinical features, and outcomes of post-tuberculosis chronic obstructive lung diseases](#)

[Inderpaul Singh Sehgal](#)¹, [Sahajal Dhooria](#)¹, [Valliappan Muthu](#)¹, [Helmut J F Salzer](#)^{2,3,4}, [Ritesh Agarwal](#)¹

Affiliations expand

- PMID: 37902135
- DOI: [10.1097/MCP.0000000000001026](https://doi.org/10.1097/MCP.0000000000001026)

Abstract

Purpose of review: Post-tuberculosis lung disease (PTLD) is an increasingly recognized and debilitating consequence of pulmonary tuberculosis (PTB). In this review, we provide a comprehensive overview of PTLD with airflow obstruction (PTLD-AFO), focusing on its

burden, pathophysiology, clinical manifestations, diagnostic methods, and management strategies.

Recent findings: The relationship between PTLD and airflow obstruction is complex and multifactorial. Approximately 60% of the patients with PTLD have some spirometric abnormality. Obstruction is documented in 18-22% of PTLD patients. The host susceptibility and host response to mycobacterium drive the pathogenic mechanism of PTLD. A balance between inflammatory, anti-inflammatory, and fibrotic pathways decides whether an individual with PTB would have PTLD after microbiological cure. An obstructive abnormality in PTLD-AFO is primarily due to destruction of bronchial walls, aberrant healing, and reduction of mucosal glands. The most common finding on computed tomography (CT) of thorax in patients with PTLD-AFO is bronchiectasis and cavitation. Therefore, the 'Cole's vicious vortex' described in bronchiectasis applies to PTLD. A multidisciplinary approach is required for diagnosis and treatment. The disability-adjusted life-years (DALYs) attributed to PTLD represent about 50% of the total estimated burden of DALYs due to tuberculosis (TB). Patients with PTLD require comprehensive care that includes psychosocial support, pulmonary rehabilitation, and vaccination against respiratory pathogens. In the absence of trials evaluating different treatments for PTLD-AFO, therapy is primarily symptomatic.

Summary: PTLD with airflow obstruction has considerable burden and causes a significant morbidity and mortality. However, many aspects of PTLD-AFO still need to be answered. Studies are required to evaluate different phenotypes, especially concerning Aspergillus-related complications. The treatment should be personalized based on the predominant phenotype of airflow obstruction. Extensive studies to understand the exact burden, pathogenesis, and treatment of PTLD-AFO are needed.

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Observational Study



Depression, anxiety, and quality of life as predictors of rehospitalization in patients with chronic heart failure

[Jovan Veskovic](#)^{1,2}, [Mina Cvetkovic](#)³, [Elvis Tahirovic](#)⁴, [Marija Zdravkovic](#)⁵, [Svetlana Apostolovic](#)⁶, [Dragana Kosevic](#)⁷, [Goran Loncar](#)^{7,8}, [Danilo Obradovic](#)⁹, [Dragan Matic](#)¹⁰, [Aleksandra Ignjatovic](#)¹¹, [Tatjana Cvetkovic](#)¹¹, [Maximilian G Posch](#)⁴, [Sara Radenovic](#)³, [Arsen D Ristić](#)⁸, [Danilo Dokic](#)⁴, [Nenad Milošević](#)⁴, [Natasa Panic](#)⁴, [Hans-Dirk Düngen](#)^{12,13}

Affiliations expand

- PMID: 37891464
- PMCID: [PMC10612261](#)
- DOI: [10.1186/s12872-023-03500-8](#)

Free PMC article

Abstract

Background: Chronic heart failure (CHF) is a severe condition, often co-occurring with depression and anxiety, that strongly affects the quality of life (QoL) in some patients. Conversely, depressive and anxiety symptoms are associated with a 2-3 fold increase in mortality risk and were shown to act independently of typical risk factors in CHF progression. The aim of this study was to examine the impact of depression, anxiety, and QoL on the occurrence of rehospitalization within one year after discharge in CHF patients.

Methods: 148 CHF patients were enrolled in a 10-center, prospective, observational study. All patients completed two questionnaires, the Hospital Anxiety and Depression Scale (HADS) and the Questionnaire Short Form Health Survey 36 (SF-36) at discharge timepoint.

Results: It was found that demographic and clinical characteristics are not associated with rehospitalization. Still, the levels of depression correlated with gender ($p \leq 0.027$) and marital status ($p \leq 0.001$), while the anxiety values were dependent on the occurrence of chronic obstructive pulmonary disease (COPD). However, levels of depression (HADS-Depression) and anxiety (HADS-Anxiety) did not correlate with the risk of rehospitalization. Univariate logistic regression analysis results showed that rehospitalized patients had significantly lower levels of Bodily pain (BP, $p = 0.014$), Vitality (VT, $p = 0.005$), Social Functioning (SF, $p = 0.007$), and General Health (GH, $p = 0.002$). In the multivariate model, poor GH (OR 0.966, $p = 0.005$) remained a significant risk factor for rehospitalization, and poor General Health is singled out as the most reliable prognostic parameter for rehospitalization (AUC = 0.665, $P = 0.002$).

Conclusion: Taken together, our results suggest that QoL assessment complements clinical prognostic markers to identify CHF patients at high risk for adverse events.

Clinical trial registration: The study is registered under <http://clinicaltrials.gov> ([NCT01501981](https://doi.org/10.1186/1745-7256-1501981), first posted on 30/12/2011), sponsored by Charité - Universitätsmedizin Berlin.

Keywords: Anxiety; Depression; Heart failure; Prediction; Quality of life; Rehospitalization.

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Conflict of interest statement

The authors declare no competing interests.

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

SUPPLEMENTARY INFO

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. 2023 Nov 1;38(11):465-471.

doi: 10.4140/TCP.n.2023.465.

Geriatric Pharmacotherapy Case Series: Chronic Obstructive Pulmonary Disease

[Nadia Khartabil](#)¹

Affiliations expand

- PMID: 37885095
- DOI: [10.4140/TCP.n.2023.465](https://doi.org/10.4140/TCP.n.2023.465)

Abstract

Patient is a 77-year-old female who is a retired teacher living with her husband. Patient presents to the clinic for a post-hospital discharge visit. She was treated for bacterial pneumonia with combination therapy of azithromycin and cefpodoxime. She was diagnosed with COPD seven years ago when she had to be treated for chronic dyspnea, cough, and sputum that kept her breathless and required hospitalization.

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Meta-Analysis

BMC Pulm Med

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. 2023 Oct 26;23(1):405.

doi: 10.1186/s12890-023-02689-w.

Impact of bronchoscopic thermal vapor ablation on lung volume reduction in patients with emphysema: a meta-analysis

[Lijia Zhi](#)¹, [Liping Liao](#)², [Zhi Wu](#)³, [Tiezhu Wang](#)³, [Yuming Ye](#)³, [Hao Li](#)³, [Li Lin](#)³, [Jia-Chao Qi](#)⁴, [Liangji Zhang](#)⁵

Affiliations expand

- PMID: 37884912
- PMCID: [PMC10601098](#)
- DOI: [10.1186/s12890-023-02689-w](#)

Free PMC article

Abstract

Background: Bronchoscopic lung volume reduction (LVR) could significantly improve pulmonary function and quality of life in patients with emphysema. We aimed to assess the efficacy and safety of bronchoscopic thermal vapor ablation (BTVA) on LVR in patients with emphysema at different stage.

Methods: A systematic search of database including PubMed, Embase and Cochrane library was conducted to determine all the studies about bronchoscopic thermal vapor ablation published through Dec 1, 2022. Related searching terms were "lung volume reduction", "bronchoscopic thermal vapor ablation", "bronchial thermal vapor ablation" "BTVA" and "emphysema", "efficacy" and "safety". We used standardized mean difference (SMD) to analyze the summary estimates for BTVA therapy.

Results: We retrieved 30 records through database search, and 4 trials were selected for meta-analysis, including 112 patients with emphysema. Meta-analysis of the pooled effect showed that levels of forced expiratory volume in 1 s (FEV1), residual volume (RV), total lung capacity (TLC), 6-min walk distance (6MWD) and St George's Respiratory Questionnaire (SGRQ) were significantly improved in patients with emphysema following BTVA treatment between 6 months vs. baseline. Additionally, no significant changes in FEV1, RV, TLC and SGRQ occurred from 3 to 6 months of follow-up except for 6MWD. The magnitude of benefit was higher at 3 months compared to 6 months. The most common complications at 6 months were treatment-related chronic obstructive pulmonary disease (COPD) exacerbations (RR: 12.49; 95% CI: 3.06 to 50.99; $p < 0.001$) and pneumonia (RR: 9.49; 95% CI: 2.27 to 39.69; $p < 0.001$).

Conclusions: Our meta-analysis provided clinically relevant information about the impact and safety of BTVA on predominantly upper lobe emphysema. Particularly, short-term significant improvement of lung function and quality of life occurred especially within the initial 3 months. Further large-scale, well-designed long-term interventional investigations are needed to clarify this issue.

Keywords: Bronchoscopic thermal vapor ablation; Efficacy; Emphysema; Lung volume reduction; Safety.

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Conflict of interest statement

The authors declare no competing interests.

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

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Curr Opin Pulm Med



. 2023 Oct 27.

doi: 10.1097/MCP.0000000000001025. Online ahead of print.

[Supplemental oxygen therapy in chronic obstructive pulmonary disease: is less is more? How much is too much?](#)

[Ayham Daher](#)¹, [Michael Dreher](#)

Affiliations expand

- PMID: 37882582
- DOI: [10.1097/MCP.0000000000001025](https://doi.org/10.1097/MCP.0000000000001025)

Abstract

Purpose of review: Currently available evidence supporting the use of supplemental oxygen therapy (SOT) in chronic obstructive pulmonary disease (COPD) is complex, and data on the mortality reduction associated with SOT usage in patients with severe daytime resting hypoxemia have not been updated since the development of other treatments.

Recent findings: No reduction in mortality was found when SOT was used in patients with moderate resting daytime, isolated nocturnal, or exercise-induced hypoxemia. However, some of these patients obtain other significant benefits during SOT, including increased exercise endurance, and a mortality reduction is possible in these 'responders'. The adverse effects of long-term oxygen therapy also need to be considered, such as reduced mobility and social stigma. Furthermore, conservative SOT could improve outcomes in the setting

of COPD exacerbations compared with higher concentration oxygen regimens. Compared with usual fixed-dose SOT, automated oxygen administration devices might reduce dyspnea during exercise and COPD exacerbations.

Summary: Current recommendations for SOT need to be revised to focus on patients who respond best and benefit most from this therapy. A conservative approach to SOT can reduce side effects compared with higher concentration oxygen regimens, and automated oxygen administration devices may help to optimize SOT.

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Neurogastroenterol Motil

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. 2023 Oct 26:e14699.

doi: 10.1111/nmo.14699. Online ahead of print.

[Selective dysfunction of the crural diaphragm in patients with chronic restrictive and obstructive lung disease](#)

[Jisha Joshua](#)¹, [Chetna Pathak](#)¹, [Ali Zifan](#)², [Ruohui Chen](#)³, [Atul Malhotra](#)², [Ravinder K Mittal](#)²

Affiliations expand

- PMID: 37882102

- DOI: [10.1111/nmo.14699](https://doi.org/10.1111/nmo.14699)

Abstract

Background: Gastroesophageal reflux (GER) is known to be associated with chronic lung diseases. The driving force of GER is the transdiaphragmatic pressure (Pdi) generated mainly by costal and crural diaphragm contraction. The latter also enhances the esophagogastric junction (EGJ) pressure to guard against GER.

Methods: The relationship between Pdi and EGJ pressure was determined using high resolution esophageal manometry in patients with interstitial lung disease (ILD, n = 26), obstructive lung disease (OLD, n = 24), and healthy subjects (n = 20).

Key results: The patient groups did not differ with respect to age, gender, BMI, and pulmonary rehabilitation history. Patients with ILD had significantly higher Pdi but lower EGJ pressures as compared to controls and OLD patients ($p < 0.001$). In control subjects, the increase in EGJ pressure at all-time points during inspiration was greater than Pdi. In contrast, the EGJ pressure during inspiration was less than Pdi in 14 patients with ILD and 7 patients with OLD. The drop in EGJ pressure was usually seen after the peak Pdi in ILD group ($p < 0.0001$) and before the peak Pdi in OLD group, ($p = 0.08$). Nine patients in the ILD group had sliding hiatus hernia, compared to none in control subjects ($p = 0.003$) and two patients in the OLD, ($p = 0.04$).

Conclusions and inferences: A higher Pdi and low EGJ pressure, and dissociation between Pdi and EGJ pressure temporal relationship suggests selective dysfunction of the crural diaphragm in patients with chronic lung diseases and may explain the higher prevalence of GERD in ILD as seen in previous studies.

Keywords: crural diaphragm; esophagogastric junction; gastroesophageal reflux; hiatus hernia; lower esophageal sphincter; transdiaphragmatic pressure gradient.

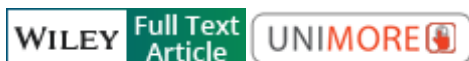
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Review

Curr Opin Support Palliat Care



. 2023 Dec 1;17(4):296-300.

doi: 10.1097/SPC.0000000000000682. Epub 2023 Oct 26.

Recent advances in bronchoscopic lung volume reduction for severe COPD patients

[Rein Posthuma](#)^{1,2,3}, [Anouk W Vaes](#)¹, [Martijn A Spruit](#)^{1,2,3}, [Lowie E G W Vanfleteren](#)⁴

Affiliations expand

- PMID: 37877448
- DOI: [10.1097/SPC.0000000000000682](https://doi.org/10.1097/SPC.0000000000000682)

Abstract

Purpose of review: Bronchoscopic lung volume reduction (BLVR) is a novel and effective treatment for a specific phenotype of chronic obstructive pulmonary disease (COPD) characterized by advanced emphysema with static lung hyperinflation and severe breathlessness. This review aims to provide an overview of the recent advances made in BLVR.

Recent findings: For achieving optimal outcomes with BLVR, patient selection and target lobe identification is crucial. BLVR has recently also been established to improve pulmonary function, exercise capacity and quality of life in COPD patients falling outside the standard treatment criteria, including patients with moderate hyperinflation, chronic

hypercapnic failure or with very low diffusion capacity. In a cluster analysis, target lobe characteristics like emphysema destruction, air trapping and perfusion were found to be important discriminators between responders and non-responders. A potential survival benefit has been demonstrated in BLVR-treated patients when compared to non-treated patients. Long-term outcomes showed sustained outcomes of BLVR; however, effects decline over time, probably due to disease progression.

Summary: BLVR using one-way endobronchial valves has become a guideline treatment offered in specialized intervention centres for a specific subgroup of COPD patients. Recent studies further characterize responders, describe extrapulmonary effects of BLVR and show positive long-term outcomes and a potential survival benefit.

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Thromb Res

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. 2023 Nov;231:58-64.

doi: 10.1016/j.thromres.2023.09.013. Epub 2023 Sep 28.

[Pulmonary embolism diagnostic strategies in patients with COPD](#)

exacerbation: Post-hoc analysis of the PEP trial

[Geoffroy Rambaud](#)¹, [Vicky Mai](#)², [Camille Motreff](#)³, [Olivier Sanchez](#)⁴, [Pierre-Marie Roy](#)⁵, [Yannick Auffret](#)¹, [Raphael Le Mao](#)³, [Frédéric Gagnadoux](#)⁶, [Nicolas Paleiron](#)⁷, [Jeannot Schmidt](#)⁸, [Jean Pastre](#)³, [Michel Nonent](#)⁹, [Cécile Tromeur](#)³, [Pierre-Yves Salaun](#)¹⁰, [Patrick Mismetti](#)¹¹, [Philippe Girard](#)¹², [Karine Lacut](#)³, [Catherine A Lemarié](#)³, [Guy Meyer](#)¹³, [Christophe Leroyer](#)³, [Grégoire Le Gal](#)¹⁴, [Laurent Bertoletti](#)¹¹, [Francis Couturaud](#)¹⁵; "PEP" investigators

Affiliations expand

- PMID: 37806116
- DOI: [10.1016/j.thromres.2023.09.013](https://doi.org/10.1016/j.thromres.2023.09.013)

Abstract

Background: The prevalence of pulmonary embolism (PE) is approximately 11-17 % in patients with an acute exacerbation of chronic obstructive pulmonary disease (AE-COPD). The optimal diagnostic strategy for PE in these patients remains undetermined.

Aims: To evaluate the safety and efficacy of standard (revised Geneva and Wells PE scores combined with fixed D-dimer cut-off) and computed tomography pulmonary angiogram (CTPA)-sparing diagnostic strategies (ADJUST-PE, YEARS, PEGeD, 4PEPS) in patients with AE-COPD.

Method: Post-hoc analyses of data from the multicenter prospective PEP study were performed. The primary outcome was the diagnostic failure rate of venous thromboembolism (VTE) during the entire study period. Secondary outcomes included diagnostic failure rate of PE and deep venous thrombosis (DVT), respectively, during the entire study period and the number of CTPA needed per diagnostic strategy.

Results: 740 patients were included. The revised Geneva and Wells PE scores combined with fixed D-dimer cut-off had a diagnostic failure rate of VTE of 0.7 % (95%CI 0.3 %-1.7 %), but >70.0 % of the patients needed imaging. All CTPA-sparing diagnostic algorithms reduced the need for CTPAs (-10.1 % to -32.4 %, depending on the algorithm), at the cost of an increased VTE diagnosis failure rate of up to 2.1 % (95%CI 1.2 %-3.4 %).

Conclusion: Revised Geneva and Wells PE scores combined with fixed D-dimer cut-off were safe, but a high number of CTPA remained needed. CTPA-sparing algorithms would reduce imaging, at the cost of an increased VTE diagnosis failure rate that exceeds the

safety threshold. Further studies are needed to improve diagnostic management in this population.

Keywords: Chronic obstructive airway disease; Chronic obstructive pulmonary disease; Deep venous thrombosis; Pulmonary embolism; Venous thromboembolism.

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Conflict of interest statement

Declaration of competing interest The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr. Couturaud reports having received research grant support from Bristol-Myers Squibb/Pfizer and Bayer and fees for board memberships or symposia from Bayer, Bristol-Myers Squibb/Pfizer, Merck Sharp and Dohme, Merck Sharp and Dohme, Sanofi, Leo Pharma, Janssen and Astra Zeneca and having received travel support from Bayer, Bristol-Myers Squibb/Pfizer, Leo Pharma, Pfizer. Dr. Bertolletti reports having received research grant support from Bayer and fees for board memberships or symposia from Actelion, Aspen, Bayer, Bristol-Myers Squibb/Pfizer and MSD, and having received travel support from Aspen, Bayer, Bristol-Myers Squibb/Pfizer, Daiichi Sankyo, Leo Pharma, MSD and Actelion. Dr. Pastre declares he has no conflict of interest related to this research. Dr. Roy declares he has no conflict of interest related to this research. Dr. Rambaud declares he has no conflict of interest related to this research. Dr. Mai declares she has no conflict of interest related to this research. Dr. Motreff declares she has no conflict of interest related to this research. Dr. Auffret declares he has no conflict of interest related to this research. Dr. Le Mao declares he has no conflict of interest related to this research. Dr. Gagnadoux declares he has no conflict of interest related to this research. Dr. Paleiron declares he has no conflict of interest related to this research. Dr. Schmidt declares he has no conflict of interest related to this research. Dr. Sanchez reports having received research grant support from Bayer, Daiichi-Sankyo and Portola Pharmaceuticals, and fees or non-financial support for consultancy activities from Actelion, GlaxoSmithKline, Boehringer Ingelheim and Chiesi. Dr. Bressollette declares he has no conflict of interest related to this research. Dr. Nonent declares he has no conflict of interest related to this research. Dr. Tromeur declares she has no conflict of interest related to this research. Dr. Salaun declares he has no conflict of interest related to this research. Dr. Mismetti reports having received research grants from Bayer, fees for board memberships from Bayer, Bristol-Myers Squibb/Pfizer and Daiichi Sankyo, for lectures from Bayer, Boehringer Ingelheim, Bristol-Myers Squibb/Pfizer, Daiichi Sankyo and Sanofi, and for development of educational presentations from Bayer and Bristol-Myers Squibb/Pfizer. Dr. Girard reports having received personal fees and non-financial support from Bayer and Leo Pharma. Dr. Lacut reports having received personal fees from Bayer-Health Care, Bristol-Myers Squibb and Boehringer Ingelheim. Dr. Lemarie declares she has no conflict of interest related to this

research. Dr. Meyer reports having received research grant support from Bayer, Boehringer Ingelheim, LEO Pharma Research Foundation and Sanofi, having been an uncompensated board member and a consultant for Bayer, Boehringer-Ingelheim, Bristol-Myers Squibb, Leo Pharma and Pfizer, and having received travel support from Bayer, Boehringer Ingelheim, Daiichi Sankyo, Leo Pharma and Sanofi. Dr. Leroyer reports having received research grant support from Pfizer and fees for board memberships or symposia from Bayer and Astra Zeneca and having received travel support from Bayer, Leo Pharma. No other potential conflict of interest relevant to this article was reported.

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Curr Opin Support Palliat Care

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. 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](https://doi.org/10.1097/SPC.0000000000000674)

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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](#)

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[Review](#)

Cytokine

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. 2023 Nov;171:156352.

doi: 10.1016/j.cyto.2023.156352. Epub 2023 Sep 11.

[Association between single-nucleotide polymorphism of cytokines genes and chronic obstructive pulmonary disease: A systematic review and meta-analysis](#)

[Ali Masjedy](#)¹, [Mahmood Salesi](#)¹, [Ali Ahmadi](#)², [Jafar Salimian](#)³, [Sadegh Azimzadeh Jamalkandi](#)⁴

Affiliations [expand](#)

- PMID: 37703677
- DOI: [10.1016/j.cyto.2023.156352](https://doi.org/10.1016/j.cyto.2023.156352)

Abstract

Chronic obstructive pulmonary disease (COPD) is a common chronic inflammatory disease with high morbidity and mortality rates worldwide. Cytokines, which are the main regulators of immune responses, play crucial roles in inflammatory diseases such as COPD. Moreover, certain genetic variations can alter cytokine expression, and changes in cytokine level or function can affect disease susceptibility. Therefore, investigating the association between genetic variations and disease progression can be useful for prevention and treatment. Several studies have explored the association between common genetic variations in cytokine genes and COPD susceptibility. In this study, we summarized the reported studies and, where possible, conducted a systematic review and meta-analysis to evaluate the genetic association between various cytokines and COPD pathogenesis. We extracted relevant articles from PubMed and Google Scholar databases using a standard systematic search strategy. We included a total of 183 studies from 78 separate articles that evaluated 50 polymorphisms in 12 cytokine genes in this study. Our analysis showed that among all reported cytokine polymorphisms (including TNF- α , TGF- β , IL1, IL1RN, IL4, IL4R, IL6, IL10, IL12, IL13, IL17, IL18, IL27, and IL33), only four variants, including TNF- α -rs1800629, TGF- β 1-rs6957, IL13-rs1800925, and IL6-rs1800796, were associated with the risk of COPD development. This updated meta-analysis strongly supports the association of TNF- α -rs1800629, TGF- β 1-rs6957, IL13-rs1800925, and IL6-rs1800796 variants with a high risk of COPD.

Keywords: Chronic obstructive pulmonary disease; Cytokine; Meta-analysis; Variant.

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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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Effects of Midazolam versus Morphine in acute cardiogenic pulmonary edema and chronic obstructive pulmonary disease: An analysis of MIMO trial

[Alberto Domínguez-Rodríguez¹](#), [Daniel Hernandez-Vaquero²](#), [Coral Suero-Mendez³](#), [Guillermo Burillo-Putze⁴](#), [Victor Gil⁵](#), [Rafael Calvo-Rodríguez⁶](#), [Pascual Piñera-Salmeron⁷](#), [Pere Llorens⁸](#), [Francisco J Martín-Sánchez⁹](#), [Pedro Abreu-Gonzalez¹⁰](#), [Òscar Miró⁵](#); [MIMO \(Midazolam versus Morphine\) Trial Investigators](#)

Affiliations expand

- PMID: 37703629
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Abstract

Aims: Chronic obstructive pulmonary disease (COPD) is an important comorbidity in heart failure. The MIMO trial showed that patients with acute cardiogenic pulmonary edema (ACPE) treated with midazolam had fewer serious adverse events than those treated with morphine. In this post hoc analysis, we examined whether the presence/ absence of COPD modifies the reduced risk of midazolam over morphine.

Methods: Patients >18 years old clinically diagnosed with ACPE and with dyspnea and anxiety were randomized (1:1) at emergency department arrival to receive either intravenous midazolam or morphine. In this post hoc analysis, we calculated the relative risk (RR) of serious adverse events in patients with and without COPD. Calculating the

CochranMantel-Haenszel interaction test, we evaluated if COPD modified the reduced risk of serious adverse events in the midazolam arm compared to morphine.

Results: Overall, 25 (22.5%) of the 111 patients randomized had a history of COPD. Patients with COPD were more commonly men with a history of previous episodes of heart failure, than participants without COPD. In the COPD group, the RR for the incidence of serious adverse events in the midazolam versus morphine arm was 0.36 (95%CI, 0.1-1.46). In the group without COPD, the RR was 0.44 (95%CI, 0.22-0.91). The presence of COPD did not modify the reduced risk of serious adverse events in the midazolam arm compared to morphine (p for interaction =0.79).

Conclusions: The reduced risk of serious adverse events in the midazolam group compared with morphine is similar in patients with and without COPD.

Keywords: Acute cardiogenic pulmonary edema; Chronic obstructive pulmonary disease; Heart failure; Midazolam; Morphine.

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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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[Review](#)

Lancet Respir Med

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. 2023 Nov;11(11):1020-1034.

COPD and multimorbidity: recognising and addressing a syndemic occurrence

[Leonardo M Fabbri](#)¹, [Bartolome R Celli](#)², [Alvar Agustí](#)³, [Gerard J Criner](#)⁴, [Mark T Dransfield](#)⁵, [Miguel Divo](#)², [Jamuna K Krishnan](#)⁶, [Lies Lahousse](#)⁷, [Maria Montes de Oca](#)⁸, [Sundeep S Salvi](#)⁹, [Daiana Stolz](#)¹⁰, [Lowie E G W Vanfleteren](#)¹¹, [Claus F Vogelmeier](#)¹²

Affiliations expand

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Abstract

Most patients with chronic obstructive pulmonary disease (COPD) have at least one additional, clinically relevant chronic disease. Those with the most severe airflow obstruction will die from respiratory failure, but most patients with COPD die from non-respiratory disorders, particularly cardiovascular diseases and cancer. As many chronic diseases have shared risk factors (eg, ageing, smoking, pollution, inactivity, and poverty), we argue that a shift from the current paradigm in which COPD is considered as a single disease with comorbidities, to one in which COPD is considered as part of a multimorbid state-with co-occurring diseases potentially sharing pathobiological mechanisms-is needed to advance disease prevention, diagnosis, and management. The term syndemics is used to describe the co-occurrence of diseases with shared mechanisms and risk factors, a novel concept that we propose helps to explain the clustering of certain morbidities in patients diagnosed with COPD. A syndemics approach to understanding COPD could have important clinical implications, in which the complex disease presentations in these patients are addressed through proactive diagnosis, assessment of severity, and integrated management of the COPD multimorbid state, with a patient-centred rather than a single-disease approach.

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Conflict of interest statement

Declaration of interests LMF declares consulting fees from Chiesi Farmaceutici; payment or honoraria for lectures, presentations, manuscript writing, or educational events from Novartis, Chiesi Farmaceutici, Chiesi Italia, GSK, AstraZeneca, and Alfasigma; and participation on a data safety monitoring board (DSMB) for Novartis and Chiesi, all outside

of the submitted work. LMF was formerly a member of the Global Initiative for Chronic Obstructive Lung Disease (GOLD). BRC declares consultancy fees from GSK, AstraZeneca, Menarini, Sanofi Aventis, and Axios; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from GSK, AstraZeneca, Menarini, Chiesi, and Regeneron; support for attending meetings or travel from GSK and Sanofi Aventis; and participation on a DSMB or advisory board for GSK, AstraZeneca, AZ Therapeutics, Sanofi Aventis, and Vertex, all outside of the submitted work. BRC is a member of GOLD. AA declares grants for research projects from GSK, AstraZeneca, and Menarini; and payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from GSK, AstraZeneca, Chiesi, Menarini, CIPLA, Zambon, and Sanofi Regeneron, all outside of the submitted work. AA holds the Chair of the Board of Directors of GOLD. GJC is member of GOLD. MTD declares grants paid to his institution from the US Department of Defense, American Lung Association, and National Institutes of Health; royalties from UpToDate; consulting fees from AstraZeneca, GSK, Novartis, Pulmonx, and Teva; and an unpaid role on the Board of Directors of the COPD Foundation, all outside of the submitted work. MD declares consulting fees from Sanofi Regeneron, outside of the submitted work. JKK declares grants paid to her institution from the American Thoracic Society Fellowship in Health Equity, Research Assistance for Primary Parents Award, COMMUNITY Center Investigator Development Core, Weill Cornell Medicine Dean's Diversity and Healthcare Disparity Research Award, and the National Institutes of Health (T32 HL134629); medical writing support from Novartis; medication samples delivered to her institution by Boehringer Ingelheim and GSK; and a donor gift to her institution from the Donna Redel Research Fund, all outside of the submitted work. LL declares fees to her institution from AstraZeneca for expert consultation, Chiesi for a lecture, and IPSA vzw, for lectures, outside of the submitted work. MM declares honoraria for lectures on COPD from AstraZeneca and GSK, outside of the submitted work. MMdO is a member of GOLD. SSS declares payments to his institution from Cipla for lectures, presentations, speakers bureaus, manuscript writing, or educational events. SSS has an unpaid leadership or fiduciary role with the Indian Chest Society, outside of the submitted work, and is a member of GOLD. DS declares grants to her institution from Curetis and AstraZeneca; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from CSL Behring, Berlin-Chemie Menarini, Novartis, GSK, AstraZeneca, Vifor, Merck, Chiesi, Grifols, MSD, and Sanofi; and participation on a DSMB or advisory board for CSL Behring, Berlin-Chemie Menarini, Novartis, GSK, AstraZeneca, Vifor, Merck, Chiesi, Grifols, MSD, and Sanofi, all outside of the submitted work. LEGWV declares research grants to his institution from The Family Kamprad Foundation (20190024), the Swedish government and country council (ALF grant ALFGBG-824371), The Swedish Heart and Lung Foundation (20200150), and Svensk Lungmedicinsk Förening; and payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from GSK, AstraZeneca, Boehringer, Novartis, Chiesi, Resmed, and Pulmonx, all outside of the submitted work. CFV declares grants to his institution from the German Ministry of Education and Science, AstraZeneca, Boehringer Ingelheim, Chiesi, CSL Behring, GSK, Grifols, and Novartis; consulting fees from Aerogen, AstraZeneca, Boehringer Ingelheim, CSL Behring, Chiesi, GSK, Insmmed, Menarini, Novartis,

and Nuvaaira; and payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from Aerogen, AstraZeneca, Boehringer Ingelheim, CSL Behring, Chiesi, GSK, Insmmed, Menarini, Novartis, Roche, and Sanofi, all outside the submitted work. CFV holds the Chair of the Science Committee of GOLD.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Randomized Controlled Trial

Ann Am Thorac Soc



. 2023 Nov;20(11):1561-1570.

doi: 10.1513/AnnalsATS.202302-104OC.

[A Hybrid Effectiveness/Implementation Clinical Trial of Adherence to Long-Term Oxygen Therapy for Chronic Obstructive Pulmonary Disease](#)

[Valentin Prieto-Centurion](#)¹, [Kristen E Holm](#)^{2,3}, [Richard Casaburi](#)⁴, [Janos Porszasz](#)⁴, [Sanjib Basu](#)⁵, [Nina E Bracken](#)^{1,6}, [Richard Gallardo 3rd](#)⁷, [Vanessa Gonzalez](#)^{5,8}, [Sai D Illendula](#)^{1,6}, [Robert A Sandhaus](#)², [Jamie L Sullivan](#)⁹, [Linda J Walsh](#)⁹, [Lynn B Gerald](#)^{1,6}, [Jerry A Krishnan](#)^{1,6}

Affiliations expand

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- DOI: [10.1513/AnnalsATS.202302-104OC](https://doi.org/10.1513/AnnalsATS.202302-104OC)

Abstract

Rationale: Interventions to promote adherence to long-term oxygen therapy (LTOT) in chronic obstructive pulmonary disease (COPD) are needed. **Objectives:** To examine the real-world effectiveness of phone-based peer coaching on LTOT adherence and other outcomes in a pragmatic trial of patients with COPD. **Methods:** In a hybrid effectiveness/implementation pragmatic trial, patients were randomized to receive phone-based proactive coaching (educational materials, five phone-based peer coaching sessions over 60 d), reactive coaching (educational materials, peer coaching when requested), or usual care. Study staff members collected baseline and outcome data via phone at 30, 60, and 90 days after randomization. Adherence to LTOT over 60 days, the primary effectiveness outcome, was defined as mean LTOT use ≥ 17.7 h/d. LTOT use was calculated using information about home oxygen equipment use in worksheets completed by study participants. Comparisons of adherence to LTOT between each coaching group and the usual care group using multivariable logistic regression models were prespecified as the primary analyses. Secondary effectiveness outcomes included Patient Reported Outcome Management Information System measures for physical, emotional, and social health. We assessed early implementation domains in the reach, adoption, and implementation framework. **Results:** In 444 participants, the proportions who were adherent to LTOT at 60 days were 74% in usual care, 84% in reactive coaching, and 70% in proactive coaching groups. Although reach, adoption by stakeholder partners, and intervention fidelity were acceptable, complete LTOT adherence data were available in only 73% of participants. Reactive coaching (adjusted odds ratio, 1.77; 97.5% confidence interval, 0.80-3.90) and proactive coaching (adjusted odds ratio, 0.70; 97.5% confidence interval, 0.34-1.46) did not improve adherence to LTOT compared with usual care. However, proactive coaching significantly reduced depressive symptoms and sleep disturbance compared with usual care and reduced depressive symptoms compared with reactive coaching. Unexpectedly, LTOT adherence was significantly lower in the proactive compared with the reactive coaching group. **Conclusions:** The results were inconclusive about whether a phone-based peer coaching strategy changed LTOT adherence compared with usual care. Further studies are needed to confirm the potential benefits of proactive peer coaching on secondary effectiveness outcomes and differences in LTOT adherence between proactive and reactive peer coaching. Clinical trial registered with ClinicalTrials.gov ([NCT02098369](https://clinicaltrials.gov/ct2/show/study/NCT02098369)).

Keywords: COPD; effectiveness-implementation hybrid trial; long-term oxygen therapy; peer coaching; pragmatic clinical trial.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated data, Grants and fundingexpand

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Intensive Care Med



. 2023 Nov;49(11):1428-1429.

doi: 10.1007/s00134-023-07206-5. Epub 2023 Sep 7.

[Different oxygenation targets for stable COPD and acute exacerbations in the ICU](#)

[G Jan Zijlstra](#)¹

Affiliations expand

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- DOI: [10.1007/s00134-023-07206-5](https://doi.org/10.1007/s00134-023-07206-5)

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- [Cited by 1 article](#)
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Publication types, MeSH termsexpand

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Microb Pathog

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doi: 10.1016/j.micpath.2023.106335. Epub 2023 Sep 4.

[Analysis of sputum microbial flora in chronic obstructive pulmonary disease patients with different phenotypes during acute exacerbations](#)

[Xiaoyan Mao](#)¹, [Yao Li](#)², [Pengfei Shi](#)², [Ziwei Zhu](#)², [Juan Sun](#)³, [Yu Xue](#)³, [Zongren Wan](#)³, [Dan Yang](#)³, [Ting Ma](#)³, [Jipeng Wang](#)³, [Rong Zhu](#)⁴

Affiliations expand

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Abstract

Background: Increasing studies have shown that the imbalance of the respiratory microbial flora is related to the occurrence of COPD, the severity and frequency of exacerbations and mortality. However, it remains unclear how the sputum microbial flora

differs during exacerbations in COPD patients manifesting emphysema phenotype, chronic bronchitis with emphysema phenotype and asthma-COPD overlap phenotype.

Methods: Sputum samples were obtained from 29 COPD patients experiencing acute exacerbations who had not received antibiotics or systemic corticosteroids within the past four weeks. Patients were divided into three groups; emphysema phenotype (E); chronic bronchitis with emphysema phenotype (B+E) and asthma-COPD overlap phenotype (ACO). We utilized metagenomic Next Generation Sequencing (mNGS) technology to analyze the sputum microbial flora in COPD patients with different phenotypes during exacerbations.

Results: There was no significant difference in alpha diversity and beta diversity among three groups. The microbial flora composition was similar in all three groups during exacerbations except for a significant increase in *Streptococcus mitis* in ACO. Through network analysis, we found *Candidatus Saccharibacteria* oral taxon TM7x and *Fusobacterium necrophorum* were the core nodes of the co-occurrence network in ACO and E respectively. They were positively correlated with some species and play a synergistic role. In B+E, *Haemophilus pittmaniae* and *Klebsiella pneumoniae* had a synergistic effect. Besides, some species among the three groups play a synergistic or antagonistic role. Through Spearman analysis, we found the relative abundance of *Streptococcus mitis* was negatively correlated with the number of hospitalizations in the past year ($r = -0.410, P = 0.027$). We also observed that the relative abundance of *Prevotella* and *Prevotella melaninogenica* was negatively correlated with age ($r = -0.534, P = 0.003$; $r = -0.567, P = 0.001$), while the relative abundance of *Streptococcus oralis* and *Actinomyces odontolyticus* was positively correlated with age ($r = 0.570, P = 0.001$; $r = 0.480, P = 0.008$). In addition, the relative abundance of *Prevotella melaninogenica* was negatively correlated with peripheral blood neutrophil ratio and neutrophil to lymphocyte ratio ($r = -0.479, P = 0.009$; $r = -0.555, P = 0.002$), while the relative abundance of *Streptococcus sanguinis* was positively correlated with peripheral blood neutrophil ratio and neutrophil to lymphocyte ratio ($r = 0.450, P = 0.014$; $r = 0.501, P = 0.006$). There was also a significant positive correlation between *Oribacterium* and blood eosinophil counts ($r = 0.491, P = 0.007$).

Conclusion: Overall, we analyzed the sputum microbiota of COPD patients with different phenotypes and its relationship with clinical indicators, and explored the relationships between microbiota and inflammation in COPD. We hope to alter the prognosis of patients by inhibiting specific bacterial taxa related to inflammation and using guide individualized treatment in the future research.

Keywords: Chronic obstructive pulmonary disease; Microbial flora; Phenotypes; Sputum; mNGS.

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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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Pediatr Pulmonol

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. 2023 Nov;58(11):3293-3302.

doi: 10.1002/ppul.26659. Epub 2023 Sep 6.

[Mechanisms of ventilatory limitation to maximum exercise in children and adolescents with chronic airway diseases](#)

[Márcio Vinícius Fagundes Donadio](#)^{1,2}, [Marta Amor Barbosa](#)¹, [Fernanda Maria Vendrusculo](#)², [Tamara Iturriaga Ramirez](#)³, [Elena Santana-Sosa](#)³, [Veronica Sanz-Santiago](#)⁴, [Margarita Perez-Ruiz](#)⁵

Affiliations expand

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- DOI: [10.1002/ppul.26659](https://doi.org/10.1002/ppul.26659)

Abstract

Introduction: Exercise intolerance is common in chronic airway diseases (CAD), but its mechanisms are still poorly understood. The aim of this study was to evaluate exercise capacity and its association with lung function, ventilatory limitation, and ventilatory efficiency in children and adolescents with cystic fibrosis (CF) and asthma when compared to healthy controls.

Methods: Cross-sectional study including patients with mild-to-moderate asthma, CF and healthy children and adolescents. Anthropometric data, lung function (spirometry) and exercise capacity (cardiopulmonary exercise testing) were evaluated. Primary outcomes were peak oxygen consumption ($\dot{V}O_2$ peak), forced expiratory volume in 1 s (FEV_1), breathing reserve (BR), ventilatory equivalent for oxygen consumption ($\dot{V}_E/\dot{V}O_2$) and for carbon dioxide production ($\dot{V}_E/\dot{V}CO_2$), both at the ventilatory threshold (VT_1) and peak exercise.

Results: Mean age of 147 patients included was 11.8 ± 3.0 years. There were differences between asthmatics and CF children when compared to their healthy peers for anthropometric and lung function measurements. Asthmatics showed lower $\dot{V}O_2$ peak when compared to both healthy and CF subjects, although no differences were found between healthy and CF patients. A lower BR was found when CF patients were compared to both healthy and asthmatic. Both CF and asthmatic patients presented higher values for $\dot{V}_E/\dot{V}O_2$ and $\dot{V}_E/\dot{V}CO_2$ at VT_1 when compared to healthy individuals. For both $\dot{V}_E/\dot{V}O_2$ and $\dot{V}_E/\dot{V}CO_2$ at peak exercise CF patients presented higher values when compared to their healthy peers.

Conclusion: Patients with CF achieved good exercise capacity despite low ventilatory efficiency, low BR, and reduced lung function. However, asthmatics reported reduced cardiorespiratory capacity and normal ventilatory efficiency at peak exercise. These results demonstrate differences in the mechanisms of ventilatory limitation to maximum exercise testing in children and adolescents with CAD.

Keywords: asthma; breathing reserve; carbon dioxide production; cystic fibrosis; equivalent for oxygen consumption.

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- [45 references](#)

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Publication types, MeSH terms, Supplementary conceptsexpand

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Respir Med



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[Clinical significance of normalized airflow obstruction in patients with chronic obstructive pulmonary disease](#)

[Yun Seok Kim](#)¹, [Yong Il Hwang](#)², [Jae Ha Lee](#)³, [Yong Bum Park](#)⁴, [Cheon Woong Choi](#)⁵, [Ki-Suck Jung](#)², [Kwang Ha Yoo](#)⁶, [Seong Yong Lim](#)⁷, [Ju Sang Kim](#)¹, [Joon Young Choi](#)⁸

Affiliations expand

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- DOI: [10.1016/j.rmed.2023.107398](https://doi.org/10.1016/j.rmed.2023.107398)

Abstract

Background: There is ongoing debate regarding the diagnostic criteria for chronic obstructive pulmonary disease (COPD); recent studies have focused on the early COPD detection and management. Here, we compared clinical features and prognosis in patients with FEV1/FVC < 0.70 at baseline, according to normalized airflow obstruction status during follow-up.

Methods: We used the Korea COPD Subgroup Study (KOCOSS) cohort database, a prospective nationwide observational COPD study. Normalized obstruction (NO) was

defined as FEV1/FVC ≥ 0.7 in the 2-year follow-up period, whereas fixed obstruction (FO) was defined as FEV1/FVC < 0.7 . Demographic and clinical data, 1-year exacerbation risk and difference in FEV1 decline over 2 years were compared between NO and FO groups.

Results: Among the 670 COPD patients with post-bronchodilator FEV1/FVC < 0.7 in this study, 95 (14.2%) displayed NO. Compared with the FO group, the NO group had higher FEV1, and DLCO, body mass index, as well as lower Saint George Respiratory Questionnaire, Beck Depression Index, and Beck Anxiety Index. Blood eosinophil count, IgE level, and FeNO did not significantly differ between two groups. There was no significant difference in exacerbation frequency between the two groups, but the NO group had a significant increase in FEV1 compared with the FO group during follow-up.

Conclusion: Transient airflow obstruction in the NO group may represent a clinical manifestation of early COPD; close monitoring is needed for such patients.

Keywords: Acute exacerbation; COPD; Early COPD; Normalized obstruction; Spirometry.

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Conflict of interest statement

Declaration of competing interest The authors have declared that no conflicts of interest exist.

SUPPLEMENTARY INFO

MeSH termsexpand

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Observational Study

Am J Respir Crit Care Med

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. 2023 Nov 1;208(9):964-974.

doi: 10.1164/rccm.202305-0863OC.

Augmentation Therapy for Severe Alpha-1 Antitrypsin Deficiency Improves Survival and Is Decoupled from Spirometric Decline-A Multinational Registry Analysis

[Daniel D Fraughen](#)¹, [Auyon J Ghosh](#)², [Brian D Hobbs](#)³, [Georg-Christian Funk](#)⁴, [Tobias Meischl](#)^{4,5}, [Christian F Clarenbach](#)⁶, [Noriane A Sievi](#)⁶, [Karin Schmid-Scherzer](#)⁴, [Oliver J McElvaney](#)^{1,7}, [Mark P Murphy](#)¹, [Adam D Roche](#)¹, [Louise Clarke](#)⁸, [Matthew Strand](#)⁹, [Florian Vafai-Tabrizi](#)⁴, [Geraldine Kelly](#)¹, [Cedric Gunaratnam](#)⁸, [Tomás P Carroll](#)¹, [Noel G McElvaney](#)¹

Affiliations expand

- PMID: 37624745
- DOI: [10.1164/rccm.202305-0863OC](https://doi.org/10.1164/rccm.202305-0863OC)

Abstract

Rationale: Intravenous plasma-purified alpha-1 antitrypsin (IV-AAT) has been used as therapy for alpha-1 antitrypsin deficiency (AATD) since 1987. Previous trials (RAPID and RAPID-OLE) demonstrated efficacy in preserving computed tomography of lung density but no effect on FEV₁. This observational study evaluated 615 people with severe AATD from three countries with socialized health care (Ireland, Switzerland, and Austria), where access to standard medical care was equal but access to IV-AAT was not. **Objectives:** To assess the real-world longitudinal effects of IV-AAT. **Methods:** Pulmonary function and mortality data were utilized to perform longitudinal analyses on registry participants with severe AATD. **Measurements and Main Results:** IV-AAT confers a survival benefit in severe AATD ($P < 0.001$). We uncovered two distinct AATD phenotypes based on an initial respiratory diagnosis: lung index and non-lung index. Lung indexes demonstrated a more rapid FEV₁ decline between the ages of 20 and 50 and subsequently entered a plateau phase of minimal decline from 50 onward. Consequentially, IV-AAT had no effect on FEV₁ decline, except in patients with a Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage 2 lung index. **Conclusions:** This real-world study demonstrates a

survival advantage from IV-AAT. This improved survival is largely decoupled from FEV₁ decline. The observation that patients with severe AATD fall into two major phenotypes has implications for clinical trial design where FEV₁ is a primary endpoint. Recruits into trials are typically older lung indexes entering the plateau phase and, therefore, unlikely to show spirometric benefits. IV-AAT attenuates spirometric decline in lung indexes in GOLD stage 2, a spirometric group commonly outside current IV-AAT commencement recommendations.

Keywords: Kaplan-Meier survival curve; forced expiratory volume; universal health care; α 1-proteinase inhibitor.

Comment in

- [Treatment for Alpha-1 Antitrypsin Deficiency: Does Augmentation Therapy Work?](#)
Brantly M. *Am J Respir Crit Care Med.* 2023 Nov 1;208(9):948-949. doi: 10.1164/rccm.202309-1585ED.PMID: 37724887 No abstract available.

SUPPLEMENTARY INFO

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

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Eur Respir J

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doi: 10.1183/13993003.00432-2023. Print 2023 Nov.

[Tailored psychological intervention for anxiety or depression in COPD](#)

(TANDEM): a randomised controlled trial

[Stephanie J C Taylor](#)^{1,2}, [Ratna Sohanpal](#)^{3,2}, [Liz Steed](#)³, [Karen Marshall](#)⁴, [Claire Chan](#)³, [Nahel Yaziji](#)⁵, [Amy C Barradell](#)⁶, [Paulino Font-Gilabert](#)⁵, [Andrew Healey](#)⁵, [Richard Hooper](#)³, [Maira J Kelly](#)³, [Kristie-Marie Mammoliti](#)⁷, [Stefan Priebe](#)³, [Arvind Rajasekaran](#)⁸, [C Michael Roberts](#)⁹, [Vickie Rowland](#)¹⁰, [Sally J Singh](#)¹¹, [Melanie Smuk](#)¹², [Martin Underwood](#)^{13,14}, [Sarah Waseem](#)¹⁵, [Patrick White](#)¹⁰, [Vari Wileman](#)¹⁶, [Hilary Pinnock](#)¹⁷

Affiliations expand

- PMID: 37620042
- PMCID: [PMC10620475](#)
- DOI: [10.1183/13993003.00432-2023](#)

Free PMC article

Abstract

Background: The TANDEM multicentre, pragmatic, randomised controlled trial evaluated whether a tailored psychological intervention based on a cognitive behavioural approach for people with COPD and symptoms of anxiety and/or depression improved anxiety or depression compared with usual care (control).

Methods: People with COPD and moderate to very severe airways obstruction and Hospital Anxiety and Depression Scale subscale scores indicating mild to moderate anxiety (HADS-A) and/or depression (HADS-D) were randomised 1.25:1 (242 intervention and 181 control). Respiratory health professionals delivered the intervention face-to-face over 6-8 weeks. Co-primary outcomes were HADS-A and HADS-D measured 6 months post-randomisation. Secondary outcomes at 6 and 12 months included: HADS-A and HADS-D (12 months), Beck Depression Inventory II, Beck Anxiety Inventory, St George's Respiratory Questionnaire, social engagement, the EuroQol instrument five-level version (EQ-5D-5L), smoking status, completion of pulmonary rehabilitation, and health and social care resource use.

Results: The intervention did not improve anxiety (HADS-A mean difference -0.60, 95% CI -1.40-0.21) or depression (HADS-D mean difference -0.66, 95% CI -1.39-0.07) at 6 months. The intervention did not improve any secondary outcomes at either time-point, nor did it influence completion of pulmonary rehabilitation or healthcare resource use. Deaths in the

intervention arm (13/242; 5%) exceeded those in the control arm (3/181; 2%), but none were associated with the intervention. Health economic analysis found the intervention highly unlikely to be cost-effective.

Conclusion: This trial has shown, beyond reasonable doubt, that this cognitive behavioural intervention delivered by trained and supervised respiratory health professionals does not improve psychological comorbidity in people with advanced COPD and depression or anxiety.

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Conflict of interest statement

Conflict of interest: L. Steed reports support for the present manuscript from the NIHR Health Technology Assessment programme (project number 13/146/02), and also reports lecture honoraria from the IPCRG, outside the submitted work. K. Marshall reports support for the present manuscript from the NIHR Health Technology Assessment programme (project number 13/146/02), and also reports lecture honoraria, outside the submitted work. S.J. Singh reports support for the present manuscript from the NIHR Health Technology Assessment programme (project number 13/146/02); in addition, S.J. Singh also reports grants from the NIHR (NIHR 202020 and senior investigator grant), Wellcome Doctoral Training Programme, HTA Project Grant (NIHR 131015), NIHR DHSC/UKRI COVID-19 Rapid Response Initiative, NIHR Global Research Group (NIHR 17/63/20) and Actegy Limited, lecture honoraria from GSK, Ministry of Justice, CIPLA and Sherbourne Gibbs, advisory board participation with NICE (Expert Adviser Panel – Long COVID) and the Wales Long COVID Advisory Board (expired), and leadership roles with the ATS (Pulmonary Rehabilitation Assembly Chair), RCP Pulmonary Rehabilitation Accreditation Scheme and NACAP Audit for Pulmonary Rehabilitation, outside the submitted work. M. Underwood is chief investigator or co-investigator on previous and current research grants from the UK NIHR, Arthritis Research UK and on grants funded by the Australian NHMRC and Norwegian MRC; he was an NIHR Senior Investigator until March 2021. He has received travel expenses for speaking at conferences from the professional organisations hosting the conferences. He is a director and shareholder of Clinvivo Ltd. He is part of an academic partnership with Serco Ltd, funded by the European Social Fund. He is a co-investigator studies that are, or have had, additional support from Stryker Ltd. Until March 2020 he received a fee as an NIHR journal editor and editors group member. V. Wileman reports support for the present manuscript from the NIHR Applied Research Collaboration (ARC) North Thames. P. White is a chief investigator or co-investigator on multiple previous and current research grants from the NIHR, and reports travel expenses for speaking at conferences from the professional organisations hosting the conferences. H. Pinnock reports support for the present manuscript from the NIHR Health Technology Assessment programme (project number 13/146/02), and also reports lecture honoraria from Sandoz, Teva and Boehringer Ingelheim, outside the submitted work. S.J.C. Taylor, R. Sohanpal, S. Priebe, A. Healey, S. Waseem, M.J. Kelly and C.M. Roberts report support for the present

manuscript from the NIHR Health Technology Assessment programme (project number 13/146/02). All other authors have nothing to disclose.

Comment in

- [Can the curse of mood disorders in COPD be lifted and enable pulmonary rehabilitation?](#)

Evans R, Doe G. *Eur Respir J*. 2023 Nov 2;62(5):2301538. doi:

10.1183/13993003.01538-2023. Print 2023 Nov. PMID: 37918881 No abstract available.

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J Intellect Disabil Res

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. 2023 Nov;67(11):1161-1173.

doi: 10.1111/jir.13078. Epub 2023 Aug 22.

[Sarcopenia predicts 5-year mortality in older adults with intellectual disabilities](#)

[B Valentin](#)^{1,2}, [D Maes-Festen](#)¹, [J Schoufour](#)², [A Oppewal](#)¹

Affiliations [expand](#)

- PMID: 37608512
- DOI: [10.1111/jir.13078](https://doi.org/10.1111/jir.13078)

Abstract

Background: People with intellectual disabilities (ID) have a lower life expectancy than their peers without ID. A contributing factor to the lower life expectancy and early mortality could be sarcopenia: low muscle mass and low muscle function. In the general population, sarcopenia strongly predicts early mortality, but this association is unknown in people with ID. Therefore, this study aims to explore the association between sarcopenia and 5-year mortality in older adults with ID.

Methods: In the Healthy Ageing and Intellectual Disabilities (HA-ID) study, the prevalence of sarcopenia was measured at baseline among 884 older adults (≥ 50 years) with ID. All-cause mortality was measured over a 5-year follow-up period. Univariable and multivariable Cox proportional hazard models were applied to determine the association between sarcopenia (no sarcopenia, pre-sarcopenia, sarcopenia, severe sarcopenia) and early mortality, adjusted for age, sex, level of ID, presence of Down syndrome, and co-morbidity (chronic obstructive pulmonary disease, diabetes type 2 and metabolic syndrome).

Results: The unadjusted hazard ratio (HR) for sarcopenia was 2.28 [95% confidence interval (CI) 1.48-3.42], $P < 0.001$, and 2.40 (95% CI 1.40-4.10, $P = 0.001$) for severe sarcopenia. When adjusted for age, sex, level of ID, and Down syndrome, sarcopenia (HR = 1.72, 95% CI 1.08-2.75, $P = 0.022$) and severe sarcopenia (HR = 1.86, 95% CI 1.07-3.23, $P = 0.028$) were significantly associated with early mortality. When additionally adjusted for co-morbidity, the adjusted HR decreased to 1.62 (95% CI 1.02-2.59, $P = 0.043$) and 1.81 (95% CI 1.04-3.15, $P = 0.035$) for sarcopenia and severe sarcopenia, respectively.

Conclusion: Sarcopenia is an independent risk factor for early mortality in older adults with ID over a 5-year follow-up period. Our results stress the need to delay the incidence and development of sarcopenia in older adults with ID.

Keywords: intellectual disabilities; mortality; older adults; sarcopenia.

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- [57 references](#)

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Chronic Obstr Pulm Dis



. 2023 Oct 26;10(4):444-449.

doi: 10.15326/jcopdf.2023.0404.

[Improving Dyspnea by Targeting Weight Loss in Patients With Chronic Obstructive Lung Disease and Severe Obesity Through Health Coaching and Remote Monitoring](#)

[Maria V Benzo¹](#), [Amelia Barwise¹](#), [Matthew M Clark²](#), [Kara Dupuy-McCauley¹](#), [Madison Roy¹](#), [Roberto P Benzo¹](#)

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- PMID: 37606647
- DOI: [10.15326/jcopdf.2023.0404](https://doi.org/10.15326/jcopdf.2023.0404)

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No abstract available

Keywords: dyspnea; obesity; quality of life.

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Environ Pollut

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. 2023 Nov 1:336:122396.

doi: 10.1016/j.envpol.2023.122396. Epub 2023 Aug 16.

[Short-term exposure to ultrafine particles and mortality and hospital admissions due to respiratory and cardiovascular diseases in Copenhagen, Denmark](#)

[Marie L Bergmann](#)¹, [Zorana J Andersen](#)¹, [Andreas Massling](#)², [Paula A Kindler](#)³, [Steffen Loft](#)¹, [Heresh Amini](#)⁴, [Thomas Cole-Hunter](#)¹, [Yuming Guo](#)⁵, [Matija Maric](#)¹, [Claus Nordstrøm](#)², [Mahmood Taghavi](#)¹, [Stéphane Tuffier](#)¹, [Rina So](#)¹, [Jiawei Zhang](#)¹, [Youn-Hee Lim](#)⁶

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- PMID: 37595732

- DOI: [10.1016/j.envpol.2023.122396](https://doi.org/10.1016/j.envpol.2023.122396)

Free article

Abstract

Ultrafine particles (UFP; particulate matter <0.1 μm in diameter) may be more harmful to human health than larger particles, but epidemiological evidence on their health effects is still limited. In this study, we examined the association between short-term exposure to UFP and mortality and hospital admissions in Copenhagen, Denmark. Daily concentrations of UFP (measured as particle number concentration in a size range 11-700 nm) and meteorological variables were monitored at an urban background station in central Copenhagen during 2002-2018. Daily counts of deaths from all non-accidental causes, as well as deaths and hospital admissions from cardiovascular and respiratory diseases were obtained from Danish registers. Mortality and hospital admissions associated with an interquartile range (IQR) increase in UFP exposure on a concurrent day and up to six preceding days prior to the death or admission were examined in a case-crossover study design. Odds ratios (OR) with 95% confidence intervals (CI) per one IQR increase in UFP were estimated after adjusting for temperature and relative humidity. We observed 140,079 deaths in total, 236,003 respiratory and 342,074 cardiovascular hospital admissions between 2002 and 2018. Hospital admissions due to respiratory and cardiovascular diseases were significantly positively associated with one IQR increase in UFP (OR: 1.04 [95% CI: 1.01, 1.07], lag 0-4, and 1.02 [1.00, 1.04], lag 0-1, respectively). Among the specific causes, the strongest associations were found for chronic obstructive pulmonary disease (COPD) mortality and asthma hospital admissions and two-day means (lag 0-1) of UFP (OR: 1.13 [1.01, 1.26] and 1.08 [1.00, 1.16], respectively, per one IQR increase in UFP). Based on 17 years of UFP monitoring data, we present novel findings showing that short-term exposure to UFP can trigger respiratory and cardiovascular diseases mortality and morbidity in Copenhagen, Denmark. The strongest associations with UFP were observed with COPD mortality and asthma hospital admissions.

Keywords: Air pollution; Cardiovascular diseases; Mortality; Particle number concentration; Respiratory tract diseases; Ultrafine particles.

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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

Thorax

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. 2023 Nov;78(11):1063-1064.

doi: 10.1136/thorax-2023-220458. Epub 2023 Aug 17.

[Reimagining emphysema for a computational age](#)

[Joseph Jacob](#)^{1,2}

Affiliations expand

- PMID: 37591700
- DOI: [10.1136/thorax-2023-220458](https://doi.org/10.1136/thorax-2023-220458)

No abstract available

Keywords: COPD Pathology; Emphysema; Imaging/CT MRI etc.

Conflict of interest statement

Competing interests: JJ declares fees from Boehringer Ingelheim, F. Hoffmann-La Roche, GlaxoSmithKline, NHSX and Takeda. Grant Funding from GlaxoSmithKline, Wellcome Trust

and Microsoft Research. Patents: UK patent application numbers 2113765.8 and GB2211487.0.

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Am J Respir Cell Mol Biol



. 2023 Nov;69(5):500-507.

doi: 10.1165/rcmb.2023-0175PS.

Does Chronic Obstructive Pulmonary Disease Originate from Different Cell Types?

[Yohannes Tesfaigzi](#)¹, [Jeffrey L Curtis](#)^{2,3}, [Irina Petrache](#)^{4,5}, [Francesca Polverino](#)⁶, [Farrah Kheradmand](#)⁶, [Ian M Adcock](#)⁷, [Stephen I Rennard](#)⁸

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- PMID: 37584669
- DOI: [10.1165/rcmb.2023-0175PS](https://doi.org/10.1165/rcmb.2023-0175PS)

Abstract

The onset of chronic obstructive pulmonary disease (COPD) is heterogeneous, and current approaches to define distinct disease phenotypes are lacking. In addition to clinical methodologies, subtyping COPD has also been challenged by the reliance on human lung samples from late-stage diseases. Different COPD phenotypes may be initiated from the susceptibility of different cell types to cigarette smoke, environmental pollution, and infections at early stages that ultimately converge at later stages in airway remodeling and destruction of the alveoli when the disease is diagnosed. This perspective provides discussion points on how studies to date define different cell types of the lung that can initiate COPD pathogenesis, focusing on the susceptibility of macrophages, T and B cells, mast cells, dendritic cells, endothelial cells, and airway epithelial cells. Additional cell types, including fibroblasts, smooth muscle cells, neuronal cells, and other rare cell types not covered here, may also play a role in orchestrating COPD. Here, we discuss current knowledge gaps, such as which cell types drive distinct disease phenotypes and/or stages of the disease and which cells are primarily affected by the genetic variants identified by whole genome-wide association studies. Applying new technologies that interrogate the functional role of a specific cell type or a combination of cell types as well as single-cell transcriptomics and proteomic approaches are creating new opportunities to understand and clarify the pathophysiology and thereby the clinical heterogeneity of COPD.

Keywords: gene-and-environment interaction; lineage tracing; lung cell types; single nucleotide polymorphisms; single-cell transcriptomics.

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Ann Am Thorac Soc

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. 2023 Nov;20(11):1642-1653.

doi: 10.1513/AnnalsATS.202303-275OC.

Sleep Testing and Mortality in a Propensity-matched Cohort of Patients with Chronic Obstructive Pulmonary Disease

[Lucas M Donovan](#)^{1,2}, [Travis Wai](#)¹, [Laura J Spece](#)^{1,2}, [Kevin I Duan](#)^{1,2}, [Matthew F Griffith](#)^{1,3}, [Aristotle Leonhard](#)², [Robert Plumley](#)¹, [Sophia A Hayes](#)², [Fernando Picazo](#)², [Kristina Crothers](#)^{1,2}, [Vishesh K Kapur](#)², [Brian N Palen](#)^{1,2}, [David H Au](#)^{1,2}, [Laura C Feemster](#)^{1,2}

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- PMID: 37579136
- DOI: [10.1513/AnnalsATS.202303-275OC](https://doi.org/10.1513/AnnalsATS.202303-275OC)

Abstract

Rationale: Many advocate the application of propensity-matching methods to real-world data to answer key questions around obstructive sleep apnea (OSA) management. One such question is whether identifying undiagnosed OSA impacts mortality in high-risk populations, such as those with chronic obstructive pulmonary disease (COPD). **Objectives:** Assess the association of sleep testing with mortality among patients with COPD and a high likelihood of undiagnosed OSA. **Methods:** We identified patients with COPD and a high likelihood of undiagnosed OSA. We then distinguished those receiving sleep testing within 90 days of index COPD encounters. We calculated propensity scores for testing based on 37 variables and compared long-term mortality in matched groups. In sensitivity analyses, we compared mortality using inverse propensity weighting and instrumental variable methods. We also compared the incidence of nonfatal events including adverse outcomes (hospitalizations and COPD exacerbations) and routine services that are regularly indicated in COPD (influenza vaccination and pulmonary function testing). We compared the incidence of each nonfatal event as a composite outcome with death and separately compared the marginal probability of each nonfatal event independently, with death as a competing risk. **Results:** Among 135,958 patients, 1,957 (1.4%) received sleep testing. We propensity matched all patients with sleep testing to an equal number without testing, achieving excellent balance on observed confounders, with standardized differences < 0.10. We observed lower mortality risk among patients with sleep testing (incidence rate ratio, 0.88; 95% confidence interval [CI], 0.79-0.99) and similar results using inverse propensity weighting and instrumental variable methods. Contrary to mortality, we found that sleep testing was associated with a similar or greater risk for nonfatal adverse events, including inpatient COPD exacerbations (subhazard ratio,

1.29; 95% CI, 1.02-1.62) and routine services like influenza vaccination (subhazard ratio, 1.26; 95% CI, 1.17-1.36). **Conclusions:** Our disparate findings can be interpreted in multiple ways. Sleep testing may indeed cause both reduced mortality and greater incidence of nonfatal adverse outcomes and routine services. However, it is also possible that our findings stem from residual confounding by patients' likelihood of accessing care. Given the limitations of propensity-based analyses, we cannot confidently distinguish these two possibilities. This uncertainty highlights the limitations of using propensity-based analyses to guide patient care and policy decisions.

Keywords: diagnostic testing; observational research; obstructive sleep apnea; propensity score methods; unmeasured confounding.

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

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Res Social Adm Pharm

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. 2023 Nov;19(11):1432-1439.

doi: 10.1016/j.sapharm.2023.07.004. Epub 2023 Jul 14.

[Predictors for unplanned hospital admissions in community dwelling adults: A dynamic cohort study](#)

[Julie Hias](#)¹, [Laura Hellemans](#)², [Shauni Nuyts](#)³, [Bert Vaes](#)⁴, [Xavier Rygaert](#)⁵, [Jos Tournoy](#)⁶, [Lorenz Van der Linden](#)⁷

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- PMID: 37573152
- DOI: [10.1016/j.sapharm.2023.07.004](https://doi.org/10.1016/j.sapharm.2023.07.004)

Abstract

Background: Polypharmacy and inappropriate medication use are associated with unplanned hospital admissions. Targeted interventions might reduce the hospitalization risk. Yet, it remains unclear which patient profiles derive the largest benefit from such interventions.

Objective: The aim of this study was to determine independent risk factors, among which polypharmacy, for unplanned hospital admissions in a cohort of community dwelling adults.

Methods: A retrospective study was performed using a large general practice registry and an insurance database in Flanders, Belgium. Community dwelling adults aged 40 years or older with data for 2013-2015 were included. The index date was the last general practitioner contact in 2014. Determinants were collected during the preceding year. Unplanned hospital admissions were determined during the year after the index date. Univariable logistic regression models were fitted on each risk factor for an unplanned hospital admission as the primary outcome. Two multivariable models were derived.

Results: In total, 40411 patients were included and 2126 (5.26%) experienced an unplanned hospital admission. Mean age was 58.3 (\pm 12.3) years. The two models identified the following determinants for an unplanned hospital admission: excessive polypharmacy, older age, male sex, number of comorbidities, atrial fibrillation, chronic obstructive pulmonary disease or stroke, low hemoglobin, use of hypnotics, antipsychotics, antidepressants or antiepileptics and prior hospital and general practitioner visits. Prior hospital visits was the largest determinant.

Conclusions: In our study we identified and confirmed the presence of known determinants for unplanned hospital admissions in community dwelling adults, most of which align with a geriatric phenotype. Our findings can inform the allocation of interventions aiming to reduce unplanned hospital admissions.

Keywords: Clinical pharmacy; Hospitalization; Polypharmacy; Risk factor.

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Conflict of interest statement

Declaration of competing interest The authors have no competing interests to declare that are relevant to the content of this article.

SUPPLEMENTARY INFO

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Respir Med



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[Mortality in individuals with COPD on long-term home non-invasive ventilation](#)

[Mathew Cherian](#)¹, [Veronique Adam](#)², [Bryan Ross](#)³, [Jean Bourbeau](#)³, [Marta Kaminska](#)⁴

Affiliations expand

- PMID: 37567515
- DOI: [10.1016/j.rmed.2023.107378](https://doi.org/10.1016/j.rmed.2023.107378)

Abstract

Background: Real-world evidence regarding survival of patients with chronic obstructive pulmonary disease (COPD) using chronic non-invasive ventilation (NIV) is scarce.

Research question: How do obesity and other factors relate to mortality in patients with COPD on chronic NIV?

Study design: and Methods: We retrospectively analyzed data from COPD patients enrolled in a home ventilation program between 2014 and 2018. Survival was compared between obese and non-obese groups using the Kaplan-Meier method. Factors associated with mortality were identified using multivariable Cox proportional regression analyses with Least Absolute Selection and Shrinkage Operator (LASSO) regularization. Univariable analyses were also done stratified by obesity.

Results: Median survival was 80.0 (95% CI: 71.0-NA) months among obese (n = 205) and 30.0 (95%CI: 19.0-42.0) months in non-obese (n = 61) patients. NIV adherence was high in both groups. Mortality was associated with male gender [HR 1.44], chronic opioids or benzodiazepines use [HR 1.07], home oxygen use [HR 1.82], fixed pressure mode of ventilation [HR 1.55], NIV inspiratory pressure [HR 1.05], and thoracic cancer [HR 1.27]; obesity [HR: 0.43], age [HR 0.99] and NIV expiratory pressure [HR 0.94] were associated with decreased mortality. In the obese, univariable analyses revealed that chest wall disease, thoracic cancer, home oxygen use, FEV₁% predicted, and ventilation parameters were associated with mortality. In the non-obese, male gender and respiratory comorbidities were related to mortality.

Interpretation: Obesity is associated with improved survival in COPD patients highly adherent to NIV. Other factors associated with mortality reflect disease severity and ventilator parameters, with differences between obese and non-obese patients.

Keywords: Chronic obstructive pulmonary disease; Non-invasive ventilation; Obesity.

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Conflict of interest statement

Declaration of competing interest The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Dr. Cherian reports no conflict of interest. Ms. Adam reports no conflict of interest. Dr. Ross reports honoraria from the Canadian Thoracic Society (CTS), CHEST, Respiplus (non-profit), Alberta Kinesiology Association (AKA), Association des Pneumologues de la Province du Québec (APPQ), and McGill University Continuing Professional Development (CPD); research funding (as Principal Investigator) from the McGill University Health Centre (MUHC) Department of Medicine Contract Academic Staff (CAS) Research Award; and research funding (as Co-Applicant) from the Canadian Institutes of Health Research (CIHR), the Réseau de Recherche en Santé Respiratoire du Québec (RSRQ), the Research Institute of the MUHC (RI MUHC), the Ministère de l'Économie et de l'Innovation (MEI) Québec, the

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Clinical Trial

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. 2023 Nov;218:107368.

doi: 10.1016/j.rmed.2023.107368. Epub 2023 Aug 9.

[Evolving to a single inhaler extrafine LABA/LAMA/ICS - Inhalation technique and adherence at the heart of COPD patient care \(TRIVOLVE\)](#)

[G Brusselle](#)¹, [U Himpe](#)², [P Fievez](#)³, [M Leys](#)⁴, [S Perez Bogerd](#)⁵, [R Peché](#)⁶, [E Vanderhelst](#)⁷, [M Lins](#)⁸, [P Capiou](#)⁹; [TRIVOLVE investigators](#)

Affiliations expand

- PMID: 37562659
- DOI: [10.1016/j.rmed.2023.107368](https://doi.org/10.1016/j.rmed.2023.107368)

Free article

Abstract

Objective: Incorrect inhaler use and poor treatment adherence have a negative impact on COPD outcomes. This multi-centre, single arm, non-interventional, phase IV study investigated whether inhalation technique, treatment adherence and patient outcomes change in patients who evolve from dual therapy or multiple inhaler triple therapy to single inhaler extrafine triple therapy (beclomethasone dipropionate (BDP, 87 µg), formoterol fumarate (FF, 5 µg) and glycopyrronium (G, 9 µg)) in combination with inhalation technique training.

Methods: A total of 126 COPD patients were included in the per protocol set. Inhalation technique and treatment adherence were assessed at baseline and at two visits at approximately 3 and 6 months of treatment with extrafine BDP/FF/G. In addition, lung function, symptom score, patient satisfaction and exacerbations (exploratory) were followed up.

Results: Before switching to single inhaler extrafine BDP/FF/G (baseline), any device errors and critical errors were detected for 28.8% and 9.6% of patients, respectively. After switching to BDP/FF/G, the percentage of patients with any device errors decreased to 14.0% (visit 2) and 16.3% (visit 3), without critical errors at the two follow-up visits. Treatment adherence increased from 67.5% at baseline to 75.8% (visit 2) and 80% (visit 3). In addition, lung function, symptom and patient satisfaction scores improved, whilst exacerbation rates substantially decreased.

Conclusions: This observational study demonstrates that in eligible COPD patients in a real-life setting, the switch from dual therapy or multiple inhaler triple therapy to single inhaler extrafine BDP/FF/G in combination with inhalation technique training is associated with improved inhalation technique and adherence.

Keywords: Adherence; COPD; Extrafine particles; Inhalation technique; Triple inhaled therapy.

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Conflict of interest statement

Declaration of competing interest Brusselle G. has, within the last 5 years, received honoraria for lectures from AstraZeneca, Boehringer-Ingelheim, Chiesi, GlaxoSmithKline, Novartis, Pfizer, Teva, UCB and Zambon; he is a member of advisory boards for AstraZeneca, Boehringer-Ingelheim, Chiesi, GlaxoSmithKline, Novartis, Sanofi/Regeneron and Teva. He reports financial support as principal investigator during the study from Chiesi sa/nv. Himpe U. received honoraria for lectures from AstraZeneca, Chiesi, GlaxoSmithKline, MSD, BMS; she is a member of advisory boards for GlaxoSmithKline. She reports financial support as principal investigator during studies from Chiesi, Astra Zeneca. She reports financial support as investigator during the study from Chiesi sa/nv. Fievez P. has no declaration of interest. Leys M. received honoraria for lectures from AstraZeneca, Chiesi, GlaxoSmithKline, Novartis, Pfizer, Janssen, Bayer, MSD; he is a member of advisory boards for AstraZeneca, Chiesi, GlaxoSmithKline, Novartis,. He reports financial support as investigator during the study from Chiesi sa/nv. Perez Bogerd S. was a member of advisory boards for AstraZeneca and has received, within the last 5 years, grants from Chiesi. She reports financial support as investigator during the study from Chiesi sa/nv. Peché R. has, within the last 5 years, received honoraria for lectures from AstraZeneca, Boehringer-Ingelheim, Chiesi, GlaxoSmithKline. He is a member of advisory boards for AstraZeneca, Boehringer-Ingelheim, Chiesi and GlaxoSmithKline. Vanderhelst E has, within the last 5 years, received honoraria for lectures from Vertex Pharmaceuticals, Boehringer-Ingelheim, Chiesi, GlaxoSmithKline. She is a member of advisory boards for Vertex Pharmaceuticals, Boehringer-Ingelheim, GlaxoSmithKline and received scientific grants from Chiesi and Boehringer-Ingelheim. Lins M. has, within the last 5 years, received honoraria for lectures from AstraZeneca, Boehringer-Ingelheim, Chiesi, GlaxoSmithKline, Novartis, Pfizer and Nyxoah. She is a member of advisory boards for AstraZeneca, GlaxoSmithKline, Novartis, Biophytis. She reports financial support as principal investigator during studies from Novartis, Chiesi, Astra Zeneca, Biophytis, Sanofi, Bayer, GSK, Johnson & Johnson. Capiou P. is a full-time employee of Chiesi sa/nv.

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. 2023 Nov-Dec;62:186-192.

doi: 10.1016/j.hrtlng.2023.07.006. Epub 2023 Aug 7.

Effectiveness of the integration of a palliative care team in the follow-up of patients with advanced chronic obstructive pulmonary disease: The home obstructive lung disease study

[D Gainza-Miranda](#)¹, [E M Sanz-Peces](#)², [M Varela Cerdeira](#)³, [C Prados Sanchez](#)⁴, [A Alonso-Babarro](#)³

Affiliations expand

- PMID: 37556860
- DOI: [10.1016/j.hrtlng.2023.07.006](https://doi.org/10.1016/j.hrtlng.2023.07.006)

Abstract

Background: Access to palliative care for patients with end-stage chronic obstructive pulmonary disease (COPD) is still very poor.

Objectives: Evaluate our palliative care program for patients with advanced COPD by assessing whether the referral criteria for advanced COPD patients were adequate in identifying patients in end-of-life care and determine the results of the palliative care team's intervention **METHODS:** This was a prospective observational study of patients admitted to a multidisciplinary unit for advanced COPD. Data on sociodemographic variables, survival, symptomatology, quality of life, ACP, and health resource utilization were analyzed.

Results: Eighty-three patients were included in this study. By the end of the follow-up period, 69 (83%) patients had died, mainly due to respiratory failure (96%). The median duration of survival from the start of follow-up was 4.27 months (95% confidence interval,

1.97-16.07). Most patients (94%) had a dyspnea level of 4. Sixty (72%) patients required opioids for dyspnea control. There were no significant differences in the quality of life of the patients during follow-up. Thirty (43%) patients died at home, 26 (38%) in a palliative care unit, and 13 (19%) in an acute care hospital. ACP was performed for 50 (72%) patients. Forty (57%) patients required palliative sedation during follow-up. Dyspnea was the reason for sedation in 34 (85%) patients. Hospital admissions and emergency room visits decreased significantly ($p = 0.01$) during follow-up.

Conclusions: Our integrated model allows for adequate selection of patients, facilitates symptom control and ACP, reduces resource utilization, and favors death at home.

Keywords: Advance care planning; Chronic obstructive pulmonary disease; End of life; Palliative medicine; 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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Thorax

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. 2023 Nov;78(11):1090-1096.

doi: 10.1136/thorax-2022-219463. Epub 2023 Jul 24.

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

[Carlos Echevarria](#)^{1,2}, [John Steer](#)^{2,3}, [Arun Prasad](#)³, [Jennifer K Quint](#)⁴, [Stephen C Bourke](#)^{2,5}

Affiliations expand

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

Abstract

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

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

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

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

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

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Conflict of interest statement

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

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Chronic Obstr Pulm Dis

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. 2023 Oct 26;10(4):422-436.

doi: 10.15326/jcopdf.2023.0387.

[Randomized Controlled Trials on Chronic Obstructive Pulmonary Disease in Africa: A Systematic Review](#)

[Eric Sven Kroeber](#)¹, [Thomas Frese](#)¹, [Eva Johanna Kantelhardt](#)², [Benjarong Nanuppakrankijkun](#)¹, [Etienne Ngeh Ngeh](#)^{3,4,5}, [Anne Schimpf](#)⁶, [Mulugeta Tamire](#)⁷, [Susanne Unverzagt](#)¹

Affiliations expand

- PMID: 37450850
- DOI: [10.15326/jcopdf.2023.0387](https://doi.org/10.15326/jcopdf.2023.0387)

Free article

Abstract

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

Methods: We performed a systematic search in 6 databases (including local African databases) and registries with updates through January 2022. We included randomized controlled trials (RCTs) that included patients diagnosed with COPD and were conducted in Africa, studying outcomes on acute respiratory episodes and rates, physical and functional abilities, and adverse events. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The study quality was assessed using the Cochrane risk of bias tool. We primarily summarized the results in narrative form.

Results: Out of 1594 identified publications, we included 18 studies with a total of 1504 participants, conducted in Egypt, South Africa, and Tunisia. Eight studies investigated interventions for patients in stable phases treated in outpatient settings, and 10 included patients with acute COPD exacerbations treated in emergency or intensive care settings. The interventions mainly included ventilatory support and pharmacological and rehabilitative interventions. Reported treatment effects were heterogeneous, ranging from no beneficial effects to clinically relevant benefits.

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

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

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Chronic Obstr Pulm Dis

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. 2023 Oct 26;10(4):343-354.

doi: 10.15326/jcopdf.2023.0402.

[Clinical Practices Surrounding the Prescription of Home Oxygen in Patients With COPD and Desaturation](#)

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

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Free article

Abstract

Purpose: While home oxygen therapy increases survival in patients with chronic obstructive pulmonary disease (COPD) who have severe resting hypoxemia, recent evidence suggests that there is no survival benefit of home oxygen for patients with COPD

who have isolated exertional desaturation. We aimed to understand clinician practice patterns surrounding the prescription of home oxygen for patients with COPD.

Methods: We conducted semi-structured qualitative interviews via videoconference with 15 physicians and 3 nurse practitioners who provide care for patients with COPD. Clinicians were recruited through the American Lung Association Airways Clinical Research Centers. Interview guides were created with the assistance of patient investigators and included questions regarding clinician practices surrounding the prescription of oxygen for patients with COPD and the use of clinical guidelines. Interviews were recorded, transcribed, and coded for themes.

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

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

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

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Chronic Obstr Pulm Dis

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. 2023 Oct 26;10(4):355-368.

doi: 10.15326/jcopdf.2023.0399.

Deep Learning Integration of Chest Computed Tomography Imaging and Gene Expression Identifies Novel Aspects of COPD

[Junxiang Chen](#)¹, [Zhonghui Xu](#)², [Li Sun](#)¹, [Ke Yu](#)¹, [Craig P Hersh](#)^{2,3}, [Adel Boueiz](#)^{2,3}, [John E Hokanson](#)⁴, [Frank C Scirba](#)⁵, [Edwin K Silverman](#)^{2,3}, [Peter J Castaldi](#)^{2,6}, [Kayhan Batmanghelich](#)¹

Affiliations expand

- PMID: 37413999
- DOI: [10.15326/jcopdf.2023.0399](https://doi.org/10.15326/jcopdf.2023.0399)

Free article

Abstract

Rationale: Chronic obstructive pulmonary disease (COPD) is characterized by pathologic changes in the airways, lung parenchyma, and persistent inflammation, but the links between lung structural changes and blood transcriptome patterns have not been fully described.

Objectives: The objective of this study was to identify novel relationships between lung structural changes measured by chest computed tomography (CT) and blood transcriptome patterns measured by blood RNA sequencing (RNA-seq).

Methods: CT scan images and blood RNA-seq gene expression from 1223 participants in the COPD Genetic Epidemiology (COPDGene[®]) study were jointly analyzed using deep learning to identify shared aspects of inflammation and lung structural changes that we labeled image-expression axes (IEAs). We related IEAs to COPD-related measurements and prospective health outcomes through regression and Cox proportional hazards models and tested them for biological pathway enrichment.

Results: We identified 2 distinct IEAs: IEA_{emph} which captures an emphysema-predominant process with a strong positive correlation to CT emphysema and a negative correlation to forced expiratory volume in 1 second and body mass index (BMI); and IEA_{airway} which captures an airway-predominant process with a positive correlation to BMI and airway wall thickness and a negative correlation to emphysema. Pathway enrichment analysis identified 29 and 13 pathways significantly associated with IEA_{emph} and IEA_{airway}, respectively (adjusted $p < 0.001$).

Conclusions: Integration of CT scans and blood RNA-seq data identified 2 IEAs that capture distinct inflammatory processes associated with emphysema and airway-predominant COPD.

Keywords: emphysema; genomics; machine learning.

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Ann Am Thorac Soc

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. 2023 Nov;20(11):1587-1594.

doi: 10.1513/AnnalsATS.202209-837OC.

[Accuracy of Pulse Oximetry for Long-Term Oxygen Therapy Assessment in Chronic Obstructive Pulmonary Disease](#)

Affiliations expand

- PMID: 37413976
- DOI: [10.1513/AnnalsATS.202209-837OC](https://doi.org/10.1513/AnnalsATS.202209-837OC)

Abstract

Rationale: Landmark studies of long-term oxygen therapy (LTOT) in patients with chronic obstructive pulmonary disease (COPD) used arterial oxygen pressure (P_{aO_2}) to define severe hypoxemia; however, oxygen saturation as measured by pulse oximetry (Sp_{O_2}) is commonly used instead. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines recommend evaluation with arterial blood gas (ABG) analysis if Sp_{O_2} is $\leq 92\%$. This recommendation has not been evaluated in stable outpatients with COPD undergoing testing for LTOT. **Objectives:** To evaluate the performance of Sp_{O_2} compared with ABG analysis of P_{aO_2} and arterial oxygen saturation (Sa_{O_2}) to detect severe resting hypoxemia in patients with COPD. **Methods:** Retrospective analysis of paired Sp_{O_2} and ABG values from stable outpatients with COPD who underwent LTOT assessment in a single center. We calculated false negatives (FNs) as an $Sp_{O_2} > 88\%$ or $> 89\%$ in the presence of pulmonary hypertension with a $P_{aO_2} \leq 55$ mm Hg or ≤ 59 mm Hg in the presence of pulmonary hypertension. Test performance was assessed using receiver operating characteristic (ROC) analysis, intraclass correlation coefficient (ICC), test bias, precision, and accuracy root-mean-square (A_{rms}). An adjusted multivariate analysis was used to evaluate factors affecting Sp_{O_2} bias. **Results:** Of 518 patients, the prevalence of severe resting hypoxemia was 74 (14.3%), with 52 missed by Sp_{O_2} (FN, 10%), including 13 (2.5%) with an $Sp_{O_2} > 92\%$ (occult hypoxemia). FNs and occult hypoxemia in Black patients were 9% and 1.5%, respectively, and were 13% and 5%, respectively, among active smokers. The correlation between Sp_{O_2} and Sa_{O_2} was acceptable (ICC = 0.78; 95% confidence interval, 0.74-0.81); and the bias of Sp_{O_2} was 0.45%, with a precision of 2.6 (-4.65 to +5.55%) and A_{rms} of 2.59. These measurements were similar in Black patients, but in active smokers, correlation was lower and bias showed greater overestimation of Sp_{O_2} . ROC analysis suggests that the optimal Sp_{O_2} cutoff to warrant LTOT evaluation by ABG analysis is $\leq 94\%$. **Conclusions:** Sp_{O_2} as the only measure of oxygenation carries a high FN rate in detecting severe resting hypoxemia in patients with COPD undergoing evaluation for LTOT. Reflex measurement of P_{aO_2} by ABG analysis should be used as recommended by GOLD, ideally at a cutoff higher than an $Sp_{O_2} \leq 92\%$, especially in active smokers.

Keywords: COPD; hypoxemia; oxygen; pulse oximetry.

Comment in

- [Pulse Oximetry Misclassifies Need for Long-Term Oxygen Therapy in Chronic Obstructive Pulmonary Disease.](#)

Fawzy A, Wise RA. Ann Am Thorac Soc. 2023 Nov;20(11):1556-1557. doi: 10.1513/AnnalsATS.202309-754ED. PMID: 37909796 No abstract available.

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MeSH terms, Substances expand

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Chronic Obstr Pulm Dis

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. 2023 Oct 26;10(4):369-379.

doi: 10.15326/jcopdf.2023.0395.

[Disparities in Guideline Concordant Statin Treatment in Individuals With Chronic Obstructive Pulmonary Disease](#)

[Jamuna K Krishnan](#)¹, [Sonal G Mallya](#)^{2,3}, [Musarrat Nahid](#)³, [Aaron D Baugh](#)⁴, [MeiLan K Han](#)⁵, [Kerri I Aronson](#)¹, [Parag Goyal](#)^{3,6}, [Laura C Pinheiro](#)³, [Samprit Banerjee](#)⁷, [Fernando J Martinez](#)¹, [Monika M Safford](#)³

Affiliations expand

- PMID: 37410623
- DOI: [10.15326/jcopdf.2023.0395](#)

Free article

Abstract

Rationale: Cardiovascular disease (CVD) affects the prognosis of patients with chronic obstructive pulmonary disease (COPD). Black women with COPD have a disproportionate risk of CVD-related mortality, yet disparities in CVD prevention in COPD are unknown.

Objectives: We aimed to identify race-sex differences in the receipt of statin treatment for CVD prevention, and whether these differences were explained by factors influencing health care utilization in the REasons for Geographic And Racial Differences in Stroke (REGARDS) COPD study sub-cohort.

Methods: We conducted a cross-sectional analysis among REGARDS Medicare beneficiaries with COPD. Our primary outcome was the presence of statin on in-home pill bottle review among individuals with an indication. Prevalence ratios (PR) for statin treatment among race-sex groups compared to White men were estimated using Poisson regression with robust variance. We then adjusted for covariates previously shown to impact health care utilization.

Results: Of the 2032 members within the COPD sub-cohort with sufficient data, 1435 participants (19% Black women, 14% Black men, 28% White women, and 39% White men) had a statin indication. All race-sex groups were less likely to receive statins than White men in unadjusted models. After adjusting for covariates that influence health care utilization, Black women (PR 0.76, 95% confidence interval [CI] 0.67 to 0.86) and White women (PR 0.84 95% CI 0.76 to 0.91) remained less likely to be treated compared to White men.

Conclusions: All race-sex groups were less likely to receive statin treatment in the REGARDS COPD sub-cohort compared to White men. This difference persisted in women after controlling for individual health care utilization factors, suggesting structural interventions are needed.

Keywords: COPD; cardiovascular disease; comorbidity; health delivery.

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Chin Med J (Engl)



. 2023 Nov 5;136(21):2587-2595.

doi: 10.1097/CM9.0000000000002487.

[Does the 2017 global initiative for chronic obstructive lung disease revision really improve the assessment of Chinese chronic obstructive pulmonary disease patients? A multicenter prospective study for more than 5 years](#)

[Yanan Cui](#)¹, [Yiming Ma](#)¹, [Zhongshang Dai](#)¹, [Yingjiao Long](#)², [Yan Chen](#)¹

Affiliations [expand](#)

- PMID: 37367695
- PMCID: [PMC10617920](#)
- DOI: [10.1097/CM9.0000000000002487](#)

Abstract

Background: The Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017 proposed a new classification that reclassified many chronic obstructive pulmonary disease (COPD) patients from group D to B. However, there is a paucity of data related to the comparison between reclassified and non-reclassified COPD patients in terms of long-term prognosis. This study aimed to investigate long-term outcomes of them and determine whether the GOLD 2017 revision improved the assessment of COPD patients.

Methods: This observational, multicenter, prospective study recruited outpatients at 12 tertiary hospitals in China from November 2016 to February 2018 and followed them up until February 2022. All enrolled patients were classified into groups A to D based on GOLD 2017, and the subjects in group B included patients reclassified from group D to B (group DB) and those remaining in group B (group BB). Incidence rates and hazard ratios (HRs) were calculated for the exacerbation of COPD and hospitalization in each group.

Results: We included and followed up 845 patients. During the first year of follow-up, the GOLD 2017 classification had a better discrimination ability for different risks of COPD exacerbation and hospitalization than GOLD 2013. Group DB was associated with a higher risk of moderate-to-severe exacerbation (HR = 1.88, 95% confidence interval [CI] = 1.37-2.59, $P < 0.001$) and hospitalization for COPD exacerbation (HR = 2.23, 95% CI = 1.29-3.85, $P = 0.004$) than group BB. However, during the last year of follow-up, the differences in the risks of frequent exacerbations and hospitalizations between group DB and BB were not statistically significant (frequent exacerbations: HR = 1.02, 95% CI = 0.51-2.03, $P = 0.955$; frequent hospitalizations: HR = 1.66, 95% CI = 0.58-4.78, $P = 0.348$). The mortality rates of the two groups were both approximately 9.0% during the entire follow-up period.

Conclusions: The long-term prognosis of patients reclassified into group B and of those remaining in group B was similar, although patients reclassified from group D to group B had worse short-term outcomes. The GOLD 2017 revision could improve the assessment of Chinese COPD patients in terms of long-term prognosis.

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Conflict of interest statement

None.

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

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Heart Lung



. 2023 Nov-Dec:62:95-100.

doi: 10.1016/j.hrtlng.2023.06.022. Epub 2023 Jun 24.

Predictors of cardiopulmonary exercise testing in COPD patients according to the Weber classification

[Flávia Rossi Caruso](#)¹, [Cássia da Luz Goulart](#)¹, [José Carlos Bonjorno Jr](#)², [Claudio Ricardo de Oliveira](#)², [Renata Gonçalves Mendes](#)¹, [Ross Arena](#)³, [Audrey Borghi-Silva](#)⁴

Affiliations expand

- PMID: 37364368
- DOI: [10.1016/j.hrtlng.2023.06.022](https://doi.org/10.1016/j.hrtlng.2023.06.022)

Abstract

Background: Weber classification stratifies cardiac patients based on peak oxygen consumption ($\dot{V}O_2$), the gold-standard measure of exercise capacity.

Objective: To determine if Weber classification is a useful tool to discriminate clinical phenotypes in COPD patients and to evaluate if disease severity and other clinical measures can predict $\dot{V}O_{2peak}$.

Methods: Three hundred and six COPD patients underwent cardiopulmonary exercise testing (CPX) and were divided according to Weber class: 1) Weber A (n = 34); 2) Weber B (n = 88); 3) Weber C (n = 138); and 4) Weber D (n = 46).

Results: Weber class D patients demonstrated a reduced $\dot{V}O_{2\text{peak}}$, heart rate (HR), minute ventilation (\dot{V}_E), oxygen (O_2) pulse, circulatory power (CP), oxygen uptake efficiency slope (OUES), oxygen saturation ($SpO_2\%$), delta (Δ)HR and ΔSpO_2 when compared to Weber A and B ($p < 0.05$). Moreover, Dyspnea and the \dot{V}_E /carbon dioxide production ($\dot{V}CO_2$) slope were higher in Weber D compared with Weber C and A ($p < 0.001$). Hierarchical regression analysis demonstrated significant predictors of $\dot{V}O_{2\text{peak}}$ ($R^2 = 0.131$; $\text{Adj } R^2 = 1.25$), including HR ($\beta = 0.5757$; $t = 5.7$; $P < 0.001$) and forced expiratory volume in one second (FEV_1) ($\beta = 0.119$; $t = 2.16$; $P < 0.03$). Among the Weber C + D groups, predictors of $\dot{V}O_{2\text{peak}}$ ($R = 0.78$; $R^2 = 0.60$; $\text{Adj } R^2 = 0.59$), dyspnea ($\beta = 0.076$; $t = 1.111$; $P < 0.27$) and maximal voluntary ventilation (MVV) ($\beta = 0.75$; $t = 1.14$; $P < 0.00$).

Conclusion: Weber classification may be a useful tool to stratify cardiorespiratory fitness in COPD patients. Other clinical measures may be useful in predicting peak $\dot{V}O_2$ in mild-to-severe COPD, moreover different phenotypes may be important tool to improve physical capacity of chronic disease patients.

Keywords: Equations; Exercise tolerance; Oxygen uptake; Rehabilitation.

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Conflict of interest statement

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

SUPPLEMENTARY INFO

MeSH terms, Substances expand

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Respir Care

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. 2023 Nov;68(11):1546-1552.

doi: 10.4187/respcare.10917. Epub 2023 Jun 13.

Minimally Important Difference of the 20-m 6-Minute Walk Test in Individuals With COPD

[Suelen R Klein](#)¹, [Anelise B Munari](#)¹, [Manuela Karloh](#)², [Francieli C Mucha](#)¹, [Isabela Jcs Silva](#)¹, [Anamaria F Mayer](#)³

Affiliations expand

- PMID: 37311628
- PMCID: PMC10589114 (available on 2024-11-01)
- DOI: [10.4187/respcare.10917](https://doi.org/10.4187/respcare.10917)

Abstract

Background: The 20-m 6-min-walk test (6MWT20) is a valid, reliable alternative for functional capacity assessment; however, its responsiveness and minimally important difference (MID) have yet to be investigated. The aim of this study was to assess the responsiveness and MID of the 6MWT20 in individuals with COPD.

Methods: Fifty-three subjects completed the study from August 2011-March 2020. The following were assessed: lung function, activities of daily living (ADLs), functional capacity 6MWT20, dyspnea, health status, quality of life, and limitations in ADLs. The primary outcome was the 6MWT20 distance.

Results: The study demonstrated that the 6MWT20 is responsive to pulmonary rehabilitation (PR), with an average improvement of 39 ± 36.3 m ($P < .001$) and an effect size of 1.07. The learning effect declined to 1.45% after PR, with an intraclass correlation coefficient of 0.99 (95% CI 0.98-0.99). The receiver operating characteristic curve indicated a cutoff point of 20 m for the MID of the 6MWT20 based on the MIDs for the modified St George Respiratory Questionnaire (sensitivity 87%, specificity 69%, area under the curve 0.80 [95% CI 0.66-0.90], $P < .001$, Youden index 0.56) and the number of steps (sensitivity 92%, specificity 73%, area under the curve 0.83 [95% CI 0.70-0.92], $P < .01$, Youden index 0.56).

Conclusions: The 6MWT20 is responsive to PR, and the MID for the test is 20 m (17-47 m).

Keywords: COPD; activities of daily living; exercise; result assessment (health care); walking.

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Conflict of interest statement

The authors have disclosed no conflicts of interest.

- [49 references](#)

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MeSH termsexpand

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Randomized Controlled Trial

Respir Care

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. 2023 Nov;68(11):1553-1560.

doi: 10.4187/respcare.09866. Epub 2023 Jun 13.

[Automated Oxygen Titration During CPAP and Noninvasive Ventilation in](#)

Healthy Subjects With Induced Hypoxemia

[Miguel Trottier](#)¹, [Pierre-Alexandre Bouchard](#)¹, [Erwan L'Her](#)², [François Lellouche](#)³

Affiliations expand

- PMID: 37311626
- PMCID: PMC10589107 (available on 2024-11-01)
- DOI: [10.4187/respcare.09866](https://doi.org/10.4187/respcare.09866)

Abstract

Background: Automated oxygen titration to maintain a stable S_{pO_2} has been developed for spontaneously breathing patients but has not been evaluated during CPAP and noninvasive ventilation (NIV).

Methods: We performed a randomized controlled crossover, double-blind study on 10 healthy subjects with induced hypoxemia during 3 situations: spontaneous breathing with oxygen support, CPAP (5 cm H₂O), and NIV (7/3 cm H₂O). We conducted in random order 3 dynamic hypoxic challenges of 5 min (F_{IO_2} 0.08 ± 0.02, 0.11 ± 0.02, and 0.14 ± 0.02). For each condition, we compared automated oxygen titration and manual oxygen titration by experienced respiratory therapists (RTs), with the aim to maintain the S_{pO_2} at 94 ± 2%. In addition, we included 2 subjects hospitalized for exacerbation of COPD under NIV and a subject managed after bariatric surgery with CPAP and automated oxygen titration.

Results: The percentage of time in the S_{pO_2} target was higher with automated compared with manual oxygen titration for all conditions, on average 59.6 ± 22.8% compared to 44.3 ± 23.9% ($P = .004$). Hyperoxemia ($S_{pO_2} > 96\%$) was less frequent with automated titration for each mode of oxygen administration (24.0 ± 24.4% vs 39.1 ± 25.3%, $P < .001$). During the manual titration periods, the RT made several changes to oxygen flow (5.1 ± 3.3 interventions that lasted 122 ± 70 s/period) compared to none during the automated titration to maintain oxygenation in the targeted S_{pO_2} . Time in the S_{pO_2} target was higher with stable hospitalized subjects in comparison with healthy subjects under dynamic-induced hypoxemia.

Conclusions: In this proof-of-concept study, automated oxygen titration was used during CPAP and NIV. The performances to maintain the S_{pO_2} target were significantly better

compared to manual oxygen titration in the setting of this study protocol. This technology may allow decreasing the number of manual interventions for oxygen titration during CPAP and NIV.

Keywords: CPAP; automated oxygen titration; hyperoxemia; hypoxemia; noninvasive ventilation; oxygen inhalation therapy.

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Conflict of interest statement

Drs Lellouche and L'Her are co-inventors of the FreeO2 system and are cofounders of a research and development company (OxyNov) to develop automated systems for respiratory support. OxyNov provided no support for the study. Mr Bouchard discloses a relationship with OxyNov. Dr Trottier has disclosed no conflicts of interest.

- [33 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Respir Care

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. 2023 Nov;68(11):1532-1539.

doi: 10.4187/respcare.10132. Epub 2023 Jun 6.

Response to Bronchodilators Administered via Different Nebulizers in Patients With COPD Exacerbation

[Breda Cushen](#)¹, [Abir Alsaid](#)², [Garrett Greene](#)³, [Richard W Costello](#)⁴

Affiliations expand

- PMID: 37280080
- PMCID: PMC10589110 (available on 2024-11-01)
- DOI: [10.4187/respcare.10132](https://doi.org/10.4187/respcare.10132)

Abstract

Background: The recommended treatment of COPD exacerbations includes administration of short-acting bronchodilators that act to reverse bronchoconstriction, restore lung volumes, and relieve breathlessness. In vitro studies demonstrate vibrating mesh nebulizers (VMNs) provide greater drug delivery to the airway compared to standard small-volume nebulizers (SVNs). We examined whether the physiological and symptom response to nebulized bronchodilators during a COPD exacerbation differed between these 2 modes of bronchodilator delivery.

Methods: Subjects hospitalized with a COPD exacerbation participated in a comparative clinical effectiveness study of 2 methods of nebulization. Using block randomization, 32 participants in this open-label trial were administered salbutamol 2.5 mg/ipratropium bromide 0.5 mg via vibrating mesh (VMN group, $n = 16$) or small-volume jet nebulizer (SVN group, $n = 16$) on one occasion. Spirometry, body plethysmography, and impulse oscillometry were performed and Borg breathlessness scores recorded pre bronchodilator and at 1 h post bronchodilator.

Results: Baseline demographics were comparable between groups. Mean FEV₁ was 48% predicted. Significant changes in lung volumes and airway impedance were seen in both groups. Inspiratory capacity (IC) increased by 0.27 ± 0.20 L and 0.21 ± 0.20 L in the VMN and SVN group, respectively, between group difference $P = .40$. FVC increased in the VMN group by 0.41 ± 0.40 L compared to 0.19 ± 0.20 L with SVN, between group difference $P = .053$; and residual volume (RV) decreased by 0.36 ± 0.80 L and 0.16 ± 0.50 L in the VMN

and SVN group, respectively, between group difference $P = .41$. The VMN group had a significant reduction in Borg breathlessness score, $P = .034$.

Conclusions: Greater improvement in symptoms, and larger absolute change in FVC, was observed in response to equivalent doses of standard bronchodilators administered by VMN, compared to SVN, but no substantial difference in change in IC.

Keywords: COPD exacerbation management; bronchodilator delivery; bronchodilator response; exacerbations of COPD; small-volume nebulizer; vibrating mesh nebulizer.

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Conflict of interest statement

The authors have disclosed no further conflicts of interest.

- [37 references](#)

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. 2023 Nov 1;58(11):775-781.

doi: 10.1097/RLI.0000000000000989. Epub 2023 May 26.

[Dark-Field Chest Radiography Outperforms Conventional Chest](#)

Radiography for the Diagnosis and Staging of Pulmonary Emphysema

[Theresa Urban](#)¹, [Andreas P Sauter](#), [Manuela Frank](#), [Konstantin Willer](#), [Wolfgang Noichl](#), [Henriette Bast](#), [Rafael Schick](#), [Julia Herzen](#), [Thomas Koehler](#), [Florian T Gassert](#), [Jannis H Bodden](#), [Alexander A Fingerle](#), [Bernhard Gleich](#), [Bernhard Renger](#), [Marcus R Makowski](#), [Franz Pfeiffer](#), [Daniela Pfeiffer](#)

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- PMID: 37276130
- PMCID: [PMC10581407](#)
- DOI: [10.1097/RLI.0000000000000989](#)

Free PMC article

Abstract

Objectives: Dark-field chest radiography (dfCXR) has recently reached clinical trials. Here we compare dfCXR to conventional radiography for the detection and staging of pulmonary emphysema.

Materials and methods: Subjects were included after a medically indicated computed tomography (CT) scan, showing either no lung impairments or different stages of emphysema. To establish a ground truth, all CT scans were assessed by 3 radiologists assigning emphysema severity scores based on the Fleischner Society classification scheme. Participants were imaged at a commercial chest radiography device and at a prototype for dfCXR, yielding both attenuation-based and dark-field images. Three radiologists blinded to CT score independently assessed images from both devices for presence and severity of emphysema (no, mild, moderate, severe). Statistical analysis included evaluation of receiver operating characteristic curves and pairwise comparison of adjacent Fleischner groups using an area under the curve (AUC)-based z test with a significance level of 0.05.

Results: A total of 88 participants (54 men) with a mean age of 64 ± 12 years were included. Compared with conventional images (AUC = 0.73), readers were better able to identify emphysema with images from the dark-field prototype (AUC = 0.85, $P = 0.005$). Although ratings of adjacent emphysema severity groups with conventional radiographs differed only for trace and mild emphysema, ratings based on images from the dark-field

prototype were different for trace and mild, mild and moderate, and moderate and confluent emphysema.

Conclusions: Dark-field chest radiography is superior to conventional chest radiography for emphysema diagnosis and staging, indicating the technique's potential as a low-dose diagnostic tool for emphysema assessment.

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Conflict of interest statement

Conflicts of interest and sources of funding: This study was supported by the European Research Council (AdG 695045); the Federal Ministry of Education and Research; the Free State of Bavaria under the Excellence Strategy of the Federal Government and the Länder; the German Research Foundation (GRK2274); Philips Medical Systems DMC; the Institute for Advanced Study, Technische Universität München; and the Karlsruhe Nano Micro Facility, a Helmholtz Research Infrastructure at Karlsruhe Institute of Technology.

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

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Thorax

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. 2023 Nov;78(11):1067-1079.

doi: 10.1136/thorax-2022-219158. Epub 2023 Jun 2.

Pulmonary emphysema subtypes defined by unsupervised machine learning on CT scans

[Elsa D Angelini](#) ^{# 1 2 3}, [Jie Yang](#) ^{# 1}, [Pallavi P Balte](#) ⁴, [Eric A Hoffman](#) ⁵, [Ani W Manichaikul](#) ⁶, [Yifei Sun](#) ⁷, [Wei Shen](#) ^{8 9}, [John H M Austin](#) ¹⁰, [Norrina B Allen](#) ¹¹, [Eugene R Bleecker](#) ¹², [Russell Bowler](#) ¹³, [Michael H Cho](#) ^{14 15}, [Christopher S Cooper](#) ¹⁶, [David Couper](#) ¹⁷, [Mark T Dransfield](#) ¹⁸, [Christine Kim Garcia](#) ⁴, [MeiLan K Han](#) ¹⁹, [Nadia N Hansel](#) ²⁰, [Emlyn Hughes](#) ²¹, [David R Jacobs](#) ²², [Silva Kasela](#) ^{23 24}, [Joel Daniel Kaufman](#) ²⁵, [John Shinn Kim](#) ^{4 26}, [Tuuli Lappalainen](#) ²³, [Joao Lima](#) ²⁰, [Daniel Malinsky](#) ⁷, [Fernando J Martinez](#) ²⁷, [Elizabeth C Oelsner](#) ⁴, [Victor E Ortega](#) ²⁸, [Robert Paine](#) ²⁹, [Wendy Post](#) ²⁰, [Tess D Pottinger](#) ⁴, [Martin R Prince](#) ³⁰, [Stephen S Rich](#) ⁶, [Edwin K Silverman](#) ¹⁴, [Benjamin M Smith](#) ^{4 31}, [Andrew J Swift](#) ^{4 32}, [Karol E Watson](#) ¹⁶, [Prescott G Woodruff](#) ³³, [Andrew F Laine](#) ^{# 1 9 10}, [R Graham Barr](#) ^{# 34 35}

Affiliations expand

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- PMCID: [PMC10592007](#)
- DOI: [10.1136/thorax-2022-219158](#)

Free PMC article

Abstract

Background: Treatment and preventative advances for chronic obstructive pulmonary disease (COPD) have been slow due, in part, to limited subphenotypes. We tested if unsupervised machine learning on CT images would discover CT emphysema subtypes with distinct characteristics, prognoses and genetic associations.

Methods: New CT emphysema subtypes were identified by unsupervised machine learning on only the texture and location of emphysematous regions on CT scans from 2853 participants in the Subpopulations and Intermediate Outcome Measures in COPD Study (SPIROMICS), a COPD case-control study, followed by data reduction. Subtypes were compared with symptoms and physiology among 2949 participants in the population-based Multi-Ethnic Study of Atherosclerosis (MESA) Lung Study and with prognosis among 6658 MESA participants. Associations with genome-wide single-nucleotide-polymorphisms were examined.

Results: The algorithm discovered six reproducible (interlearner intraclass correlation coefficient, 0.91-1.00) CT emphysema subtypes. The most common subtype in SPIROMICS, the combined bronchitis-apical subtype, was associated with chronic bronchitis, accelerated lung function decline, hospitalisations, deaths, incident airflow limitation and a gene variant near *DRD1*, which is implicated in mucin hypersecretion ($p=1.1 \times 10^{-8}$). The second, the diffuse subtype was associated with lower weight, respiratory hospitalisations and deaths, and incident airflow limitation. The third was associated with age only. The fourth and fifth visually resembled combined pulmonary fibrosis emphysema and had distinct symptoms, physiology, prognosis and genetic associations. The sixth visually resembled vanishing lung syndrome.

Conclusion: Large-scale unsupervised machine learning on CT scans defined six reproducible, familiar CT emphysema subtypes that suggest paths to specific diagnosis and personalised therapies in COPD and pre-COPD.

Keywords: COPD epidemiology; Emphysema; Imaging/CT MRI etc.

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Conflict of interest statement

Competing interests: EDA, PPB, AM, YS, WS, JHMA, MHC, DC, EH, DRJ, SK, JDK, TL, JL, ECO, WP, MRP, SSR, EKS, KEW and AFL reports receiving grants from the National Institutes of Health (NIH). JY performed the work at Columbia University but is now an employee of Google. EAH reports receiving grants from the NIH; being a founder and shareholder of VIDA Diagnostics; and holding patents for an apparatus for analysing CT images to determine the presence of pulmonary tissue pathology, an apparatus for image display and analysis, and a method for multiscale meshing of branching biological structures. EBA reports receiving grants from the American Heart Association and the NIH. CBC reports receiving personal fees from GlaxoSmithKline. MTD reports receiving a grant from the NHLBI and personal fees from AstraZeneca, GlaxoSmithKline, Pulmonx, PneumRx/BTG and Quark. MKH reports consulting for GlaxoSmithKline, AstraZeneca and Boehringer Ingelheim receiving research support from Novartis and Sunovion. NNH reports receiving grants from the NIH, Boehringer Ingelheim, and the COPD Foundation. JDK reports receiving grants from US Environmental Protection Agency and the NIH. FJM reports serving on COPD advisory boards for AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Sunovion and Teva; serving as a consultant for ProterixBio and Verona; serving on the steering committees of studies sponsored by the NHLBI, AstraZeneca, and GlaxoSmithKline; having served on data safety and monitoring boards of COPD studies supported by Genentech and GlaxoSmithKline. BMS reports receiving grants from the NIH, Canadian Institutes of Health Research (CIHR), Fonds de la recherche en santé du Québec (FRQS), the Research Institute of the McGill University Health Centre, the Quebec Lung Association and AstraZeneca. PGW reports receiving personal fees for consultancy from

Theravance, AstraZeneca, Regeneron, Sanofi, Genentech, Roche and Janssen. RGB reports receiving grants from the COPD Foundation, the US Environmental Protection Agency (EPA), the American Lung Association and the NIH.

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

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Review

Semin Nucl Med

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. 2023 Nov;53(6):809-819.

doi: 10.1053/j.semnuclmed.2023.05.003. Epub 2023 May 29.

Practice of ¹⁸F-FDG-PET/CT in ICU Patients: A Systematic Review

[Bram van Leer](#)¹, [Nick D van Rijsewijk](#)², [Maarten W N Nijsten](#)³, [Riemer H J A Slart](#)⁴, [Janesh Pillay](#)⁵, [Andor W J M Glaudemans](#)²

Affiliations [expand](#)

- PMID: 37258380

- DOI: [10.1053/j.semnuclmed.2023.05.003](https://doi.org/10.1053/j.semnuclmed.2023.05.003)

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Abstract

¹⁸F-FDG-PET/CT imaging has become a key tool to evaluate infectious and inflammatory diseases. However, application of ¹⁸F-FDG-PET/CT in patients in the intensive care unit (ICU) is limited, which is remarkable since the development of critical illness is closely linked to infection and inflammation. This limited use is caused by perceived complexity and risk of planning and executing ¹⁸F-FDG-PET/CT in such patients. The aim of this systematic review was to investigate the feasibility of ¹⁸F-FDG-PET/CT in ICU patients with special emphasis on patient preparation, transport logistics and safety. Therefore, a systematic search was performed in PubMed, Embase, and Web of Science using the search terms: intensive care, critically ill, positron emission tomography and ¹⁸F-FDG or derivatives. A total of 1183 articles were found of which 10 were included. Three studies evaluated the pathophysiology of acute respiratory distress syndrome, acute lung injury and acute chest syndrome. Three other studies applied ¹⁸F-FDG-PET/CT to increase understanding of pathophysiology after traumatic brain injury. The remaining four studies evaluated infection of unknown origin. These four studies showed a sensitivity and specificity between 85%-100% and 57%-88%, respectively. A remarkable low adverse event rate of 2% was found during the entire ¹⁸F-FDG-PET/CT procedure, including desaturation and hypotension. In all studies, a team consisting of an intensive care physician and nurse was present during transport to ensure continuation of necessary critical care. Full monitoring during transport was used in patients requiring mechanical ventilation or vasopressor support. None of the studies used specific patient preparation for ICU patients. However, one article described specific recommendations in their discussion. In conclusion, ¹⁸F-FDG-PET/CT has been shown to be feasible and safe in ICU patients, even when ventilated or requiring vasopressors. Specific recommendations regarding patient preparation, logistics and scanning are needed. Including ¹⁸F-FDG-PET/CT in routine workup of infection of unknown origin in ICU patients showed potential to identify source of infection and might improve outcome.

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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 types, MeSH terms, Substancesexpand

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J Intern Med

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. 2023 Nov;294(5):616-627.

doi: 10.1111/joim.13656. Epub 2023 May 31.

[Elevated low-density lipoprotein cholesterol: An inverse marker of morbidity and mortality in patients with myocardial infarction](#)

[Jessica Schubert](#)¹, [Bertil Lindahl](#)^{1,2}, [Håkan Melhus](#)¹, [Henrik Renlund](#)², [Margrét Leosdóttir](#)^{3,4}, [Ali Yari](#)⁵, [Peter Ueda](#)⁶, [Tomas Jernberg](#)⁵, [Emil Hagström](#)^{1,2}

Affiliations expand

- PMID: 37254886
- DOI: [10.1111/joim.13656](https://doi.org/10.1111/joim.13656)

Abstract

Background: The incidence of atherosclerotic cardiovascular disease increases with levels of low-density lipoprotein cholesterol (LDL-C). Yet, a paradox may exist where lower LDL-C levels at myocardial infarction (MI) are associated with poorer prognoses.

Objective: To assess the association between LDL-C levels at MI with risk factor burden and cause-specific outcomes.

Methods: Statin-naïve patients hospitalized for a first MI and registered in SWEDEHEART were included. Data were linked to Swedish registers. Primary outcomes were all-cause mortality and nonfatal MI. Associations between LDL-C and outcomes were assessed using adjusted proportional hazards models.

Results: Among 63,168 patients (median age, 66 years), the median LDL-C level was 3.0 mmol/L (interquartile range 2.4-3.6). Patient age and comorbidities increased as LDL-C decreased. During a median follow-up of 4.5 years, 10,236 patients died, and 4973 had nonfatal MI. Patients with the highest LDL-C had a lower risk of mortality (hazard ratio [HR] 0.75; 95% confidence interval [CI] 0.71-0.80). The risk of hospitalization for pneumonia, hip fracture, chronic obstructive pulmonary disease, and new cancer diagnosis was lower with higher LDL-C (HR range, 0.40-0.81). Patients with the highest LDL-C had a greater risk of recurrent MI (HR 1.16; 95% CI 1.07-1.26).

Conclusions: Patients with the highest LDL-C levels at MI had the lowest incidence of mortality and morbidity. This seems to reflect lower age at MI, less underlying morbidities, paired with the modifiability of LDL-C. However, supporting the causal association between LDL-C and ischemic heart disease, elevated LDL-C was simultaneously associated with an increased risk of nonfatal MI.

Keywords: atherosclerosis; cholesterol; lipid lowering; myocardial infarction; observational; prevention.

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. 2023 Nov;37(11):1521-1532.

doi: 10.1177/02692155231174124. Epub 2023 May 15.

Determination of the minimal important difference for inspiratory muscle strength in people with severe and very severe COPD

[Marc Beaumont](#)^{1,2}, [Charles Couasnon](#)³, [Loïc Péran](#)¹, [Anne Cécile Berriet](#)¹, [Catherine Le Ber](#)¹, [Romain Pichon](#)^{3,4}

Affiliations expand

- PMID: 37186772
- DOI: [10.1177/02692155231174124](https://doi.org/10.1177/02692155231174124)

Abstract

Objective: Inspiratory muscle training is recommended for people with chronic obstructive pulmonary disease (COPD) with inspiratory muscle weakness. Clinical interpretation of changes in inspiratory muscle strength could be helped by the determination of cut-off values. The aim of this study was to estimate the minimal important difference for inspiratory muscle strength assessed with maximal inspiratory pressure (MIP) in people with COPD.

Design: Post hoc analysis of a randomized controlled trial (EMI2 study) including people with severe to very severe COPD undergoing a pulmonary rehabilitation program was conducted. The determination of the minimal important difference was realized using both anchor-based and distribution-based methods.

Setting: The study includes patients admitted to the rehabilitation program unit of the Centre Hospitalier des Pays de Morlaix (Morlaix, France) between March 5, 2014 and September 8, 2016.

Participants: Seventy-three people with severe to very severe COPD (age 62.2 ± 8.0 years, forced expiratory volume in 1 s $36.4 \pm 9.5\%$ of theoretical) were analyzed.

Intervention: Patients followed a standardized pulmonary rehabilitation program 5 days a week for 4 weeks. The program included aerobic training, ground-based outdoor walking training, and strengthening of lower and upper limb muscles.

Main measures: At the end of the pulmonary rehabilitation program, MIP improved by 14.8 ± 14.9 cmH₂O ($p < 0.05$). Regarding the anchor-based method, only the modified Medical Research Council was selected as an appropriate anchor. The receiver operating characteristic curve analysis reported a minimal important difference of 13.5 cmH₂O (sensitivity: 75% specificity: 67.5%). Using distribution-based methods, the estimate of minimal important difference was 7.9 cmH₂O (standard error of measurement method) and 10.9 cmH₂O (size effect method).

Results: The estimations proposed by this study ranged from 7.9 to 13.5 cmH₂O.

Conclusions: The measurement of minimal important difference is a simple tool for assessing the changes of inspiratory muscle strength during a pulmonary rehabilitation program. We propose a minimal important difference of 13.5 cmH₂O for the improvement of MIP. Further studies are needed to confirm this estimation. ClinicalTrials.gov identifier: [NCT02074813](https://clinicaltrials.gov/ct2/show/study/NCT02074813).

Keywords: COPD; minimal important difference; pulmonary rehabilitation; respiratory muscles.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Associated dataexpand

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. 2023 Nov;37(11):1479-1491.

doi: 10.1177/02692155231172005. Epub 2023 Apr 25.

Efficacy of aerobic training and resistance training combined with external diaphragm pacing in patients with chronic obstructive pulmonary disease: A randomized controlled study

[Yiming Xu](#)¹, [Donghong Yang](#)¹, [Beibei Lu](#)¹, [Yin Zhang](#)¹, [Lei Ren](#)¹, [Honghua Shen](#)¹

Affiliations expand

- PMID: 37122164
- DOI: [10.1177/02692155231172005](https://doi.org/10.1177/02692155231172005)

Abstract

Objective: To evaluate the efficacy of aerobic training, resistance training combined with external diaphragm pacing in patients with chronic obstructive pulmonary disease.

Design: Randomized controlled trial.

Setting: The Fourth Rehabilitation Hospital of Shanghai, China.

Participants: 82 (67.0 ± 6.5 years, 59.8% male) patients with stable chronic obstructive pulmonary disease were randomized to intervention group 1 ($n = 27$), intervention group 2 ($n = 28$), and control group ($n = 27$).

Intervention: Intervention group 1 received aerobic and resistance training, while intervention group 2 received additional external diaphragm pacing. Control group received aerobic training only.

Main measures: 1-year follow-up of physical activity, body composition, respiratory function and diaphragm function.

Results: Intervention groups 1 and 2 showed statistically improvements in the difference value compared with control group in terms of 6-min walk distance (-95.28 ± 20.09 and -101.92 ± 34.91 vs -63.58 ± 23.38), forced expiratory volume in 1 s (-0.042 ± 0.027 and -0.130 ± 0.050 vs -0.005 ± 0.068), fat-free mass (-2.11 ± 3.74 and -3.82 ± 3.74 vs 0.28 ± 1.49) and chronic obstructive pulmonary disease assessment test value (2.16 ± 0.85 and 2.38 ± 1.02 vs 1.50 ± 0.93). Intervention group 2 showed significant difference in arterial oxygen pressure (-4.46 ± 3.22 vs -1.92 ± 3.45), diaphragm excursion during deep breaths (-0.82 ± 0.74 vs -0.38 ± 0.29), and diaphragm thickness fraction (-8.77 ± 3.22 vs -4.88 ± 2.69) compared with control group.

Conclusion: The combination of aerobic training, resistance training, and external diaphragm pacing obtained significant improvements in physical activity, respiratory function, body composition, arterial oxygen pressure, and diaphragm function in patients with chronic obstructive pulmonary disease.

Trial registration: ChiCTR1800020257, www.chictr.org.cn/index.aspx.

Keywords: aerobic training; chronic obstructive pulmonary disease; external diaphragm pacing; resistance training.

SUPPLEMENTARY INFO

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. 2023 Oct 31:2023.01.30.526265.

doi: 10.1101/2023.01.30.526265. Preprint

Human pluripotent stem cell-derived respiratory airway progenitors generate alveolar epithelial cells and recapitulate features of idiopathic pulmonary fibrosis

[Mikael G Pezet](#), [Juan A Torres](#), [Tania A Thimraj](#), [Ivana Matkovic Leko](#), [Nadine Schrode](#), [John W Murray](#), [Kristin Beaumont](#), [Hans-Willem Snoeck](#)

- PMID: 36778291
- PMCID: [PMC9915513](#)
- DOI: [10.1101/2023.01.30.526265](#)

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Abstract

Human lungs contain unique cell populations in distal respiratory airways (RAs). These populations accumulate in patients with lung injury, chronic obstructive pulmonary disease (COPD) and idiopathic pulmonary fibrosis (IPF). Their lineage potentials and roles are unknown, however. As they are absent in rodents, deeper understanding of these cells requires a human in vitro model. Here we report the generation from human pluripotent stem cells (hPSCs) of expandable spheres (induced respiratory airway progenitors (iRAPs)) consisting of all RA-associated cell types. iRAPs could differentiate into type 1 (AT1) and type 2 alveolar (AT2) epithelial cells in defined conditions, showing that alveolar cells can

be derived from RAs. iRAPs with deletion of HPS1, which causes pulmonary fibrosis in humans, display defects that are hallmarks of IPF, indicating involvement of intrinsic dysfunction of RA-associated cells in IPF. iRAPs thus provide a model to gain insight into human lung regeneration and into pathogenesis of IPF.

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Semin Thromb Hemost

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. 2023 Nov;49(8):809-815.

doi: 10.1055/s-0042-1756190. Epub 2022 Sep 15.

[Pulmonary Embolism and Chronic Obstructive Pulmonary Disease](#)

[Laurent Bertoletti](#)^{1,2,3,4}, [Francis Couturaud](#)^{4,5,6}, [Olivier Sanchez](#)^{4,7,8}, [David Jimenez](#)^{9,10,11}

Affiliations [expand](#)

- PMID: 36108648
- DOI: [10.1055/s-0042-1756190](https://doi.org/10.1055/s-0042-1756190)

Abstract

Chronic obstructive pulmonary disease (COPD) is a frequent and devastating chronic respiratory disease. COPD is ranked among the top five causes of death worldwide. Patients with COPD suffer from persistent dyspnea, with periods of acute worsening, called exacerbations. Such exacerbations may be severe. In fact, one-third of COPD patients will be hospitalized because of an exacerbation. Hospitalization due to respiratory failure has been identified as a powerful predisposing risk factor for venous thromboembolism (VTE) for many years. Therefore, COPD is recognized as a moderate risk factor for VTE, with an odds ratio between 2 and 9, similar to other risk factors such as estrogen-containing contraceptives or (any) cancer. However, unlike other risk factors such as contraception, the presence of COPD can modify the initial presentation of VTE and worsen the short-term prognosis of patients who have acute pulmonary embolism (PE), particularly during a COPD exacerbation. It is not only that both stable COPD and acute exacerbations of COPD might increase the risk of VTE, but PE itself may mimic the symptoms of a COPD exacerbation. Hence, some authors have evaluated the prevalence of PE among COPD patients with acute worsening. This clinical review (1) gives an update on epidemiological data, clinical presentation, and prognosis of PE associated with COPD; (2) presents the results of the Prevalence de l'Embolie Pulmonaire chez les patients admis pour exacerbation de BPCO study, which aimed at determining the frequency of PE in COPD patients hospitalized for an acute exacerbation; (3) discusses the results of the Significance of Pulmonary Embolism in COPD Exacerbations study, the first randomized trial having compared the efficacy of a systematic search for PE versus routine care on admission for a COPD exacerbation; and (4) provides a selection of remaining unmet needs on the association between COPD and PE.

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Conflict of interest statement

L.B. reports grants from Bayer, grants and personal fees from MSD, personal fees and nonfinancial support from BMS/Pfizer, and personal fees and nonfinancial support from Léo-Pharma, outside the submitted work. F.C. reports grants, personal fees and nonfinancial support from Bayer, personal fees from MSD, grants, personal fees and nonfinancial support from BMS/Pfizer, nonfinancial support from Léo-Pharma, personal fees from Astra-Zeneca, and nonfinancial support from Janssen, outside the submitted work; D.J. reports personal fees from Bayer, personal fees and nonfinancial support from BMS/Pfizer, personal fees from Léo-Pharma, grants and personal fees from SANOFI, personal fees from Boehringer-Ingelheim, grants and personal fees from Daiichi Sankyo, and grants and personal fees from ROVI, outside the submitted work; O.S. reports personal fees and nonfinancial support from Bayer, grants and personal fees from MSD, grants, personal fees, and nonfinancial support from BMS/Pfizer, personal fees from Léo-Pharma, personal fees from SANOFI, and personal fees from Boehringer-Ingelheim, outside the submitted work.

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MeSH termsexpand

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

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J Geriatr Oncol

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. 2023 Nov 2:101654.

doi: 10.1016/j.jgo.2023.101654. Online ahead of print.

A care pathway for older patients with multimorbidity including cancer – Design of the GERONTE pathway

[P A L Nelleke Seghers](#)¹, [Siri Rostoft](#)², [Shane O'Hanlon](#)³, [Lien Degol](#)⁴, [Cindy Kenis](#)⁵, [Hans Wildiers](#)⁶, [Pierre Soubeyran](#)⁷, [Marije E Hamaker](#)⁸

Affiliations expand

- PMID: 37925337
- DOI: [10.1016/j.jgo.2023.101654](https://doi.org/10.1016/j.jgo.2023.101654)

No abstract available

Keywords: Care coordination; Geriatric oncology; Multimorbidity; Patient- centred care pathway; Quality of life.

Conflict of interest statement

Declaration of Competing Interest Pierre Soubeyran: Board member with TEVA, Sandoz, BMS and Eisai. All other authors: No competing interests to declare.

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Lancet Healthy Longev



. 2023 Nov;4(11):e618-e628.

doi: [10.1016/S2666-7568\(23\)00195-2](https://doi.org/10.1016/S2666-7568(23)00195-2).

[Socioeconomic inequalities in physical, psychological, and cognitive multimorbidity in middle-aged and older adults in 33 countries: a cross-sectional study](#)

[Yujie Ni](#)¹, [Yaguan Zhou](#)¹, [Mika Kivimäki](#)², [Ying Cai](#)³, [Rodrigo M Carrillo-Larco](#)⁴, [Xin Xu](#)¹, [Xiaochen Dai](#)⁵, [Xiaolin Xu](#)⁶

Affiliations expand

- PMID: 37924843
- DOI: [10.1016/S2666-7568\(23\)00195-2](https://doi.org/10.1016/S2666-7568(23)00195-2)

Abstract

Background: Many physical, psychological, and cognitive disorders are highly clustered among populations with low socioeconomic status. However, the extent to which socioeconomic status is associated with different combinations of these disorders is unclear, particularly outside high-income countries. We aimed to evaluate these associations in 33 countries including high-income countries, upper-middle-income countries, and one lower-middle-income country.

Methods: This cross-sectional multi-region study pooled individual-level data from seven studies on ageing between 2017 and 2020. Education and total household wealth were used to measure socioeconomic status. Physical disorder was defined as having one or more of the self-reported chronic conditions. Psychological and cognitive disorders were measured by study-specific instruments. The outcome included eight categories: no disorders, physical disorder, psychological disorder, cognitive disorder, and their four combinations. Multivariable-adjusted logistic regression models were used to estimate odds ratios (ORs) and 95% CIs for the associations of socioeconomic status with these outcomes separately for high-income countries, upper-middle-income countries, and the lower-middle-income country.

Findings: Among 167 376 individuals aged 45 years and older, the prevalence of multimorbidity was 24.5% in high-income countries, 33.9% in upper-middle-income countries, and 8.1% in the lower-middle-income country (India). Lower levels of education, household wealth, and a combined socioeconomic status score were strongly associated with physical, psychological, and cognitive multimorbidity in high-income countries and upper-middle-income countries, with ORs (low vs high socioeconomic status) for physical-psychological-cognitive multimorbidity of 12.36 (95% CI 10.29-14.85; $p < 0.0001$) in high-income countries and of 23.84 (18.85-30.14; $p < 0.0001$) in upper-middle-income countries. The associations in the lower-middle-income country were mixed. Participants with both a low level of education and low household wealth had the highest odds of multimorbidity (eg, OR for physical-psychological-cognitive multimorbidity 21.21 [15.95-28.19; $p < 0.0001$] in high-income countries, 37.07 [25.66-53.56; $p < 0.0001$] in upper-middle-income countries, and 54.96 [7.66-394.38; $p < 0.0001$] in the lower-middle-income country).

Interpretation: In study populations from high-income countries, upper-middle-income countries, and the lower-middle-income country, the odds of multimorbidity, which included physical, psychological, and cognitive disorders, were more than ten times greater in individuals with low socioeconomic status. Equity-oriented policies and programmes that reduce social inequalities in multimorbidity are urgently needed to achieve Sustainable Development Goals.

Funding: Zhejiang University, Fundamental Research Funds for the Central Universities, The Key Laboratory of Intelligent Preventive Medicine of Zhejiang Province, Wellcome Trust, Medical Research Council, National Institute on Aging, and Academy of Finland.

Translation: For the Chinese translation of the abstract see Supplementary Materials section.

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Conflict of interest statement

Declaration of interests XiaoX was supported by Zhejiang University, Fundamental Research Funds for the Central Universities, and The Key Laboratory of Intelligent Preventive Medicine of Zhejiang Province. MK was supported by the Wellcome Trust (grant number 221854/Z/20/Z), the Medical Research Council (grant numbers R024227 and S011676), the National Institute on Aging (grant numbers R01AG056477 and R01AG062553), and Academy of Finland (grant number 350426). All other authors declare no competing interests.

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Int J Behav Nutr Phys Act

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. 2023 Nov 3;20(1):130.

doi: 10.1186/s12966-023-01531-0.

Different types of screen time, physical activity, and incident dementia, Parkinson's disease, depression and multimorbidity status

[Hanzhang Wu](#)^{1,2,3}, [Yeqing Gu](#)⁴, [Wenxiu Du](#)^{1,2}, [Ge Meng](#)^{1,5}, [Hongmei Wu](#)^{1,2}, [Shunming Zhang](#)^{1,2}, [Xuena Wang](#)^{1,2}, [Juanjuan Zhang](#)^{1,2}, [Yaogang Wang](#)^{6,7}, [Tao Huang](#)⁸, [Kaijun Niu](#)^{9,10,11,12,13,14}

Affiliations expand

- PMID: 37924067

- DOI: [10.1186/s12966-023-01531-0](https://doi.org/10.1186/s12966-023-01531-0)

Abstract

Background: Several previous studies have shown that excessive screen time is associated with an increased prevalence of dementia, Parkinson's disease (PD), and depression. However, the results have been inconsistent. This study aimed to prospectively investigate the association between different types of screen time and brain structure, as well as the incidence of dementia, Parkinson's disease, depression, and their multimorbidity status.

Methods: We included 473,184 participants initially free of dementia, PD, and depression from UK Biobank, as well as 39,652 participants who had magnetic resonance imaging (MRI) data. Screen time exposure variables including TV viewing and computer using were self-reported by participants. Cox proportional hazards regression models were used to estimate the association between different types of screen time and the incidence of dementia, Parkinson's disease, depression, and their multimorbidity status. Multiple linear regression models were used to assess the linear relationship between different types of screen time and MRI biomarkers in a subgroup of participants.

Results: During the follow up, 6,096, 3,061, and 23,700 participants first incident cases of dementia, PD, and depression respectively. For moderate versus the lowest computer uses, the adjusted HRs (95% CIs) were 0.68 (0.64, 0.72) for dementia, 0.86 (0.79, 0.93) for PD, 0.85 (0.83, 0.88) for depression, 0.64 (0.55, 0.74) for dementia and depression multimorbidity, and 0.59 (0.47, 0.74) for PD and depression multimorbidity. The multivariable HRs (95% CIs) for the highest versus the lowest group of TV viewing time were 1.28 (1.17, 1.39) for dementia, 1.16 (1.03, 1.29) for PD, 1.35 (1.29, 1.40) for depression, 1.49 (1.21, 1.84) for dementia and depression multimorbidity, and 1.44 (1.05, 1.97) for PD and depression multimorbidity. Moderate computer using time was negatively associated with white matter hyperintensity volume ($\beta = -0.042$; 95% CI -0.067, -0.017), and positively associated with hippocampal volume ($\beta = 0.059$; 95% CI 0.034, 0.084). Participants with the highest TV viewing time were negatively associated with hippocampal volume ($\beta = -0.067$; 95% CI -0.094, -0.041). In isotemporal substitution analyses, substitution of TV viewing or computer using by equal time of different types of PA was associated with a lower risk of all three diseases, with strenuous sports showing the strongest benefit.

Conclusion: We found that moderate computer use was associated with a reduced risk of dementia, PD, depression and their multimorbidity status, while increased TV watching was associated with a higher risk of these disease. Notably, different screen time may affect the risk of developing diseases by influencing brain structures. Replacing different types of screen time with daily-life PA or structured exercise is associated with lower dementia, PD, and depression risk.

Keywords: Dementia; Depression; Magnetic resonance imaging; Parkinson's disease; Screen time.

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PLoS Med

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. 2023 Nov 3;20(11):e1004310.

doi: 10.1371/journal.pmed.1004310. Online ahead of print.

[Sociodemographic characteristics and longitudinal progression of multimorbidity: A multistate modelling analysis of a large primary care records dataset in England](#)

[Sida Chen](#)¹, [Tom Marshall](#)², [Christopher Jackson](#)¹, [Jennifer Cooper](#)², [Francesca Crowe](#)², [Krish Nirantharakumar](#)², [Catherine L Saunders](#)³, [Paul Kirk](#)¹, [Sylvia Richardson](#)¹, [Duncan Edwards](#)³, [Simon Griffin](#)³, [Christopher Yau](#)^{4,5}, [Jessica K Barrett](#)¹

Affiliations [expand](#)

- PMID: 37922316

- DOI: [10.1371/journal.pmed.1004310](https://doi.org/10.1371/journal.pmed.1004310)

Abstract

Background: Multimorbidity, characterised by the coexistence of multiple chronic conditions in an individual, is a rising public health concern. While much of the existing research has focused on cross-sectional patterns of multimorbidity, there remains a need to better understand the longitudinal accumulation of diseases. This includes examining the associations between important sociodemographic characteristics and the rate of progression of chronic conditions.

Methods and findings: We utilised electronic primary care records from 13.48 million participants in England, drawn from the Clinical Practice Research Datalink (CPRD Aurum), spanning from 2005 to 2020 with a median follow-up of 4.71 years (IQR: 1.78, 11.28). The study focused on 5 important chronic conditions: cardiovascular disease (CVD), type 2 diabetes (T2D), chronic kidney disease (CKD), heart failure (HF), and mental health (MH) conditions. Key sociodemographic characteristics considered include ethnicity, social and material deprivation, gender, and age. We employed a flexible spline-based parametric multistate model to investigate the associations between these sociodemographic characteristics and the rate of different disease transitions throughout multimorbidity development. Our findings reveal distinct association patterns across different disease transition types. Deprivation, gender, and age generally demonstrated stronger associations with disease diagnosis compared to ethnic group differences. Notably, the impact of these factors tended to attenuate with an increase in the number of preexisting conditions, especially for deprivation, gender, and age. For example, the hazard ratio (HR) (95% CI; p-value) for the association of deprivation with T2D diagnosis (comparing the most deprived quintile to the least deprived) is 1.76 ([1.74, 1.78]; $p < 0.001$) for those with no preexisting conditions and decreases to 0.95 ([0.75, 1.21]; $p = 0.69$) with 4 preexisting conditions. Furthermore, the impact of deprivation, gender, and age was typically more pronounced when transitioning from an MH condition. For instance, the HR (95% CI; p-value) for the association of deprivation with T2D diagnosis when transitioning from MH is 2.03 ([1.95, 2.12], $p < 0.001$), compared to transitions from CVD 1.50 ([1.43, 1.58], $p < 0.001$), CKD 1.37 ([1.30, 1.44], $p < 0.001$), and HF 1.55 ([1.34, 1.79], $p < 0.001$). A primary limitation of our study is that potential diagnostic inaccuracies in primary care records, such as underdiagnosis, overdiagnosis, or ascertainment bias of chronic conditions, could influence our results.

Conclusions: Our results indicate that early phases of multimorbidity development could warrant increased attention. The potential importance of earlier detection and intervention of chronic conditions is underscored, particularly for MH conditions and higher-risk

populations. These insights may have important implications for the management of multimorbidity.

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Conflict of interest statement

I have read the journal's policy and the authors of this manuscript have the following competing interests: JB has previously received funding for unrelated work from F. Hoffmann-La Roche Ltd. KN reports grants from NIHR, MRC, Diabetes UK, Vifor, and AstraZeneca, and personal fees from Merck Sharp & Dohme, Sanofi, and Boehringer Ingelheim, outside of and unrelated to the submitted work. TM has previously received funding for unrelated work: from Cancer Research UK and from the Health Research Board (Ireland) for advisory board participation and travel. SJG received payment from Novo Nordisk, Napp and Astra Zeneca for lectures at 6 educational events over the last 3 years. Napp supported SJG's attendance at EASD 2018 and he received payment from Eli Lilly associated with membership of an independent data monitoring committee for a randomised trial of a medication to lower glucose. PK, SR and KN are co-investigators on the HDRUK grant titled Measuring & Understanding Multimorbidity using Routine Data in the UK (MUrMuR-UK). CY has received remuneration for unrelated consultancy services to F. Hoffmann-La Roche and Singula Bio. The other authors have declared that no competing interests exist.

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J Multidiscip Healthc

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. 2023 Oct 26:16:3167-3177.

doi: 10.2147/JMDH.S412283. eCollection 2023.

[A Qualitative Study on Distributed Leadership in Integrated Care: Exploring the Experiences of Elderly Multimorbid Patients with GP Collaboration](#)

[Harald Braut](#)¹, [Marianne Storm](#)², [Aslaug Mikkelsen](#)¹

Affiliations [expand](#)

- PMID: 37915976
- PMID: [PMC10615873](#)
- DOI: [10.2147/JMDH.S412283](#)

Free PMC article

Abstract

Objective: This study explores how the collaboration between elderly multimorbid patients and general practitioners contributes to the patient's experience of integrated care in the municipality. The research also investigates whether the municipality's integrative mechanisms creating integrated care can be understood as distributed leadership.

Method: In this qualitative study, we conducted a thematic analysis of semi-structured interviews with twenty elderly multimorbid patients living at home and their general practitioners.

Results: Analysis of patients' and general practitioners' experience of healthcare service characterized by collective efforts identified four themes: 1) an impression of collective processes as difficult for patients to access and influence; 2) that the fluidity and location of leadership is dependent on the individual patient and his or her health condition; 3) that collective implementation of healthcare services is separated in time, geography and between organizations; and 4) that patients experience individual healthcare workers as specialized and unable to support the medical and holistic goals of the collective. The Direction, Alignment, and Commitment or DAC framework, is used to investigate the capabilities of the collective.

Conclusion: To promote distributed leadership and create a patient experience of integrated care in the municipality, healthcare organizations must develop collective processes that enhance patient participation to a greater extent. General practitioners and other healthcare personnel should be encouraged to play a more central role in solving elderly multimorbid patients' healthcare needs in the municipality.

Keywords: distributed leadership; family practice; integrated care; multidisciplinary healthcare; multimorbidity; qualitative research.

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Conflict of interest statement

Dr Harald Braut has experience working as a GP. The authors report no other conflicts of interest in this work.

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Geriatr Gerontol Int

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. 2023 Nov 2.

doi: 10.1111/ggi.14720. Online ahead of print.

Association of possible sarcopenia with major chronic diseases and multimorbidity among middle-aged and older adults: Findings from a national cross-sectional study in China

[Xiaoguang Zhao](#)^{1,2}, [Hongjun Zhang](#)³, [Jiabin Yu](#)^{1,2}, [Jin Wang](#)¹

Affiliations expand

- PMID: 37915295
- DOI: [10.1111/ggi.14720](https://doi.org/10.1111/ggi.14720)

Abstract

Aim: This study investigated the prevalence of possible sarcopenia (PSA) in a large sample of middle-aged and older adults, and determined the association between PSA, major chronic diseases and the number of chronic diseases.

Methods: A total of 14 917 adults aged ≥ 40 years were included in the analysis. The handgrip strength and the five-time chair stand test were used to assess PSA. The participants' major chronic diseases were divided into 14 categories. Four categories were created based on the participants' number of chronic illnesses: 0, 1, 2 and ≥ 3 .

Results: The present study found an overall prevalence of PSA of 23.6% among Chinese middle-aged and older adults aged ≥ 40 years, with the risk increasing with advancing age. PSA was significantly associated with most categories of chronic diseases and multimorbidity. The closely independent associations were obtained for stroke; emotional, nervous or psychiatric problems; chronic lung disease, asthma, heart disease, hypertension and arthritis or rheumatism. Compared with participants with 0 chronic disease, those with two or more chronic diseases had higher odds for PSA. However, the association between PSA and the number of chronic diseases varied in different sex and age groups.

Conclusions: The findings suggest that PSA is associated with major chronic diseases among middle-aged and older adults. People with two or more chronic diseases have a greater likelihood of PSA compared with those without chronic diseases, and the association between PSA and the number of chronic diseases largely depended on sex and age. *Geriatr Gerontol Int* 2023; ••: ••-••.

Keywords: China; chronic diseases; middle-aged and older adults; multimorbidity; sarcopenia.

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- [40 references](#)

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. 2023 Nov 1;13(1):18798.

doi: 10.1038/s41598-023-46227-4.

[Incidence, prevalence and characteristics of multimorbidity in different age groups among urban hospitalized patients in China](#)

[Dixiang Song](#)^{#1}, [Deshan Liu](#)^{#1}, [Weihai Ning](#)¹, [Yujia Chen](#)¹, [Jingjing Yang](#)¹, [Chao Zhao](#)¹, [Hongwei Zhang](#)²

Affiliations [expand](#)

- PMID: 37914899

- PMID: [PMC10620234](#)
- DOI: [10.1038/s41598-023-46227-4](#)

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Abstract

The aim of the study was to investigate the incidence, prevalence and characteristics of multimorbidity in urban inpatients of different age groups. This study used data from the National Insurance Claim for Epidemiology Research (NICER) to calculate the overall incidence, prevalence, geographic and age distribution patterns, health care burden, and multimorbidity patterns for multimorbidity in 2017. According to our study, the overall prevalence of multimorbidity was 6.68%, and the overall prevalence was 14.87% in 2017. The prevalence of multimorbidity increases with age. The pattern of the geographic distribution of multimorbidity shows that the prevalence of multimorbidity is relatively high in South East China. The average annual health care expenditure of patients with multimorbidity increased with age and rose rapidly, especially among older patients. Patients with cancer and chronic kidney disease have higher treatment costs. Patients with hypertension or ischemic heart disease had a significantly higher relative risk of multimorbidity than other included noncommunicable diseases (NCDs). Hyperlipidemia has generated the highest number of association rules, which may suggest that hyperlipidemia may be both a risk factor for other NCDs and an outcome of them.

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Conflict of interest statement

The authors declare no competing interests.

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- [5 figures](#)

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Pediatr Cardiol



. 2023 Nov 1.

doi: 10.1007/s00246-023-03312-9. Online ahead of print.

[The Impact of Morbidities Following Pediatric Cardiac Surgery on Family Functioning and Parent Quality of Life](#)

[Jo Wray](#)¹, [Deborah Ridout](#)², [Alison Jones](#)³, [Peter Davis](#)⁴, [Paul Wellman](#)⁵, [Warren Rodrigues](#)⁶, [Emma Hudson](#)⁷, [Victor Tsang](#)⁶, [Christina Pagel](#)⁸, [Katherine L Brown](#)⁶

Affiliations expand

- PMID: 37914854
- DOI: [10.1007/s00246-023-03312-9](https://doi.org/10.1007/s00246-023-03312-9)

Abstract

We previously selected and defined nine important post-operative morbidities linked to paediatric cardiac surgery, and prospectively measured their incidence following 3090 consecutive operations. Our aim was to study the impact of these morbidities on family functioning and parental quality of life over 6 months in a subset of cases. As part of a prospective case matched study in five of the ten children's cardiac centers in the UK, we compared outcomes for parents of children who had a 'single morbidity', 'multiple morbidities', 'extracorporeal life support (ECLS)' or 'no morbidity'. Outcomes were evaluated using the PedsQL Family impact module (FIM) at 6 weeks and 6 months post-surgery. Outcomes were modelled using mixed effects regression, with adjustment for case mix and clustering within centers. We recruited 340 patients with morbidity (60% of eligible

patients) and 326 with no morbidity over 21 months. In comparison to the reference group of 'no morbidity', after adjustment for case mix, at 6 weeks parent health-related quality of life (HRQoL) and total FIM scores were lower (worse) only for ECLS ($p < 0.005$), although a higher proportion of parents in both the ECLS and multi-morbidity groups had low/very low scores ($p < .05$). At 6 months, parent outcomes had improved for all groups but parent HRQoL and total score for ECLS remained lower than the 'no morbidity' group ($p < .05$) and a higher proportion of families had low or very low scores in the ECLS (70%) group ($p < .01$). Post-operative morbidities impact parent HRQoL and aspects of family functioning early after surgery, with this impact lessening by 6 months. Families of children who experience post-operative morbidities should be offered timely psychological support.

Keywords: Family functioning; Health-related quality of life; Impact; Post-operative morbidities.

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[Review](#)

Neurosci Biobehav Rev

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. 2023 Oct 31:155:105436.

doi: 10.1016/j.neubiorev.2023.105436. Online ahead of print.

Prevalence of co-occurring conditions in children and adults with autism spectrum disorder: A systematic review and meta-analysis

[Martina Micai](#)¹, [Laura Maria Fatta](#)¹, [Letizia Gila](#)¹, [Angela Caruso](#)¹, [Tommaso Salvitti](#)¹, [Francesca Fulceri](#)¹, [Antonio Ciaramella](#)¹, [Roberto D'Amico](#)², [Cinzia Del Giovane](#)³, [Marco Bertelli](#)⁴, [Giovanna Romano](#)⁵, [Holger Jens Schünemann](#)⁶, [Maria Luisa Scattoni](#)⁷

Affiliations expand

- PMID: 37913872
- DOI: [10.1016/j.neubiorev.2023.105436](https://doi.org/10.1016/j.neubiorev.2023.105436)

Abstract

This systematic review estimates the prevalence of co-occurring conditions (CCs) in children and adults with autism. A comprehensive search strategy consulting existing guidelines, diagnostic manuals, experts, carers, and autistic people was developed. PubMed and PsycInfo databases from inception to May 2022 were searched. PROSPERO registration: CRD42019132347. Two blind authors screened and extracted the data. Prevalence estimates for different CCs were summarized by using random effects models. Subgroup analyses were performed for age groups (children/adolescents vs adults) and study designs (population/registry-based vs clinical sample-based). Of 19,932 studies, 340 publications with about 590,000 participants were included and meta-analyzed to estimate the prevalence of 38-point prevalence, 27-lifetime, and 3 without distinction between point and lifetime prevalence. Point prevalence of developmental coordination disorder, sleep-wake problem, gastrointestinal problem, ADHD, anxiety disorder, overweight/obesity, feeding and eating disorder, elimination disorder, disruptive behavior, and somatic symptoms and related disorder were the most frequent CCs. Prevalence differed depending on the age group and study design. Knowing specific CCs linked to autism helps professional investigations and interventions for improved outcomes.

Keywords: Autism spectrum disorder; Co-occurring Condition; Comorbidity; Dual diagnosis; Frequency; Incidence; Meta-analysis; Multimorbidity; Prevalence; Systematic review.

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Conflict of interest statement

Declaration of Competing Interest None.

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Epidemiol Serv Saude



. 2023 Oct 30;32(3):e2023045.

doi: 10.1590/S2237-96222023000300007.en. eCollection 2023.

[Multimorbidity and the use of health services in the Brazilian population: National Health Survey 2019](#)

[Article in English, Portuguese]

[Ana Sara Semeão de Souza](#)¹

Affiliations [expand](#)

- PMID: 37909521
- PMCID: [PMC10615183](#)

- DOI: [10.1590/S2237-96222023000300007.en](https://doi.org/10.1590/S2237-96222023000300007.en)

Free PMC article

Abstract

in [English](#), [Spanish](#), [Portuguese](#)

Objective: To describe the prevalence of health service use due to multimorbidity according to sociodemographic and health characteristics of the Brazilian population; to analyze the relationship between multimorbidity and the use of health services.

Methods: This was a cross-sectional study using data from the 2019 National Health Survey. The outcomes were seeking health services in the last 15 days, medical consultation and hospitalization in the previous 12 months. Multimorbidity was defined as ≥ 2 chronic diseases. Associations were assessed using Poisson regression.

Results: Of the 81,768 individuals, prevalence of seeking health services among individuals with multimorbidity was 38.0% higher (95%CI 1.31;1.45), medical appointments, 11.0% higher (95%CI 1.10;1.12), and 56.0% higher for hospitalizations (95%CI 1.44;1.70), compared to those without multimorbidity. This relationship was higher for seeking health services and medical appointments among male.

Conclusion: The use of health services was higher among those with multimorbidity, but different between the types of health services used and sexes.

Main results: Having multimorbidity increased the use of health services, even after progressive adjustment by sociodemographic characteristics and health needs. This relationship was greater among males for medical consultations.

Implications for services: Greater use of health services by individuals with multiple non-communicable diseases (NCDs) points to the need for changes in care models, with focus on continuity of care.

Perspectives: Health services should focus on continuous, coordinated and comprehensive approaches to the care of people with multimorbidity, thus seeking to increase the efficiency and quality of care provided to this population.

Conflict of interest statement

CONFLICTS OF INTEREST

The author do not have any conflicts of interest to declare.

- [29 references](#)

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Int J Geriatr Psychiatry

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. 2023 Nov;38(11):e6021.

doi: 10.1002/gps.6021.

[Association of multimorbidity patterns with motoric cognitive risk syndrome among older adults: Evidence from a China longitudinal study](#)

[Feiyang Xiong](#)^{1,2}, [Yizhong Wang](#)³, [Jun Zhu](#)⁴, [Shixue Li](#)^{1,2}, [Qiangdong Guan](#)⁴, [Zhengyue Jing](#)^{4,5}

Affiliations expand

- PMID: 37909119

- DOI: [10.1002/gps.6021](https://doi.org/10.1002/gps.6021)

Abstract

Objectives: Motoric cognitive risk syndrome (MCR), a pre-dementia syndrome, is characterized by slow gait and subjective cognitive complaints among older adults. This study assessed the relationship between multimorbidity, its patterns, and MCR.

Methods: Data for this study were obtained from three waves (2011, 2013, and 2015) of the China Health and Retirement Longitudinal Study. Participants who were aged 60 years and older and had complete data at baseline as well as complete data about MCR at follow-up were selected. Patients without MCR at baseline were selected for further analyses. Longitudinal associations between multimorbidity, its patterns, and MCR were examined using a Cox proportional hazards model. Multimorbidity patterns were classified using latent class analysis.

Results: A total of 4923 respondents were included at baseline, 43.47% of whom had multimorbidity. Additionally, the prevalence of MCR at baseline was 12.61%. After adjusting for covariates, multimorbidity was positively associated with MCR (hazard ratio [HR] = 1.33, 95% confidence interval [CI] = 1.06-1.68). A higher number of multimorbidity was also significantly associated with an increased risk of developing MCR (HR = 1.10, 95% CI = 1.02-1.19). Three multimorbidity patterns were selected: relatively healthy pattern, respiratory pattern, and cardiovascular pattern. Older adults with the cardiovascular pattern were 1.57 times more likely to develop MCR than those with the relatively healthy pattern (HR = 1.57, 95% CI = 1.16-2.13). There was no significant difference between the relatively healthy pattern and the respiratory pattern (HR = 1.31, 95% CI = 0.91-1.92).

Conclusions: MCR is highly prevalent among older Chinese adults. MCR may be exacerbated by multimorbidity. For older adults with multimorbidity (especially cardiovascular multimorbidity), attention should be paid to MCR to achieve early detection, diagnosis, and treatment.

Keywords: cardiovascular multimorbidity; cognitive complaints; motoric cognitive risk syndrome; multimorbidity.

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- [48 references](#)

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MeSH terms, Grants and funding expand

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Pharmacogenomics J



. 2023 Nov 1.

doi: 10.1038/s41397-023-00317-8. Online ahead of print.

British South Asian ancestry participants views of pharmacogenomics clinical implementation and research: a thematic analysis

[Emma F Magavern](#)¹, [Faiza Durrani](#)², [Mehru Raza](#)², [Robin Lerner](#)², [Mohammed Riadul Islam](#)³, [Genes & Health Research Team](#); [Megan Clinch](#)^{#4}, [Mark J Caulfield](#)^{#5}

Affiliations expand

- PMID: 37907686
- DOI: [10.1038/s41397-023-00317-8](https://doi.org/10.1038/s41397-023-00317-8)

Abstract

Background: South Asian ancestry populations are underrepresented in genomic studies and therapeutics trials. British South Asians suffer from multi-morbidity leading to polypharmacy. Our objective was to elucidate British South Asian ancestry community perspectives on pharmacogenomic implementation and sharing pharmacogenomic clinical data for research.

Methods: Four focus groups were conducted (9-12 participants in each). Two groups were mixed gender, while one group was male only and one was female only. Simultaneous interpretation was available to participants in Urdu and Bengali. Focus groups were recorded and abridged transcription and thematic analysis were undertaken.

Results: There were 42 participants, 64% female. 26% were born in the UK or Europe. 52% were born in Bangladesh and 17% in Pakistan. 36% reported university level education. Implementation of pharmacogenomics was perceived to be beneficial to individuals but pose a risk of overburdening resource limited systems. Pharmacogenomic research was perceived to be beneficial to the community, with concerns about data privacy and misuse. Data sharing was desirable if the researchers did not have a financial stake, and benefits would be shared. Trust was the key condition for the acceptability of both clinical implementation and research. Trust was linked with medication compliance. Education, outreach, and communication facilitate trust.

Conclusions (significance and impact of the study): Pharmacogenomics implementation with appropriate education and communication has the potential to enhance trust and contribute to increased medication compliance. Trust drives data sharing, which would enable enhanced representation in research. Representation in scientific evidence base could cyclically enhance trust and compliance.

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. 2023 Oct 31;13(1):18764.

doi: 10.1038/s41598-023-44813-0.

[Effect of multimorbidity on hypertension management](#)

[Eunjeong Ji](#)¹, [Soyeon Ahn](#)¹, [Jung-Yeon Choi](#)², [Cheol-Ho Kim](#)², [Kwang-Il Kim](#)^{3,4}

Affiliations expand

- PMID: 37907571
- PMCID: [PMC10618203](#)
- DOI: [10.1038/s41598-023-44813-0](#)

Free PMC article

Abstract

Multimorbidity, the coexistence of multiple health conditions, is associated with functional decline, disability, and mortality. We aimed to investigate the effects of multimorbidity on hypertension treatment and control rates by analyzing data from the Korean National Health and Nutrition Examination Survey database, which is a cross-sectional, nationally representative survey conducted by the Korean government. Multimorbidity, defined as having two or more chronic diseases, was evaluated by blood pressure measurements, blood chemistry examinations, and questionnaires. We classified the participants according to the number of multimorbidities from 0 to ≥ 6 . Association analysis was performed to identify the patterns of multimorbidity related to hypertension control. From 2016 to 2020, 30,271 adults (≥ 20 years) were included in the analysis (age: 52.1 ± 16.8 years, male: 44.0%), and 14,278 (47.2%) had multimorbidity. The number of chronic conditions was significantly higher in older adults, women, and hypertensive patients. Multimorbidity was associated with hypertension treatment. The number of chronic conditions was significantly higher in controlled compared to uncontrolled patients (3.6 ± 1.7 vs 2.9 ± 1.6 , $p < 0.001$). But the control rate of hypertension among treated patients was lower in patients with multimorbidity (75.6% in hypertension only group vs 71.8% in multimorbidity group, $p = 0.009$). Multimorbidity patterns showed distinct features in treated and controlled hypertensive patients. In conclusion, multimorbidity has a beneficial effect on the treatment of hypertension, but the control rate of systolic blood pressure was lower among the patients with multimorbidity. More attention should be paid to the hypertensive patients with multimorbidity to improve the control rate of hypertension.

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Conflict of interest statement

The authors declare no competing interests.

- [20 references](#)

- [4 figures](#)

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BMJ Open

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. 2023 Oct 31;13(10):e077335.

doi: 10.1136/bmjopen-2023-077335.

[Impact, scope of practice and competencies of Advanced Practice Nurses within APN-led models of care for young and middle-aged adult patients with multimorbidity and/or complex chronic conditions in hospital settings: a scoping review protocol](#)

[Gabriele Bales](#)^{1,2}, [Wolfgang Hasemann](#)³, [Reto W Kressig](#)^{3,4}, [Hanna Mayer](#)⁵

Affiliations [expand](#)

- PMID: 37907288

- PMID: [PMC10619075](#)
- DOI: [10.1136/bmjopen-2023-077335](#)

Free PMC article

Abstract

Introduction: The increase of young and middle-aged adult patients with multimorbid and/or complex chronic conditions has created new challenges for healthcare systems and services. Advanced Practice Nurses (APNs) play an essential role in treating these patients because of their expertise and advanced nursing skills. Little is known about competencies, scope of practice and impact of APNs within APN-led care models for young and middle-aged adult patients with multimorbidity and/or complex chronic conditions in hospital settings. The objective of this scoping review is to describe the impact, scope of practice and competencies of APNs within APN-led care models for young and middle-aged adult patients in hospital settings.

Methods and analysis: This scoping review will be conducted using the methodological framework proffered by Arksey and O'Malley, incorporating the methodological enhancement of Levac *et al.* It will comply with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) for Scoping Reviews' guidelines of Tricco *et al.* Systematic research will be conducted in the databases MEDLINE (PubMed), CINAHL (EBSCO), EMBASE (Ovid), CENTRAL and PsycINFO (Ovid) using all recognised keywords, index terms and search strings. Grey literature will be scanned. Bibliography of all selected studies will be hand searched. Studies will be selected based on defined inclusion and exclusion criteria, screened by title and abstracts. Data from full-text articles meeting the inclusion criteria will be extracted independently by two authors. Disagreements in evaluation will be discussed and resolved by consensus. Results will be reported in the form of descriptive tables. Narrative summery is used to present the results of the review in the context of the study's objectives and questions.

Ethics and dissemination: This scoping review does not require ethics approval. The review will be handed in as part of a doctoral thesis and published in a peer-reviewed journal.

Trial registration number osf: 4PM38.

Keywords: hospitals; literature; nursing care.

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Conflict of interest statement

Competing interests: None declared.

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J R Soc Med

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. 2023 Oct 31:1410768231206033.

doi: 10.1177/01410768231206033. Online ahead of print.

[Prevalence of multiple long-term conditions \(multimorbidity\) in England: a whole population study of over 60 million people](#)

[Jonathan Valabhji](#)^{1,2,3}, [Emma Barron](#)¹, [Adrian Pratt](#)⁴, [Nasrin Hafezparast](#)⁵, [Rupert Dunbar-Rees](#)⁵, [Ellie Bragan Turner](#)⁵, [Kate Roberts](#)⁶, [Jacqueline Mathews](#)⁶, [Robbie Deegan](#)⁴, [Victoria Cornelius](#)¹, [Jason Pickles](#)¹, [Gary Wainman](#)¹, [Chirag Bakhai](#)^{1,7}, [Desmond G Johnston](#)^{2,3}, [Edward W Gregg](#)⁸, [Kamlesh Khunti](#)⁹

Affiliations expand

- PMID: 37905525
- DOI: [10.1177/01410768231206033](https://doi.org/10.1177/01410768231206033)

Abstract

Objectives: To determine the prevalence of multiple long-term conditions (MLTC) at whole English population level, stratifying by age, sex, socioeconomic status and ethnicity.

Design: A whole population study.

Setting: Individuals registered with a general practice in England and alive on 31 March 2020.

Participants: 60,004,883 individuals.

Main outcome measures: MLTC prevalence, defined as two or more of 35 conditions derived from a number of national patient-level datasets. Multivariable logistic regression was used to assess the independent associations of age, sex, ethnicity and deprivation decile with odds of MLTC.

Results: The overall prevalence of MLTC was 14.8% (8,878,231), varying from 0.9% (125,159) in those aged 0-19 years to 68.2% (1,905,979) in those aged 80 years and over. In multivariable regression analyses, compared with the 50-59 reference group, the odds ratio was 0.04 (95% confidence interval (CI): 0.04-0.04; $p < 0.001$) for those aged 0-19 years and 10.21 (10.18-10.24; $p < 0.001$) for those aged 80 years and over. Odds were higher for men compared with women, 1.02 (1.02-1.02; $p < 0.001$), for the most deprived decile compared with the least deprived, 2.26 (2.25-2.27; $p < 0.001$), and for Asian ethnicity compared with those of white ethnicity, 1.05 (1.04-1.05; $p < 0.001$). Odds were lower for black, mixed and other ethnicities (0.94 (0.94-0.95) $p < 0.001$, 0.87 (0.87-0.88) $p < 0.001$ and 0.57 (0.56-0.57) $p < 0.001$, respectively). MLTC for persons aged 0-19 years were dominated by asthma, autism and epilepsy, for persons aged 20-49 years by depression and asthma, for persons aged 50-59 years by hypertension and depression and for those aged 60 years and older, by cardiometabolic factors and osteoarthritis. There were large numbers of combinations of conditions in each age group ranging from 5936 in those aged 0-19 years to 205,534 in those aged 80 years and over.

Conclusions: While this study provides useful insight into the burden across the English population to assist health service delivery planning, the heterogeneity of MLTC presents challenges for delivery optimisation.

Keywords: Epidemiologic studies; epidemiology; health policy; health service research; medical management; quality improvement.

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BMC Geriatr

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. 2023 Oct 30;23(1):700.

doi: 10.1186/s12877-023-04371-6.

[Association between multimorbidity and informal long-term care use in China: a nationwide cohort study](#)

[Shu Chen](#)^{1,2}, [Yafei Si](#)^{3,4}, [Katja Hanewald](#)^{3,4}, [Bingqin Li](#)⁵, [Chenkai Wu](#)⁶, [Xiaolin Xu](#)^{7,8,9}, [Hazel Bateman](#)^{3,4}

Affiliations expand

- PMID: 37904087
- PMCID: [PMC10617137](#)
- DOI: [10.1186/s12877-023-04371-6](#)

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Abstract

Background: The impact of multimorbidity on long-term care (LTC) use is understudied, despite its well-documented negative effects on functional disabilities. The current study

aims to assess the association between multimorbidity and informal LTC use in China. We also explored the socioeconomic and regional disparities.

Methods: The study included 10,831 community-dwelling respondents aged 45 years and older from the China Health and Retirement Longitudinal Study in 2011, 2015, and 2018 for analysis. We used a two-part model with random effects to estimate the association between multimorbidity and informal LTC use. Heterogeneity of the association by socioeconomic position (education and income) and region was explored via a subgroup analysis. We further converted the change of informal LTC hours associated with multimorbidity into monetary value and calculated the 95% uncertainty interval (UI).

Results: The reported prevalence of multimorbidity was 60.0% (95% CI: 58.9%, 61.2%) in 2018. We found multimorbidity was associated with an increased likelihood of receiving informal LTC (OR = 2.13; 95% CI: 1.97, 2.30) and more hours of informal LTC received (IRR = 1.20; 95% CI: 1.06, 1.37), *ceteris paribus*. Participants in the highest income quintile received more hours of informal LTC care (IRR = 1.62; 95% CI: 1.31, 1.99). The estimated monetary value of increased informal LTC hours among participants with multimorbidity was equivalent to 3.7% (95% UI: 2.2%, 5.4%) of China's GDP in 2018.

Conclusion: Our findings substantiate the threat of multimorbidity to LTC burden. It is imperative to strengthen LTC services provision, especially among older adults with multimorbidity and ensure equal access among those with lower income.

Keywords: Economic burden; Informal long-term care; Multimorbidity; Regional disparities; Socio-economic disparities.

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Conflict of interest statement

The authors declare no competing interests.

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

SUPPLEMENTARY INFO

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

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. 2023 Oct 30;13(1):18607.

doi: 10.1038/s41598-023-42603-2.

[Findings from the Indonesian family life survey on patterns and factors associated with multimorbidity](#)

[Meliana Griselda](#)^{#1,2}, [Sofa D Alfian](#)^{#3,4,5}, [Imam A Wicaksono](#)^{1,6}, [Martin Wawruch](#)⁷, [Rizky Abdulah](#)^{1,6}

Affiliations expand

- PMID: 37903815
- PMCID: [PMC10616186](#)
- DOI: [10.1038/s41598-023-42603-2](#)

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Abstract

The prevalence of multimorbidity tends to increase with age, but it is now also reported in the middle-aged population, which has a negative impact on healthcare systems and health outcomes. This study aims to analyze the patterns and factors associated with multimorbidity in Indonesia. This national cross-sectional population-based survey used publicly available data from the Indonesian Family Life Survey (IFLS-5) for 2014 among middle-aged (40-59 years old) and elderly (≥ 60 years old) respondents. Information on all chronic diseases was assessed using a self-reported questionnaire. Sociodemographic and health-related behavioral factors were obtained from self-reported data. Binary logistic

regression analysis was used to identify the factors associated with multimorbidity. Adjusted odds ratios (AORs) with 95% confidence intervals (CIs) were reported. The study recruited 11,867 respondents. The prevalence of multimorbidity was 18.6% (95% CI 17.9-19.3) with which 15.6% among middle age (95% CI 14.95-16.25) and 24.9% among the elderly (95% CI 24.12-25.68). Hypertension was the most commonly reported disease (23.2%) in all combinations of multimorbidity and among all age groups. Socio-demographic factors: elderly (AOR: 1.66; 95% CI 1.46-1.89), female (AOR: 1.42; 95% CI 1.20-1.69), living in the urban area (AOR: 1.22; 95% CI 1.09-1.38), higher educational level (AOR: 2.49; 95% CI 1.91-3.26), unemployed (AOR: 1.63; 95% CI 1.44-1.84), and higher economic level (AOR: 1.41; 95% CI 1.18-1.68) were associated with multimorbidity. Poor health behavior factors: being former smokers (AOR: 2.03; 95% CI 1.65-2.51) and obesity (AOR: 1.53; 95% CI 1.35-1.75) were also associated with multimorbidity. The prevalence of multimorbidity in the middle-aged and elderly population in Indonesia is relatively high, particularly in populations with poor health behaviors. Therefore, healthcare professionals should integrate more patient-specific factors when designing and implementing tailored interventions to manage multimorbidity in Indonesia.

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Conflict of interest statement

The authors declare no competing interests.

- [87 references](#)
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PLoS Med

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. 2023 Oct 27;20(10):e1004300.

doi: 10.1371/journal.pmed.1004300. eCollection 2023 Oct.

Ethnic differences in early onset multimorbidity and associations with health service use, long-term prescribing, years of life lost, and mortality: A cross-sectional study using clustering in the UK Clinical Practice Research Datalink

[Fabiola Eto](#)¹, [Miriam Samuel](#)¹, [Rafael Henkin](#)², [Meera Mahesh](#)³, [Tahania Ahmad](#)¹, [Alisha Angdembe](#)², [R Hamish McAllister-Williams](#)^{4 5 6}, [Paolo Missier](#)⁷, [Nick J Reynolds](#)⁷, [Michael R Barnes](#)², [Sally Hull](#)¹, [Sarah Finer](#)¹, [Rohini Mathur](#)¹

Affiliations expand

- PMID: 37889900
- PMCID: [PMC10610074](#)
- DOI: [10.1371/journal.pmed.1004300](#)

Free PMC article

Abstract

Background: The population prevalence of multimorbidity (the existence of at least 2 or more long-term conditions [LTCs] in an individual) is increasing among young adults, particularly in minority ethnic groups and individuals living in socioeconomically deprived areas. In this study, we applied a data-driven approach to identify clusters of individuals who had an early onset multimorbidity in an ethnically and socioeconomically diverse population. We identified associations between clusters and a range of health outcomes.

Methods and findings: Using linked primary and secondary care data from the Clinical Practice Research Datalink GOLD (CPRD GOLD), we conducted a cross-sectional study of 837,869 individuals with early onset multimorbidity (aged between 16 and 39 years old when the second LTC was recorded) registered with an English general practice between 2010 and 2020. The study population included 777,906 people of White ethnicity (93%), 33,915 people of South Asian ethnicity (4%), and 26,048 people of Black African/Caribbean ethnicity (3%). A total of 204 LTCs were considered. Latent class analysis stratified by ethnicity identified 4 clusters of multimorbidity in White groups and 3 clusters in South Asian and Black groups. We found that early onset multimorbidity was more common among South Asian (59%, 33,915) and Black (56% 26,048) groups compared to the White population (42%, 777,906). Latent class analysis revealed physical and mental health conditions that were common across all ethnic groups (i.e., hypertension, depression, and painful conditions). However, each ethnic group also presented exclusive LTCs and different sociodemographic profiles: In White groups, the cluster with the highest rates/odds of the outcomes was predominantly male (54%, 44,150) and more socioeconomically deprived than the cluster with the lowest rates/odds of the outcomes. On the other hand, South Asian and Black groups were more socioeconomically deprived than White groups, with a consistent deprivation gradient across all multimorbidity clusters. At the end of the study, 4% (34,922) of the White early onset multimorbidity population had died compared to 2% of the South Asian and Black early onset multimorbidity populations (535 and 570, respectively); however, the latter groups died younger and lost more years of life. The 3 ethnic groups each displayed a cluster of individuals with increased rates of primary care consultations, hospitalisations, long-term prescribing, and odds of mortality. Study limitations include the exclusion of individuals with missing ethnicity information, the age of diagnosis not reflecting the actual age of onset, and the exclusion of people from Mixed, Chinese, and other ethnic groups due to insufficient power to investigate associations between multimorbidity and health-related outcomes in these groups.

Conclusions: These findings emphasise the need to identify, prevent, and manage multimorbidity early in the life course. Our work provides additional insights into the excess burden of early onset multimorbidity in those from socioeconomically deprived and diverse groups who are disproportionately and more severely affected by multimorbidity and highlights the need to ensure healthcare improvements are equitable.

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Conflict of interest statement

FE receive salary for this work by MRC (MR/S027297/1). SF and RM receive salary contributions for their work on the Genes & Health programme, by a Life Sciences Consortium that includes Astra Zeneca PLC, Bristol-Myers Squibb Company,

GlaxoSmithKline Research and Development Limited, Maze Therapeutics Inc, Merck Sharp & Dohme LLC, Novo Nordisk A/S, Pfizer Inc, Takeda Development Centre Americas Inc. RM is supported by Barts Charity (MGU0504). RM has received consulting fees from AMGEN unrelated to this work. RHM has received fees from American Center for Psychiatry & Neurology United Arab Emirates, British Association for Psychopharmacology, European College of Neuropsychopharmacology, International Society for Affective Disorders, Janssen, LivaNova, Lundbeck, My Tomorrows, OCM Comunicazione s.n.c., Pfizer, Qatar International Mental Health Conference, Sunovion, Syntropharma, UK Medical Research Council and Wiley; grant support from National Institute for Health Research Efficacy and Mechanism Evaluation Panel and Health Technology Assessment Panel; and non-financial support from COMPASS Pathways and Magstim. PM is funded by the National Institute for Health Research (NIHR) Newcastle Biomedical Research Centre, by NIHR AIM AI-MULTIPLY, and by NIHR ADMISSION (MR/V033654/1). NJR is funded by the National Institute for Health Research (NIHR) Newcastle Biomedical Research Centre, by the NIHR Newcastle In Vitro Diagnostics Co-operative and NIHR AIM AI-MULTIPLY. N.J.R. is also a NIHR Senior Investigator, (Senior Investigator Award) NIHR200168. NJR reports grants from PSORT industrial partners as listed (<http://www.psort.org.uk/>); other research grants from GSK Stiefel and Novartis. MRB is funded by the National Institute for Health Research (NIHR) AIM AI-MULTIPLY Consortium (NIHR203982). MRB reports research grants from Benevolent AI, Janssen and Novartis. TA is funded by the NIHR Applied Research Collaboration North Thames Award (NIHR 200163). AA is funded by the NIHR (31672 AI-MULTIPLY, 2022-2025). RH is funded by the Health Data Research UK (grant ref: LOND1).

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- [6 figures](#)

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J Gerontol A Biol Sci Med Sci

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. 2023 Oct 27:glad249.

doi: 10.1093/gerona/glad249. Online ahead of print.

Cross-sectional association between plasma biomarkers and multimorbidity patterns in older adults

[Aitana Vázquez-Fernández](#)¹, [Alberto Lana Pérez](#)², [Ellen A Struijk](#)¹, [Verónica Vega-Cabello](#)¹, [Juan Cárdenas-Valladolid](#)^{3,4,5}, [Miguel Ángel Salinero-Fort](#)^{4,6,7,8}, [Fernando Rodríguez-Artalejo](#)^{1,9}, [Esther Lopez-García](#)^{1,9}, [Francisco Félix Caballero](#)¹

Affiliations expand

- PMID: 37886823
- DOI: [10.1093/gerona/glad249](https://doi.org/10.1093/gerona/glad249)

Abstract

Multimorbidity is the simultaneous presence of two or more chronic conditions. Metabolomics could identify biomarkers potentially related to multimorbidity. We aimed to identify groups of biomarkers and their association with different multimorbidity patterns. Cross-sectional analyses were conducted within the Seniors-ENRICA-2 cohort in Spain, with information from 700 individuals aged ≥ 65 years. Biological samples were analyzed using high-throughput proton nuclear magnetic resonance metabolomics. Biomarkers groups were identified with exploratory factor analysis, and multimorbidity was classified into three types: cardiometabolic, neuropsychiatric, and musculoskeletal. Logistic regression was used to estimate the association between biomarkers groups and multimorbidity patterns, after adjusting for potential confounders including sociodemographics, lifestyle, and body mass index. Three factors were identified: the "lipid metabolism" mainly reflected biomarkers related to lipid metabolism, such as very-low-density lipoprotein and low-density lipoprotein cholesterol; the "high-density lipoprotein cholesterol" mainly included high-density lipoprotein cholesterol subclasses and other lipids not included in the first factor; and the "amino acid/glycolysis/ketogenesis", composed of some amino acids, glycolysis-related metabolites and ketone bodies. Higher scores in the "lipid metabolism" factor were associated with a higher likelihood of cardiometabolic multimorbidity, odds ratio for tertile 3 vs. tertile 1 was 1.79 (95% confidence interval: 1.17-2.76). The "high-density lipoprotein cholesterol" factor was associated with lower odds of cardiometabolic multimorbidity [0.51 (0.32-0.82)], and the

"amino acid/glycolysis/ketogenesis" factor was associated with more frequent cardiometabolic multimorbidity [1.85 (1.18-2.90)]. Different metabolomic biomarkers are associated with different multimorbidity patterns, therefore multiple biomarker measurements are needed for a complete picture of the molecular mechanisms of multimorbidity.

Keywords: biomarkers; chronic disease; metabolomics; multimorbidity.

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. 2023 Oct 26.

doi: 10.1055/a-2199-2344. Online ahead of print.

[Mortality related risk factors: Results from the Brandenburg Endocarditis Register](#)

[Roya Ostovar](#)¹, [Filip Schroeter](#)², [Farzaneh Seifi Zinab](#)³, [Dirk Fritzsche](#)⁴, [Hans-Heinrich Minden](#)⁵, [Nirmeen Lasheen](#)⁶, [Martin Hartrumpf](#)², [Oliver Ritter](#)⁷, [Gesine Dörr](#)⁸, [Johannes Maximilian Albes](#)⁹

Affiliations expand

- PMID: 37884029
- DOI: [10.1055/a-2199-2344](https://doi.org/10.1055/a-2199-2344)

Abstract

Objective: Endocarditis as a potentially life-threatening disease with high complication and mortality rates. In recent years, an increase has been reported throughout Europe. In the aging society, successful treatment is complex and challenging owing to the high rate of multimorbidity.

Methods: We initiated a statewide prospective multicenter endocarditis registry in 2020. Perioperative risk factors, comorbidities, microbiological, laboratory and imaging diagnostics, complications and mortality including 1-year follow-up were collected. The present midterm analysis includes factors influencing mortality in the first 313 patients.

Result: In-hospital mortality and 1-year mortality were 28.4% and 40.9%, respectively. Preoperative risk factors such as age $p < 0.001$, EuroSCORE II $p < 0.001$, Coronary artery disease $p = 0.022$, pacemaker probe infection $p = 0.033$, preoperative LVEF, SIRS, pulmonary edema, heart failure, septic emboli, acute renal failure, impaired coagulation, hypalbuminemia ($p < 0.001$, respectively), NTproBNP $p = 0.001$. Presence of perianular abscess, perforation and shunt were associated with increased mortality ($p = 0.004$, $p = 0.001$, $p = 0.004$, respectively). In addition, Cardiopulmonary bypass time influenced mortality ($p = 0.002$). Main postoperative causes of death were multi-organ failure, renal failure, vasoplegia and low-output syndrome ($p < 0.001$, respectively). Previous endocarditis was 7.7%. 35.5% were prosthetic valve recipients. 33.6% were Redo surgery.

Conclusions: Our first Registry data show the complexity of endocarditis patients and the challenging treatment. Some risk factors can be treated preoperatively. For instance, hypalbuminemia and the duration of the procedure which can be controlled with adequate albumin substitution and carefully planned procedures restricted to the essential requirements, i.e. hybrid approaches with consecutive interventions.

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Conflict of interest statement

The authors declare that they have no conflict of interest.

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PLoS One



. 2023 Oct 26;18(10):e0293314.

doi: 10.1371/journal.pone.0293314. eCollection 2023.

[Comorbidity clusters and in-hospital outcomes in patients admitted with acute myocardial infarction in the USA: A national population-based study](#)

[Salwa S Zghebi](#)^{1,2}, [Martin K Rutter](#)^{3,4}, [Louise Y Sun](#)⁵, [Waqas Ullah](#)⁶, [Muhammad Rashid](#)^{7,8}, [Darren M Ashcroft](#)^{9,10}, [Douglas T Steinke](#)⁹, [Stephen Weng](#)¹¹, [Evangelos Kontopantelis](#)^{1,12}, [Mamas A Mamas](#)^{7,8}

Affiliations expand

- PMID: 37883354
- PMCID: [PMC10602297](#)
- DOI: [10.1371/journal.pone.0293314](#)

Free PMC article

Abstract

Background: The prevalence of multimorbidity in patients with acute myocardial infarction (AMI) is increasing. It is unclear whether comorbidities cluster into distinct phenogroups and whether are associated with clinical trajectories.

Methods: Survey-weighted analysis of the United States Nationwide Inpatient Sample (NIS) for patients admitted with a primary diagnosis of AMI in 2018. In-hospital outcomes included mortality, stroke, bleeding, and coronary revascularisation. Latent class analysis of 21 chronic conditions was used to identify comorbidity classes. Multivariable logistic and linear regressions were fitted for associations between comorbidity classes and outcomes.

Results: Among 416,655 AMI admissions included in the analysis, mean (\pm SD) age was 67 (\pm 13) years, 38% were females, and 76% White ethnicity. Overall, hypertension, coronary heart disease (CHD), dyslipidaemia, and diabetes were common comorbidities, but each of the identified five classes (C) included \geq 1 predominant comorbidities defining distinct phenogroups: cancer/coagulopathy/liver disease class (C1); least burdened (C2); CHD/dyslipidaemia (largest/referent group, (C3)); pulmonary/valvular/peripheral vascular disease (C4); diabetes/kidney disease/heart failure class (C5). Odds ratio (95% confidence interval [CI]) for mortality ranged between 2.11 (1.89-2.37) in C2 to 5.57 (4.99-6.21) in C1. For major bleeding, OR for C1 was 4.48 (3.78; 5.31); for acute stroke, ORs ranged between 0.75 (0.60; 0.94) in C2 to 2.76 (2.27; 3.35) in C1; for coronary revascularization, ORs ranged between 0.34 (0.32; 0.36) in C1 to 1.41 (1.30; 1.53) in C4.

Conclusions: We identified distinct comorbidity phenogroups that predicted in-hospital outcomes in patients admitted with AMI. Some conditions overlapped across classes, driven by the high comorbidity burden. Our findings demonstrate the predictive value and potential clinical utility of identifying patients with AMI with specific comorbidity clustering.

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Conflict of interest statement

SSZ, LYS, EK, MKR, DS, DMA MAM, MR declare no competing interests. SW is a currently an employee of GSK. This does not alter our adherence to PLOS ONE policies on sharing data and materials.

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

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Med Sci Monit



. 2023 Oct 26:29:e941455.

doi: 10.12659/MSM.941455.

[Identifying Predominant Causes of Death Among Hospitalized COVID-19 Patients During Poland's Second and Third Waves](#)

[Irina Niecwietajewa](#)¹, [Michał Frączek](#)², [Maria Mroczkowska](#)³, [Mariusz Frączek](#)⁴

Affiliations expand

- PMID: 37880930
- PMCID: [PMC10617245](#)
- DOI: [10.12659/MSM.941455](#)

Free PMC article

Abstract

BACKGROUND Number of confirmed COVID-19 deaths per million population in Poland between November 2020 and May 2021 was one of the largest in Europe. This retrospective study was conducted at a single center in Poland between November 2020 and May 2021 to evaluate the morbidity and mortality rates in 581 patients hospitalized with COVID-19. **MATERIAL AND METHODS** A retrospective single-center study was conducted in a dedicated COVID-19 hospital from November, 2020 to May, 2021. The data of 581 hospitalized patients were analyzed. Multimorbidity was assessed using the Charlson Comorbidity Index, including chronic kidney, respiratory, cardiovascular diseases, diabetes mellitus, cancer, and dementia. The observation period covered admission to the hospital for severe COVID-19 until discharge or death. Diagnosis of COVID-19 was confirmed by quantitative reverse transcription polymerase chain reaction test. Statistical analysis was carried out in the IBM SPSS Statistics program. **RESULTS** The mortality rate was 35% of all admitted patients. Lung damage was the cause of death in 60%, bacterial superinfection in 26%, arterial thrombosis or thromboembolism in 9%, and heart failure in 5% of patients. The chi-square test showed a significant relationship between sex and the cause of death related to COVID-19 pneumonia and bacterial ventilator-associated pneumonia (VAP). **CONCLUSIONS** The findings from this study supports findings from other countries that between November 2020 and May 2021, before SARS-CoV-2 vaccination programs were fully implemented and before effective medications and antiviral agents were developed, patients with severe COVID-19 had high rates of morbidity and mortality.

Conflict of interest statement

Conflict of interest: None declared

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

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Br J Psychiatry



. 2023 Nov;223(5):518-525.

doi: 10.1192/bjp.2023.112.

Severe mental illness, race/ethnicity, multimorbidity and mortality following COVID-19 infection: nationally representative cohort study

[Jayati Das-Munshi](#)¹, [Ioannis Bakolis](#)², [Laia Bécares](#)³, [Jacqueline Dyer](#)⁴, [Matthew Hotopf](#)⁵, [Josephine Ocloo](#)², [Robert Stewart](#)⁵, [Ruth Stuart](#)⁵, [Alex Dregan](#)⁶

Affiliations expand

- PMID: 37876350
- PMCID: [PMC7615273](#)
- DOI: [10.1192/bjp.2023.112](#)

Free PMC article

Abstract

Background: The association of COVID-19 with death in people with severe mental illness (SMI), and associations with multimorbidity and ethnicity, are unclear.

Aims: To determine all-cause mortality in people with SMI following COVID-19 infection, and assess whether excess mortality is affected by multimorbidity or ethnicity.

Method: This was a retrospective cohort study using primary care data from the Clinical Practice Research Database, from February 2020 to April 2021. Cox proportional hazards

regression was used to estimate the effect of SMI on all-cause mortality during the first two waves of the COVID-19 pandemic.

Results: Among 7146 people with SMI (56% female), there was a higher prevalence of multimorbidity compared with the non-SMI control group ($n = 653\,024$, 55% female). Following COVID-19 infection, the SMI group experienced a greater risk of death compared with controls (adjusted hazard ratio (aHR) 1.53, 95% CI 1.39-1.68). Black Caribbean/Black African people were more likely to die from COVID-19 compared with White people (aHR = 1.22, 95% CI 1.12-1.34), with similar associations in the SMI group and non-SMI group (P for interaction = 0.73). Following infection with COVID-19, for every additional multimorbidity condition, the aHR for death was 1.06 (95% CI 1.01-1.10) in the SMI stratum and 1.16 (95% CI 1.15-1.17) in the non-SMI stratum (P for interaction = 0.001).

Conclusions: Following COVID-19 infection, patients with SMI were at an elevated risk of death, further magnified by multimorbidity. Black Caribbean/Black African people had a higher risk of death from COVID-19 than White people, and this inequity was similar for the SMI group and the control group.

Keywords: COVID-19; Mortality; ethnicity; multimorbidity; severe mental illness.

Conflict of interest statement

Conflict of Interest

Professor Robert Stewart reports funding received from Janssen, GSK and Takeda. All other authors do not declare conflicts of interest.

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

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. 2023 Oct 6:65:102265.

doi: 10.1016/j.eclinm.2023.102265. eCollection 2023 Nov.

Chronic diseases and multimorbidity patterns, their recent onset, and risk of new-onset Parkinson's disease and related functional degeneration in older adults: a prospective cohort study

[Ziyang Ren](#)^{1,2}, [Yunhan Xu](#)³, [Jinfang Sun](#)⁴, [Yanqing Han](#)⁵, [Lin An](#)³, [Jufen Liu](#)^{1,2}

Affiliations expand

- PMID: 37855021
- PMCID: [PMC10579290](#)
- DOI: [10.1016/j.eclinm.2023.102265](#)

Free PMC article

Abstract

Background: Certain chronic diseases contribute to increased risks of Parkinson's disease (PD), but the association between time-varying multimorbidity patterns and new-onset PD remains underexplored.

Methods: Data were from the Survey of Health, Ageing and Retirement in Europe (SHARE) waves 5-8 conducted between January 2013 and March 2020. Eleven chronic diseases were included, with ≥ 2 denoting multimorbidity. Three multimorbidity patterns were further defined: somatic multimorbidity (SMM), neuropsychiatric multimorbidity (NPM), and cardiometabolic multimorbidity (CMM). PD-related function degeneration included

functional limitations, mobility limitations, depressive symptoms, and cognitive decline. Time-dependent analyses, competing-risk analyses, and mixed-effect models were utilised.

Findings: In this prospective cohort study, 557 developed new-onset PD during follow-ups among 64,273 participants included at baseline, as defined by participants' self-reported physician diagnoses. Participants with (vs. without) multimorbidity, SMM, NPM, and CMM were at 1.40-2.70 times higher PD risk after considering the competing role of all-cause death, which remained significant in all sensitivity analyses and were more pronounced in lower-income participants (P for interaction <0.05). Similarly, they tended to develop functional degeneration faster than those without these multimorbidity patterns ($P < 0.05$). Participants with recent-onset (newly diagnosed in 2015) multimorbidity patterns were at 1.45-3.72 times higher risk of PD than those never diagnosed. Interestingly, they were at comparable or even higher (though P values for >0.05) PD risk compared to participants with multimorbidity patterns diagnosed in 2013 or before. Furthermore, recent-onset (vs. prior diagnosed) NPM exhibited faster functional deterioration and cognitive decline (P for difference <0.05).

Interpretation: Our findings suggest that promoting early prevention of multimorbidity, especially recent-onset multimorbidity and NPM, could prevent some subsequent cases of PD and related functional degeneration among older adults. However, further studies are needed to confirm this association.

Funding: The National Key Research and Development Program, Ministry of Science and Technology, China; Zhongnanshan Medical Foundation of Guangdong Province; Major Project of the National Social Science Fund of China; Fundamental Research Funds for the Central Universities.

Keywords: Chronic disease; Functional degeneration; Multimorbidity; Parkinson's disease; Time-dependent.

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Conflict of interest statement

The authors declare no conflict of interest regarding this manuscript.

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

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Review

Clin Geriatr Med



. 2023 Nov;39(4):635-645.

doi: 10.1016/j.cger.2023.04.008. Epub 2023 May 11.

Adverse Drug Event Prevention and Detection in Older Emergency Department Patients

[Jennifer L Koehl](#)¹

Affiliations expand

- PMID: 37798069
- DOI: [10.1016/j.cger.2023.04.008](https://doi.org/10.1016/j.cger.2023.04.008)

Abstract

Older adults are given therapies to enhance the quality and longevity of life, but with the benefits of medication therapy also comes the potential for adverse drug events (ADEs). Avoiding ADEs has become a national health priority with substantial impact on health outcomes and health care costs. The presence of multimorbidity, changes in physiologic function, and polypharmacy make older adults more vulnerable to medication-related ADEs. Use of interactive support tools in the form of geriatric-friendly medication order sets and geriatric consultations along with pharmacist-led medication review and optimization are imperative to decrease the occurrence of ADEs and unnecessary prescribing cascades.

Keywords: Adverse drug event; Deprescribe; Medication review; Polypharmacy; Potentially inappropriate medication; Prescribing cascade.

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SUPPLEMENTARY INFO

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J Psychosom Res



. 2023 Nov;174:111490.

doi: 10.1016/j.jpsychores.2023.111490. Epub 2023 Sep 11.

[Exploring the relationship between depression and multimorbidity in Chinese middle-aged and older people based on propensity score matching](#)

[Bei Yang](#)¹, [Hua He](#)², [Qiao Nie](#)², [Yi Yang](#)³

Affiliations expand

- PMID: 37713765
- DOI: [10.1016/j.jpsychores.2023.111490](https://doi.org/10.1016/j.jpsychores.2023.111490)

Abstract

Background: This study aimed to explore the relationship between depression and multimorbidity among middle-aged and older people in China.

Methods: The cross-sectional study used the 2018 China Longitudinal Study of Health and Retirement and included a sample of 19,761 middle-aged and older adults aged 45 years and above. Propensity score matching was used to match samples of individuals with and without depression symptoms. The association between depression symptoms and multimorbidity and dose-response relationships were analyzed using logistic regression and restricted cubic spline (RCS) models for matched samples.

Results: Logistic regression analysis showed that the prevalence of multimorbidity was 1.49 times higher among middle-aged and older adults in the depression symptom group compared to the non-depression group (95% CI:1.24, 1.80). The RCS curves for the relationship between depression and multimorbidity showed an overall increasing trend ($P = 0.028$). And prevalence of arthritis and digestive disease in the depressed and non-depressed groups is 3.6% and 3.9%, respectively.

Limitations: It was difficult to draw conclusions about causation since the study was cross-sectional, and CESD-10 scores do not represent the population study finally diagnosed with depression, the conclusions should be promoted with caution.

Conclusions: Middle-aged and older people with depressive symptoms are more likely to have multimorbidity than non-depressed individuals. Furthermore, the likelihood of multimorbidity increases with higher depression scores, and the binary combinations were similarly distributed. Therefore, attention should be paid to the management of mental health in the middle-aged and older adult population to alleviate and prevent any mental health issues they might face.

Keywords: Chronic disease; Depression; Dose-response relationship; Multimorbidity; Propensity score matching.

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Conflict of interest statement

Declaration of Competing Interest All authors declare that there is no conflict of interest.

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Med Care



. 2023 Nov 1;61(11):765-771.

doi: 10.1097/MLR.0000000000001919. Epub 2023 Sep 13.

[Health Status of US Patients With One or More Health Conditions: Using a Novel Electronic Patient-reported Outcome Measure Producing Single Metric Measures](#)

[Xin Zhang](#)¹, [Karin M Vermeulen](#), [Paul F M Krabbe](#)

Affiliations expand

- PMID: 37708354
- PMCID: [PMC10563950](#)
- DOI: [10.1097/MLR.0000000000001919](#)

Free PMC article

Abstract

Background: Most existing research studying health status impacted by morbidity has focused on a specific health condition, and most instruments used for measuring health

status are neither patient-centered nor preference-based. This study aims to report on the health status of patients impacted by one or more health conditions, measured by a patient-centered and preference-based electronic patient-reported outcome measure.

Methods: A cross-sectional study was conducted among patients with one or more health conditions in the United States. A novel generic, patient-centered, and preference-based electronic patient-reported outcome measure: Château Santé-Base, was used to measure health status. Individual health state was expressed as a single metric number (value). We compared these health-state values between sociodemographic subgroups, between separate conditions, between groups with or without comorbidity, and between different combinations of multimorbidity.

Results: The total sample comprised 3913 patients. Multimorbidity was present in 62% of the patients. The most prevalent health conditions were pain (50%), fatigue/sleep problems (40%), mental health problems (28%), respiratory diseases (22%), and diabetes (18%). The highest (best) and lowest health-state values were observed in patients with diabetes and mental health problems. Among combinations of multimorbidity, the lowest values were observed when mental health problems were involved, the second lowest values were observed when fatigue/sleep problems and respiratory diseases coexisted.

Conclusions: This study compared health status across various single, and multiple (multimorbidity and comorbidity) health conditions directly, based on single metric health-state values. The insights are valuable in clinical practice and policy-making.

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Conflict of interest statement

P.F.M.K. developed the patient-reported outcome measure, the preference-based measurement model, and the mobile applications presented in this paper, and uses them as extensions of academic and commercial activities. These activities adhere to the policies of Medical Care on sharing data and materials. X.Z. is employed by the Chinese Scholarship Council (CSC) and the University Medical Center Groningen (UMCG). K.M.V. declares no conflict of interest.

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

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Diabetes Ther



. 2023 Nov;14(11):1903-1913.

doi: 10.1007/s13300-023-01463-9. Epub 2023 Sep 14.

[A Longitudinal Clinical Trajectory Analysis Examining the Accumulation of Co-morbidity in People with Type 2 Diabetes \(T2D\) Compared with Non-T2D Individuals](#)

[Adrian Heald](#)^{1,2}, [Rui Qin](#)³, [Richard Williams](#)^{4,5}, [John Warner-Levy](#)⁶, [Ram Prakash Narayanan](#)⁷, [Israel Fernandez](#)⁸, [Yonghong Peng](#)³, [J Martin Gibson](#)^{6,9}, [Kevin McCay](#)³, [Simon G Anderson](#)¹⁰, [William Ollier](#)³

Affiliations expand

- PMID: 37707702
- PMCID: [PMC10570249](#)
- DOI: [10.1007/s13300-023-01463-9](#)

Free PMC article

Abstract

Background: Type 2 diabetes mellitus (T2D) is commonly associated with an increasing complexity of multimorbidity. While some progress has been made in identifying genetic

and non-genetic risk factors for T2D, understanding the longitudinal clinical history of individuals before/after T2D diagnosis may provide additional insights.

Methods: In this study, we utilised longitudinal data from the DARE (Diabetes Alliance for Research in England) study to examine the trajectory of clinical conditions in individuals with and without T2D. Data from 1932 individuals (T2D n = 1196 vs. matched non-T2D controls n = 736) were extracted and subjected to trajectory analysis over a period of up to 50 years (25 years pre-diagnosis/25 years post-diagnosis). We also analysed the cumulative proportion of people with diagnosed coronary artery disease (CAD) in their general practice (GP) record with an analysis of lower respiratory tract infection (RTI) as a comparator group.

Results: The mean age of diagnosis of T2D was 52.6 (95% confidence interval 52.0-53.4) years. In the years leading up to T2D diagnosis, individuals who eventually received a T2D diagnosis consistently exhibited a considerable increase in several clinical phenotypes. Additionally, immediately prior to T2D diagnosis, a significantly greater prevalence of hypertension (35%)/RTI (34%)/heart conditions (17%)/eye, nose, throat infection (19%) and asthma (12%) were observed. The corresponding trajectory of each of these conditions was much less dramatic in the matched controls. Post-T2D diagnosis, proportions of T2D individuals exhibiting hypertension/chronic kidney disease/retinopathy/infections climbed rapidly before plateauing. At the last follow-up by quintile of disadvantage, the proportion (%) of people with diagnosed CAD was 6.4% for quintile 1 (least disadvantaged) and 11% for quintile 5 (F = 3.4, p = 0.01 for the difference between quintiles).

Conclusion: These findings provide novel insights into the onset/natural progression of T2D, suggesting an early phase of inflammation-related disease activity before any clinical diagnosis of T2D is made. Measures that reduce social inequality have the potential in the longer term to reduce the social gradient in health outcomes reported here.

Keywords: DARE cohort; Longitudinal; Multi-morbidity; Type 2 Diabetes.

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Conflict of interest statement

No authors have any conflict of interest.

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

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Review

Lancet Respir Med



. 2023 Nov;11(11):1020-1034.

doi: 10.1016/S2213-2600(23)00261-8. Epub 2023 Sep 8.

[COPD and multimorbidity: recognising and addressing a syndemic occurrence](#)

[Leonardo M Fabbri](#)¹, [Bartolome R Celli](#)², [Alvar Agustí](#)³, [Gerard J Criner](#)⁴, [Mark T Dransfield](#)⁵, [Miguel Divo](#)², [Jamuna K Krishnan](#)⁶, [Lies Lahousse](#)⁷, [Maria Montes de Oca](#)⁸, [Sundeep S Salvi](#)⁹, [Daiana Stolz](#)¹⁰, [Lowie E G W Vanfleteren](#)¹¹, [Claus F Vogelmeier](#)¹²

Affiliations expand

- PMID: 37696283
- DOI: [10.1016/S2213-2600\(23\)00261-8](https://doi.org/10.1016/S2213-2600(23)00261-8)

Abstract

Most patients with chronic obstructive pulmonary disease (COPD) have at least one additional, clinically relevant chronic disease. Those with the most severe airflow obstruction will die from respiratory failure, but most patients with COPD die from non-respiratory disorders, particularly cardiovascular diseases and cancer. As many chronic diseases have shared risk factors (eg, ageing, smoking, pollution, inactivity, and poverty), we argue that a shift from the current paradigm in which COPD is considered as a single disease with comorbidities, to one in which COPD is considered as part of a multimorbid state-with co-occurring diseases potentially sharing pathobiological mechanisms-is needed to advance disease prevention, diagnosis, and management. The term syndemics is used to describe the co-occurrence of diseases with shared mechanisms and risk factors, a

novel concept that we propose helps to explain the clustering of certain morbidities in patients diagnosed with COPD. A syndemics approach to understanding COPD could have important clinical implications, in which the complex disease presentations in these patients are addressed through proactive diagnosis, assessment of severity, and integrated management of the COPD multimorbid state, with a patient-centred rather than a single-disease approach.

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Conflict of interest statement

Declaration of interests LMF declares consulting fees from Chiesi Farmaceutici; payment or honoraria for lectures, presentations, manuscript writing, or educational events from Novartis, Chiesi Farmaceutici, Chiesi Italia, GSK, AstraZeneca, and Alfasigma; and participation on a data safety monitoring board (DSMB) for Novartis and Chiesi, all outside of the submitted work. LMF was formerly a member of the Global Initiative for Chronic Obstructive Lung Disease (GOLD). BRC declares consultancy fees from GSK, AstraZeneca, Menarini, Sanofi Aventis, and Axios; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from GSK, AstraZeneca, Menarini, Chiesi, and Regeneron; support for attending meetings or travel from GSK and Sanofi Aventis; and participation on a DSMB or advisory board for GSK, AstraZeneca, AZ Therapeutics, Sanofi Aventis, and Vertex, all outside of the submitted work. BRC is a member of GOLD. AA declares grants for research projects from GSK, AstraZeneca, and Menarini; and payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from GSK, AstraZeneca, Chiesi, Menarini, CIPLA, Zambon, and Sanofi Regeneron, all outside of the submitted work. AA holds the Chair of the Board of Directors of GOLD. GJC is member of GOLD. MTD declares grants paid to his institution from the US Department of Defense, American Lung Association, and National Institutes of Health; royalties from UpToDate; consulting fees from AstraZeneca, GSK, Novartis, Pulmonx, and Teva; and an unpaid role on the Board of Directors of the COPD Foundation, all outside of the submitted work. MD declares consulting fees from Sanofi Regeneron, outside of the submitted work. JKK declares grants paid to her institution from the American Thoracic Society Fellowship in Health Equity, Research Assistance for Primary Parents Award, COMMUNITY Center Investigator Development Core, Weill Cornell Medicine Dean's Diversity and Healthcare Disparity Research Award, and the National Institutes of Health (T32 HL134629); medical writing support from Novartis; medication samples delivered to her institution by Boehringer Ingelheim and GSK; and a donor gift to her institution from the Donna Redel Research Fund, all outside of the submitted work. LL declares fees to her institution from AstraZeneca for expert consultation, Chiesi for a lecture, and IPSA vzw, for lectures, outside of the submitted work. MM declares honoraria for lectures on COPD from AstraZeneca and GSK, outside of the submitted work. MMdO is a member of GOLD. SSS declares payments to his institution from Cipla for lectures, presentations, speakers bureaus, manuscript writing, or educational events. SSS has an unpaid leadership or fiduciary role with the Indian Chest Society, outside of the submitted

work, and is a member of GOLD. DS declares grants to her institution from Curetis and AstraZeneca; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from CSL Behring, Berlin-Chemie Menarini, Novartis, GSK, AstraZeneca, Vifor, Merck, Chiesi, Grifols, MSD, and Sanofi; and participation on a DSMB or advisory board for CSL Behring, Berlin-Chemie Menarini, Novartis, GSK, AstraZeneca, Vifor, Merck, Chiesi, Grifols, MSD, and Sanofi, all outside of the submitted work. LEGWV declares research grants to his institution from The Family Kamprad Foundation (20190024), the Swedish government and country council (ALF grant ALFGBG-824371), The Swedish Heart and Lung Foundation (20200150), and Svensk Lungmedicinsk Förening; and payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from GSK, AstraZeneca, Boehringer, Novartis, Chiesi, Resmed, and Pulmonx, all outside of the submitted work. CFV declares grants to his institution from the German Ministry of Education and Science, AstraZeneca, Boehringer Ingelheim, Chiesi, CSL Behring, GSK, Grifols, and Novartis; consulting fees from Aerogen, AstraZeneca, Boehringer Ingelheim, CSL Behring, Chiesi, GSK, Insmmed, Menarini, Novartis, and Nuaira; and payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from Aerogen, AstraZeneca, Boehringer Ingelheim, CSL Behring, Chiesi, GSK, Insmmed, Menarini, Novartis, Roche, and Sanofi, all outside the submitted work. CFV holds the Chair of the Science Committee of GOLD.

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Neurourol Urodyn

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. 2023 Nov;42(8):1745-1755.

doi: 10.1002/nau.25279. Epub 2023 Sep 7.

Multimorbidity associated with urinary incontinence among older women and men with complex needs in Aotearoa | New Zealand

[Philip J Schluter](#)^{1,2}, [Hamish A Jamieson](#)^{3,4}

Affiliations expand

- PMID: 37675660
- DOI: [10.1002/nau.25279](https://doi.org/10.1002/nau.25279)

Abstract

Aims: To investigate the association between multimorbidity and urinary incontinence (UI) among community living older adults with complex needs in sex-specific crude and adjusted analyses.

Methods: Since 2012 in Aotearoa | New Zealand (NZ) all community-living older people with complex needs who require publicly funded assistance undergo a comprehensive standardized geriatric needs assessment using the interRAI-HC instrument. Consenting adults aged ≥ 65 years who undertook this assessment between July 5, 2012 and December 31, 2020 were investigated. Multimorbidity was defined as having ≥ 2 chronic conditions. Recent bladder incontinence episodes were elicited and UI dichotomized into continent and incontinent groups.

Results: The study included 140 401 participants with an average age of 82.0 years (range: 65-107 years), of whom 85 746 (61.1%) were female. Overall, 36 185 (42.2%) females and 17 988 (32.9%) males reported UI. Participants had a median of 3 (range: 0-12) chronic conditions, with 109 135 (77.9%) classified as having multimorbidity. In adjusted modified Poisson regression analyses, the prevalence ratio for UI was 1.21 (95% confidence interval [CI]: 1.19, 1.24) times higher in females and 1.18 (95% CI: 1.14, 1.22) times higher for males with multimorbidity compared to those without multimorbidity.

Conclusions: Although significant, the estimated sex-specific effect sizes were modest for the association between multimorbidity and UI in this population. However, despite using the comprehensive interRAI-HC instrument, several potentially core chronic conditions were not adequately captured. Although increasingly recognized as an important and

growing public health issue, capturing all relevant chronic conditions challenges many epidemiological investigations into multimorbidity.

Keywords: comprehensive standardized community care assessment; epidemiology; multimorbidity; national study; older persons; urinary incontinence.

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Review

Ageing Res Rev

-
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-

. 2023 Nov:91:102044.

doi: 10.1016/j.arr.2023.102044. Epub 2023 Aug 28.

[Biomarkers of aging in frailty and age-associated disorders: State of the art and future perspective](#)

[Stefano Salvioli](#)¹, [Maria Sofia Basile](#)², [Leonardo Bencivenga](#)³, [Sara Carrino](#)⁴, [Maria Conte](#)⁴, [Sarah Damanti](#)⁵, [Rebecca De Lorenzo](#)⁵, [Eleonora Fiorenzato](#)⁶, [Alessandro Gialluisi](#)⁷, [Assunta](#)

[Ingannato](#)⁸, [Angelo Antonini](#)⁹, [Nicola Baldini](#)¹⁰, [Miriam Capri](#)⁴, [Simone Cenci](#)⁵, [Licia Iacoviello](#)⁷, [Benedetta Nacmias](#)⁸, [Fabiola Olivieri](#)¹¹, [Giuseppe Rengo](#)¹², [Patrizia Rovere Querini](#)⁵, [Fabrizia Lattanzio](#)¹³

Affiliations expand

- PMID: 37647997
- DOI: [10.1016/j.arr.2023.102044](https://doi.org/10.1016/j.arr.2023.102044)

Free article

Abstract

According to the Geroscience concept that organismal aging and age-associated diseases share the same basic molecular mechanisms, the identification of biomarkers of age that can efficiently classify people as biologically older (or younger) than their chronological (i.e. calendar) age is becoming of paramount importance. These people will be in fact at higher (or lower) risk for many different age-associated diseases, including cardiovascular diseases, neurodegeneration, cancer, etc. In turn, patients suffering from these diseases are biologically older than healthy age-matched individuals. Many biomarkers that correlate with age have been described so far. The aim of the present review is to discuss the usefulness of some of these biomarkers (especially soluble, circulating ones) in order to identify frail patients, possibly before the appearance of clinical symptoms, as well as patients at risk for age-associated diseases. An overview of selected biomarkers will be discussed in this regard, in particular we will focus on biomarkers related to metabolic stress response, inflammation, and cell death (in particular in neurodegeneration), all phenomena connected to inflammaging (chronic, low-grade, age-associated inflammation). In the second part of the review, next-generation markers such as extracellular vesicles and their cargos, epigenetic markers and gut microbiota composition, will be discussed. Since recent progresses in omics techniques have allowed an exponential increase in the production of laboratory data also in the field of biomarkers of age, making it difficult to extract biological meaning from the huge mass of available data, Artificial Intelligence (AI) approaches will be discussed as an increasingly important strategy for extracting knowledge from raw data and providing practitioners with actionable information to treat patients.

Keywords: Artificial Intelligence; Biomarkers of aging; Frailty; Inflammaging; Multimorbidity.

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Conflict of interest statement

Declaration of Competing Interest The authors declare no conflict of interest.

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Review

Ageing Res Rev



. 2023 Nov;91:102039.

doi: 10.1016/j.arr.2023.102039. Epub 2023 Aug 28.

[Risk factors for multimorbidity in adulthood: A systematic review](#)

[Clare Tazzeo](#)¹, [Alberto Zucchelli](#)², [Davide Liborio Vetrano](#)¹, [Jacopo Demurtas](#)³, [Lee Smith](#)⁴, [Daniel Schoene](#)⁵, [Dolores Sanchez-Rodriguez](#)⁶, [Graziano Onder](#)⁷, [Cafer Balci](#)⁸, [Silvia Bonetti](#)⁹, [Giulia Grande](#)¹, [Gabriel Torbahn](#)¹⁰, [Nicola Veronese](#)¹¹, [Alessandra Marengoni](#)¹²

Affiliations expand

- PMID: 37647994
- DOI: [10.1016/j.arr.2023.102039](https://doi.org/10.1016/j.arr.2023.102039)

Abstract

Background: Multimorbidity, the coexistence of multiple chronic diseases in an individual, is highly prevalent and challenging for healthcare systems. However, its risk factors remain poorly understood.

Objective: To systematically review studies reporting multimorbidity risk factors.

Methods: A PRISMA-compliant systematic review was conducted, searching electronic databases (MEDLINE, EMBASE, Web of Science, Scopus). Inclusion criteria were studies addressing multimorbidity transitions, trajectories, continuous disease counts, and specific patterns. Non-human studies and participants under 18 were excluded. Associations between risk factors and multimorbidity onset were reported.

Results: Of 20,806 identified studies, 68 were included, with participants aged 18-105 from 23 countries. Nine risk factor categories were identified, including demographic, socioeconomic, and behavioral factors. Older age, low education, obesity, hypertension, depression, low physical function were generally positively associated with multimorbidity. Results for factors like smoking, alcohol consumption, and dietary patterns were inconsistent. Study quality was moderate, with 16.2% having low risk of bias.

Conclusions: Several risk factors seem to be consistently associated with an increased risk of accumulating chronic diseases over time. However, heterogeneity in settings, exposure and outcome, and baseline health of participants hampers robust conclusions.

Keywords: Multimorbidity; Multiple chronic diseases; Risk factors.

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Conflict of interest statement

Declaration of Competing Interest All authors declare that there are no conflicts of interest.

SUPPLEMENTARY INFO

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Patient

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. 2023 Nov;16(6):569-578.

doi: 10.1007/s40271-023-00645-8. Epub 2023 Aug 29.

Operationalizing the Chronic Care Model with Goal-Oriented Care

[Agnes Grudniewicz](#)¹, [Carolyn Steele Gray](#)², [Pauline Boeckxstaens](#)³, [Jan De Maeseneer](#)³, [James Mold](#)⁴

Affiliations expand

- PMID: 37642918
- PMCID: [PMC10570240](#)
- DOI: [10.1007/s40271-023-00645-8](#)

Free PMC article

Abstract

The Chronic Care Model has guided quality improvement in health care for almost 20 years, using a patient-centered, disease management approach to systems and care teams. To further advance efforts in person-centered care, we propose strengthening the Chronic Care Model with the goal-oriented care approach. Goal-oriented care is person-centered in that it places the focus on what matters most to each person over the course of their life. The person's goals inform care decisions, which are arrived at collaboratively between clinicians and the person. In this paper, we build on each of the elements of the Chronic Care Model with person-centered, goal-oriented care and provide clinical examples on how to operationalize this approach. We discuss how this adapted approach can support our health care systems, in particular in the context of growing multi-morbidity.

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Conflict of interest statement

Dr Mold has published two books on goal-oriented care from which he receives royalties. The remaining authors do not have any conflicts of interest to declare.

- [55 references](#)

SUPPLEMENTARY INFO

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J Formos Med Assoc

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. 2023 Nov;122(11):1226.

doi: 10.1016/j.jfma.2023.08.012. Epub 2023 Aug 23.

[Response to comment on "Multimorbidity and prior falls correlate with risk of 30-day hospital readmission in aged 80+: A prospective cohort study"](#)

[Ding-Cheng Chan](#)¹, [Feng-Ping Lu](#)²

Affiliations expand

- PMID: 37625982

- DOI: [10.1016/j.jfma.2023.08.012](https://doi.org/10.1016/j.jfma.2023.08.012)

Free article

No abstract available

Conflict of interest statement

Declaration of competing interest The authors have no conflicts of interest relevant to this article.

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. 2023 Nov 1:340:523-528.

doi: 10.1016/j.jjad.2023.08.067. Epub 2023 Aug 16.

[Association of cognitive frailty and abdominal obesity with cardiometabolic multimorbidity among](#)

middle-aged and older adults: A longitudinal study

[Xinhong Zhu](#)¹, [Linlin Ding](#)², [Xiaona Zhang](#)², [Zhenfang Xiong](#)²

Affiliations expand

- PMID: 37595895
- DOI: [10.1016/j.jad.2023.08.067](https://doi.org/10.1016/j.jad.2023.08.067)

Abstract

Background: Cognitive frailty and abdominal obesity are deemed to be important targets for disease prevention. However, a possible cardiometabolic multimorbidity (CMM) link with cognitive frailty and abdominal obesity is unknown. The aim of this study was to investigate the association of cognitive frailty and abdominal obesity with CMM in the middle-aged and older people.

Methods: The sample comprised 11,503 participants aged 45 and over from the China Health and Retirement Longitudinal Study (CHARLS) 2011. Cognitive frailty was defined as the coexisting cognitive impairment and physical frailty. Abdominal obesity was assessed using waist circumference. CMM was defined as the presence of two or more cardiometabolic diseases (CMDs), including diabetes, heart disease, and stroke. A total of 9177 participants without CMM recruited from CHARLS 2011 and were followed up in 2018.

Results: Compared with 0 CMD, coexisting cognitive frailty and abdominal obesity was associated with the risk of 1 CMD (OR: 1.734, 95 % CI: 1.133-2.655), and ≥ 2 CMDs (OR: 7.218, 95%CI: 3.216-16.198). Longitudinal analysis showed that individuals with both cognitive frailty and abdominal obesity (HR: 2.162, 95%CI: 1.032-4.531) were more likely to have new onset CMM than cognitive frailty alone peers (HR: 1.667, 95 % CI: 0.721-3.853). Among the participants with first CMD, the likelihood of CMM was substantially higher in the co-existence of cognitive frailty and abdominal obesity (HR: 3.073, 95%CI: 1.254-7.527) than in the abdominal obesity alone (HR: 1.708, 95%CI: 1.201-2.427). Cognitive frailty alone was not significantly associated with CMM.

Conclusion: Cognitive frailty is not independently associated with the risk of CMM, but cognitive frailty and abdominal obesity together has a greater risk of CMM.

Keywords: Abdominal obesity; Cardiometabolic disease; Cardiometabolic multimorbidity; Cognitive frailty; Cognitive impairment.

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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 types, MeSH termsexpand

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Am J Gastroenterol

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. 2023 Oct 27.

doi: 10.14309/ajg.0000000000002472. Online ahead of print.

[Cost of Care for Patients With Cirrhosis](#)

[Fasiha Kanwal](#)^{1,2,3,4}, [Richard Nelson](#)⁵, [Yan Liu](#)^{1,2,3,4}, [Jennifer R Kramer](#)^{2,3,4}, [Ruben Hernaez](#)^{1,2,3,4}, [George Cholankeril](#)¹, [Abbas Rana](#)⁶, [Avegail Flores](#)¹, [Donna Smith](#)^{3,4}, [Yumei Cao](#)^{2,3,4}, [Bettina Beech](#)⁷, [Steven M Asch](#)^{8,9}

Affiliations expand

- PMID: 37561079
- DOI: [10.14309/ajg.0000000000002472](https://doi.org/10.14309/ajg.0000000000002472)

Abstract

Introduction: There are limited longitudinal data on the cost of treating patients with cirrhosis, which hampers value-based improvement initiatives.

Methods: We conducted a retrospective cohort study of patients with cirrhosis seen in the Veterans Affairs health care system from 2011 to 2015. Patients were followed up through 2019. We identified a sex-matched and age-matched control cohort without cirrhosis. We estimated incremental annual health care costs attributable to cirrhosis for 4 years overall and in subgroups based on severity (compensated, decompensated), cirrhosis complications (ascites, encephalopathy, varices, hepatocellular cancer, acute kidney injury), and comorbidity (Deyo index).

Results: We compared 39,361 patients with cirrhosis with 138,964 controls. The incremental adjusted costs for caring of patients with cirrhosis were \$35,029 (95% confidence interval \$32,473-\$37,585) during the first year and ranged from \$14,216 to \$17,629 in the subsequent 3 years. Cirrhosis complications accounted for most of these costs. Costs of managing patients with hepatic encephalopathy (year 1 cost, \$50,080) or ascites (\$50,364) were higher than the costs of managing patients with varices (\$20,488) or hepatocellular cancer (\$37,639) in the first year. Patients with acute kidney injury or those who had multimorbidity were the most costly at \$64,413 and \$66,653 in the first year, respectively.

Discussion: Patients with cirrhosis had substantially higher health care costs than matched controls and multimorbid patients had even higher costs. Cirrhosis complications accounted for most of the excess cost, so preventing complications has the largest potential for cost saving and could serve as targets for improvement.

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- [36 references](#)

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Observational Study

J Surg Res

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. 2023 Nov;291:660-669.

doi: 10.1016/j.jss.2023.06.049. Epub 2023 Aug 7.

Emergency Surgery, Multimorbidity and Hospital-Free Days: A Retrospective Observational Study

[Claire B Rosen](#)¹, [Sanford E Roberts](#)², [Chris J Wirtalla](#)³, [Luke J Keele](#)³, [Elinore J Kaufman](#)⁴, [Scott Halpern](#)⁵, [Rachel R Kelz](#)⁴

Affiliations expand

- PMID: 37556878
- PMCID: PMC10530175 (available on 2024-11-01)
- DOI: [10.1016/j.jss.2023.06.049](https://doi.org/10.1016/j.jss.2023.06.049)

Abstract

Introduction: Analyzing hospital-free days (HFDs) offers a patient-centered approach to health services research. We hypothesized that, within emergency general surgery (EGS), multimorbidity would be associated with fewer HFDs, whether patients were managed operatively or nonoperatively.

Methods: EGS patients were identified using national Medicare claims data (2015-2018). Patients were classified as multimorbid based on the presence of a Qualifying Comorbidity Set and stratified by treatment: operative (received surgery within 48 h of index admission) and nonoperative. HFDs were calculated through 180 d, beginning on the day of index

admission, as days alive and spent outside of a hospital, an Emergency Department, or a long-term acute care facility. Univariate comparisons were performed using Kruskal-Wallis tests and risk-adjusted HFDs were compared between multimorbid and nonmultimorbid patients using multivariable zero-inflated negative binomial regression models.

Results: Among 174,891 operative patients, 45.5% were multimorbid. Among 398,756 nonoperative patients, 59.2% were multimorbid. Multimorbid patients had fewer median HFDs than nonmultimorbid patients among operative and nonoperative cohorts ($P < 0.001$). At 6 mo, among operative patients, multimorbid patients had 6.5 fewer HFDs ($P < 0.001$), and among nonoperative patients, multimorbid patients had 7.9 fewer HFDs ($P < 0.001$). When length of stay was included as a covariate, nonoperative multimorbid patients still had 7.9 fewer HFDs than nonoperative, nonmultimorbid patients ($P < 0.001$).

Conclusions: HFDs offer a patient-centered, composite outcome for claims-based analyses. For EGS patients, multimorbidity was associated with less time alive and out of the hospital, especially when patients were managed nonoperatively.

Keywords: Days alive and at home; Emergency general surgery; Hospital-free days; Multimorbidity; Outcomes; Treatment.

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Conflict of interest statement

Declarations of interest: None

- [37 references](#)

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. 2023 Nov 1:340:258-268.

doi: 10.1016/j.jad.2023.07.117. Epub 2023 Aug 2.

Urban-rural disparities in the prevalence and trends of depressive symptoms among Chinese elderly and their associated factors

[Yu Wu](#)¹, [Binbin Su](#)¹, [Chen Chen](#)¹, [Yihao Zhao](#)¹, [Panliang Zhong](#)¹, [Xiaoying Zheng](#)²

Affiliations expand

- PMID: 37536424
- DOI: [10.1016/j.jad.2023.07.117](https://doi.org/10.1016/j.jad.2023.07.117)

Free article

Abstract

Background: This study aimed to examine urban-rural disparities in the prevalence and trends of depressive symptoms (DS) among Chinese elderly and associated factors.

Methods: A total of 8025, 7808, and 4887 respondents aged 60 years and above were selected from the China Family Panel Studies (CFPS) in 2016, 2018, and 2020, respectively. DS was assessed using a short version of Center for Epidemiologic Studies Depression Scale (CES-D). Twenty-two associated factors from six categories were included in random forest (RF) models. All urban-rural comparisons were conducted based on good model performance.

Results: The DS prevalence among all rural elderly was significantly higher than corresponding urban elderly. This disparity continued to widen among younger elderly, while it continued to narrow among older elderly. The top 10 common leading factors were sleep quality, self-rated health, life satisfaction, memory ability, child relationship, IADL disability, marital status, educational level, and gender. Urban-rural disparities in sleep quality, interpersonal trust, and child relationship continued to widen, while disparities in multimorbidity, hospitalization status, and frequency of family dinner continued to narrow.

Limitation: This study may exist recall bias and lacks causal explanation.

Conclusions: Significant and continuing disparities in the DS prevalence were observed between urban and rural elderly in China, showing opposite trends in younger and older elderly. The top 10 leading associated factors for DS were nearly consistent across urban and rural elderly, with sleep quality having strongest contribution. Urban-rural disparities in associated factors also showed different trends. This study provides a reference for mental health promotion among Chinese elderly.

Keywords: Depressive symptoms; Elderly; Machine learning; Random forest; Urban-rural disparity.

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Conflict of interest statement

Declaration of competing interest There are no actual or potential conflicts of interest, including any financial, personal, or other relationships with other people or organizations.

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Publication types, MeSH termsexpand

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J Gerontol A Biol Sci Med Sci

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. 2023 Oct 28;78(11):2162-2169.

doi: 10.1093/gerona/glad178.

[Bidirectional Association Between Multimorbidity and Frailty and the Role of Depression in Older Europeans](#)

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

Affiliations expand

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

Abstract

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

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

Results: There was a bidirectional relationship between frailty and multimorbidity. More severe multimorbidity predicted greater frailty ($\beta = 0.159$; $p < .001$) and vice versa ($\beta = 0.107$; $p < .001$). All paths from multimorbidity to frailty were stronger than the paths from frailty to multimorbidity ($b1-a1$: $\beta = 0.051$; $p < .001$). Likewise, early multimorbidity change was a significant predictive factor for late frailty change ($\beta = 0.064$; $p < .001$) and vice versa ($\beta = 0.048$; $p < .001$). Depression in Wave 5 (T5) mediated the association between frailty in Wave 4 (T4) and multimorbidity in Wave 6 (T6; indirect effect: $\beta = 0.004$; bootstrap 95% confidence interval: 0.003, 0.006).

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

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

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J Formos Med Assoc

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. 2023 Nov;122(11):1224-1225.

doi: 10.1016/j.jfma.2023.07.009. Epub 2023 Jul 21.

[Comment on "Multimorbidity and prior falls correlate with risk of 30-day hospital readmission in aged 80+: A prospective cohort study"](#)

[Lina Liu](#)¹, [Suzhi Liu](#)²

Affiliations [expand](#)

- PMID: 37481432

- DOI: [10.1016/j.jfma.2023.07.009](https://doi.org/10.1016/j.jfma.2023.07.009)

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No abstract available

Conflict of interest statement

Declaration of competing interest The authors have no conflicts of interest relevant to this article.

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Clin Lung Cancer

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. 2023 Nov;24(7):e259-e267.e8.

doi: 10.1016/j.clc.2023.06.004. Epub 2023 Jun 14.

[Comparison of Stage I Non-Small-Cell Lung Cancer Treatments for Patients Living With HIV: A Simulation Study](#)

[Keith Sigel](#)¹, [Michael J Silverberg](#)², [Kristina Crothers](#)³, [Lesley Park](#)⁴, [Inna Lishchenko](#)⁵, [Xuesong Han](#)⁶, [Wendy Leyden](#)², [Minal Kale](#)⁵, [Kimberly Stone](#)⁵, [Carlie Sigel](#)⁷, [Juan Wisnivesky](#)⁵, [Chung Yin Kong](#)⁵

Affiliations [expand](#)

- PMID: 37407294
- DOI: [10.1016/j.clcc.2023.06.004](https://doi.org/10.1016/j.clcc.2023.06.004)

Abstract

Introduction: Non-small-cell lung cancer (NSCLC) is a leading cause of death for people living with HIV (PWH). Nevertheless, there are no clinical trial data regarding the management of early-stage lung cancer in PWH. Using data from large HIV and cancer cohorts we parameterized a simulation model to compare treatments for stage I NSCLC according to patient characteristics.

Materials and methods: To parameterize the model we analyzed PWH and NSCLC patient outcomes and quality of life data from several large cohort studies. Comparative effectiveness of 4 stage I NSCLC treatments (lobectomy, segmentectomy, wedge resection, and stereotactic body radiotherapy) was estimated using evidence synthesis methods. We then simulated trials comparing treatments according to quality adjusted life year (QALY) gains by age, tumor size and histology, HIV disease characteristics and major comorbidities.

Results: Lobectomy and segmentectomy yielded the greatest QALY gains among all simulated age, tumor size and comorbidity groups. Optimal treatment strategies differed by patient sex, age, and HIV disease status; wedge resection was among the optimal strategies for women aged 80 to 84 years with tumors 0 to 2 cm in size. Stereotactic body radiotherapy was included in some optimal strategies for patients aged 80 to 84 years with multimorbidity and in sensitivity analyses was a non-inferior option for many older patients or those with poor HIV disease control.

Conclusion: In simulated comparative trials of treatments for stage I NSCLC in PWH, extensive surgical resection was often associated with the greatest projected QALY gains although less aggressive strategies were predicted to be non-inferior in some older, comorbid patient groups.

Keywords: Comorbidities; Lobectomy; Microsimulation; Segmentectomy; Stereotactic body radiation; Wedge resection.

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Qual Life Res



. 2023 Nov;32(11):3269-3277.

doi: 10.1007/s11136-023-03473-3. Epub 2023 Jul 5.

Treatment burden and health-related quality of life of patients with multimorbidity: a cross-sectional study

[Eyob Alemayehu Gebreyohannes](#) ^{#1 2 3}, [Begashaw Melaku Gebresillassie](#) ⁴, [Frehiwot Mulugeta](#) ⁴, [Etsegenet Dessu](#) ⁴, [Tamrat Befekadu Abebe](#) ^{#5}

Affiliations expand

- PMID: 37405663
- PMCID: [PMC10522511](#)
- DOI: [10.1007/s11136-023-03473-3](#)

Free PMC article

Abstract

Purpose: The aim of this study was to investigate treatment burden and its relationship with health-related quality of life (HRQoL) among patients with multimorbidity (two or more chronic diseases) who were taking prescription medications and attending the

outpatient department of the University of Gondar Comprehensive Specialized Teaching Hospital.

Methods: A cross-sectional study was conducted between March 2019 and July 2019. Treatment burden was measured using the Multimorbidity Treatment Burden Questionnaire (MTBQ), while HRQoL was captured using the Euroqol-5-dimensions-5-Levels (EQ-5D-5L).

Results: A total of 423 patients participated in the study. The mean global MTBQ, EQ-5D index, and EQ-VAS scores were 39.35 (\pm 22.16), 0.83 (\pm 0.20), and 67.32 (\pm 18.51), respectively. Significant differences were observed in the mean EQ-5D-Index (F [2, 81.88] 33.1) and EQ-VAS (visual analogue scale) scores (F [2, 75.48] = 72.87) among the treatment burden groups. Follow up post-hoc analyses demonstrated significant mean differences in EQ-VAS scores across the treatment burden groups and in EQ-5D index between the no/low treatment burden and high treatment burden, as well as between the medium treatment burden and high treatment burden. In the multivariate linear regression model, every one SD increase in the global MTBQ score (i.e., 22.16) was associated with a decline of 0.08 in the EQ-5D index (β - 0.38, 95%CI - 0.48, - 0.28), as well as a reduction of 9.4 in the EQ-VAS score (β - 0.51, 95%CI -0.60, - 0.42).

Conclusion: Treatment burden was inversely associated with HRQoL. Health care providers should be conscious in balancing treatment exposure with patients' HRQoL.

Keywords: Cross-sectional studies; Multimorbidity; Patient-reported outcome measures; Polypharmacy; Quality of life; Treatment burden.

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Conflict of interest statement

Authors declare no competing interests.

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Ethn Health

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. 2023 Nov;28(8):1145-1160.

doi: 10.1080/13557858.2023.2224949. Epub 2023 Jun 18.

Chronic disease multimorbidity and substance use among African American men: veteran–non–veteran differences

[M Daniel Bennett Jr](#)¹, [Justin T McDaniel](#)², [David L Albright](#)³

Affiliations expand

- PMID: 37331990
- DOI: [10.1080/13557858.2023.2224949](https://doi.org/10.1080/13557858.2023.2224949)

Abstract

Objectives: The purpose of the study was to explore the extent to which prior military service may moderate the relationship between chronic disease multimorbidity and substance use among African American men in the United States.

Design: Data for this cross-sectional study was downloaded from the 2016–2019 United States (US) National Survey on Drug Use and Health. We estimated three survey-weighted multivariable logistic regression models, where use of each of the following substances served as the dependent variables: illicit drugs, opioids, and tobacco. Differences in these outcomes were examined along two primary independent variables: veteran status and multimorbidity (and an interaction term for these variables). We also controlled for the following covariates: age, education, income, rurality, criminal behavior, and religiosity.

Results: From the 37,203,237 (weighted N) African American men in the sample, approximately 17% reported prior military service. Veterans with ≥ 2 chronic diseases had higher rates of illicit drug use (aOR = 1.37, 95% CI = 1.01, 1.87; 32% vs. 28%) than non-

veterans with ≥ 2 chronic diseases. Non-veterans with one chronic disease had higher rates of tobacco use (aOR = 0.80, 95% CI = 0.69, 0.93; 29% vs. 26%) and opioid misuse (aOR = 0.49, 95% CI = 0.36, 0.67; 29% vs. 18%) than veterans with one chronic disease.

Discussion: Chronic disease multi-morbidity appears to be a context in which African American veterans may be at greater risk for certain undesirable health behaviors than African American non-veterans and at lower risk for others. This may be due to exposure to trauma, difficulty accessing care, socio-environmental factors, and co-occurring mental health conditions. These complex interactions may contribute to higher rates of SUDs among African American veterans compared to African American non-veterans.

Keywords: African American; chronic disease; substance use; veterans.

SUPPLEMENTARY INFO

MeSH termsexpand

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Qual Life Res

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. 2023 Nov;32(11):3099-3108.

doi: 10.1007/s11136-023-03458-2. Epub 2023 Jun 16.

[Response shift in parent-reported psychopathology in children with chronic physical illness](#)

[Tolulope T Sajobi](#)^{1,2}, [Olawale F Ayilara](#)³, [Gurkiran K Dhuga](#)⁴, [Mark A Ferro](#)⁴

Affiliations expand

- PMID: 37326699
- DOI: [10.1007/s11136-023-03458-2](https://doi.org/10.1007/s11136-023-03458-2)

Abstract

Purpose: Because physical-mental comorbidity in children is relatively common, this study tested for response shift (RS) in children with chronic physical illness using a parent-reported measure of child psychopathology.

Methods: Data come from Multimorbidity in Children and Youth across Life-course (MY LIFE), a prospective study of $n = 263$ children aged 2-16 years with physical illness in Canada. Parents provided information on child psychopathology using the Ontario Child Health Study Emotional Behavioral Scales (OCHS-EBS) at baseline and 24 months. Oort's structural equation modeling was used to test for different forms of RS in parent-reported assessments between baseline and 24 months. Model fit was evaluated using root mean square error of approximation (RMSEA), comparative fit index (CFI), and standardized root mean residual (SRMR).

Results: There were $n = 215$ (81.7%) children with complete data and were included in this analysis. Of these, $n = 105$ (48.8%) were female and the mean (SD) age was 9.4 (4.2) years. A two-factor measurement model provided good fit to the data [RMSEA (90% CI) = 0.05 (0.01, 0.10); CFI = 0.99; SRMR = 0.03]. Non-uniform recalibration RS was detected on the conduct disorder subscale of the OCHS-EBS. This RS effect had negligible impact on the longitudinal change in externalizing and internalizing disorders construct over time.

Conclusions: Response shift detected on the conduct disorder subscale of the OCHS-EBS, indicated that parents of children with physical illness may recalibrate their responses on child psychopathology over 24 months. Researchers and health professionals should be aware of RS when using the OCHS-EBS to assess child psychopathology over time.

Keywords: Children; Mental health; Multimorbidity; Physical health; Quality of life; Response shift.

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- [59 references](#)

SUPPLEMENTARY INFO

MeSH terms, Grants and funding expand

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Arch Gerontol Geriatr

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. 2023 Nov;114:105067.

doi: 10.1016/j.archger.2023.105067. Epub 2023 May 19.

[Multimorbidity patterns in the German general population aged 40 years and over](#)

[Massuma Amirzada](#)¹, [Elżbieta Buczak-Stec](#)², [Hans-Helmut König](#)³, [André Hajek](#)³

Affiliations expand

- PMID: 37257215
- DOI: [10.1016/j.archger.2023.105067](https://doi.org/10.1016/j.archger.2023.105067)

Abstract

Aim: The aim of this study was to identify and describe multimorbidity patterns among middle-aged and older community-dwelling individuals in Germany. Moreover, we aimed to determine potential gender differences in multimorbidity patterns.

Methods: We analysed data from the most recent (sixth) wave (2017) of the large nationally representative German Ageing Survey (DEAS). Altogether n = 6,554 individuals participated, mean age was 62.0 (ranging from 43 to 92 years). Latent Class Analysis was

performed to identify multimorbidity patterns, based on 13 chronic conditions and diseases. Multimorbidity was defined as the presence of at least two chronic conditions.

Results: Altogether, 53.3% of individuals were multimorbid. We identified and clinically described five multimorbidity patterns: the relatively healthy class (45.1%), the high morbidity class (10.8%), the arthrosis/inflammatory/mental illnesses class (20.6%), the hypertension-metabolic illness class (21.7%), and the cardiovascular/cancer class (1.7%). Our analysis revealed that women compared to men have higher relative risk (IRR = 1.61, 95% CI 1.25-2.06) of being in the arthrosis/inflammatory/mental illnesses class, compared to the relatively healthy class. Furthermore, we found that, depending on which multimorbidity pattern individuals belong to, they differ greatly in terms of socio-demographic factors, health behaviour, and lifestyle factors.

Conclusions: We showed that the many chronic diseases cluster in a non-random way. Five clinically meaningful multimorbidity patterns were identified. Gender differences were apparent only in one class, namely in the arthrosis/inflammatory/mental illnesses class.

Keywords: LCA; Latent class analysis; Multimorbidity clusters; Multimorbidity patterns; Multiple chronic conditions; Old age.

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Conflict of interest statement

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

SUPPLEMENTARY INFO

MeSH termsexpand

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[Review](#)



Observed daytime sleepiness in in-hospital geriatric patients and risk of falls

[Jeanina Schlitzer](#)¹, [Michaela Friedhoff](#)², [Barbara Nickel](#)², [Helmut Frohnhofer](#)^{3,4}

Affiliations expand

- PMID: 37222819
- DOI: [10.1007/s00391-023-02191-2](https://doi.org/10.1007/s00391-023-02191-2)

Abstract

in [English](#), [German](#)

Background: Daytime sleepiness and falls are frequent in geriatric in-hospital patients; however, the relationship between both events is not clear. To test the hypothesis that observed daytime sleepiness is associated with falls in geriatric in-hospital patients data collected from medical records of patients who were admitted to an acute geriatric department were retrospectively analyzed.

Methods: The data from the medical records of patients who were admitted to the geriatric department of the Alfried-Krupp-Hospital in Essen, Germany in the period from January 2018 to March 2020 were retrospectively analyzed. Personal data, data concerning the geriatric assessment, observed daytime sleepiness, and falls were recorded.

Results: From a total of 1485 patients who were consecutively admitted to hospital, the data of 1317 (87%) patients could be included for further analysis. During the hospital stay 146 (11%) patients fell at least once, 35 (3%) patients had more than 1 fall and 64 falls (44%) occurred while patients were standing (bipedal fall). Daytime sleepiness was observed in 73% of the patients with bipedal falls and in 65% patients with nonbipedal falls ($p < 0.01$). Falls correlated significantly with the history of a recent fall, the length of

hospital stay, the Barthel index (BI) on admission, the mini mental state examination (MMSE), dementia and observed daytime sleepiness. No correlation was found between falls and age, multimorbidity, and the number of drugs used. Drugs related to falls were medications to treat Parkinson's disease, antidepressants and neuroleptics. In a multiple logistic regression analysis in-hospital falls were significantly and independently associated with a history of falls, length of in-hospital stay, dementia, and observed daytime sleepiness.

Conclusion: Observed daytime sleepiness is associated with in-hospital falls in geriatric patients. Prospective interventional studies are needed to confirm this relationship, and to quantify the impact of sleepiness on the risk of falling. Additionally, the impact of treatment for observed daytime sleepiness on the risk of falling should be assessed. The assessment of sleepiness should become a routine task in geriatrics.

Keywords: Falls; Length of stay; Multimorbidity; Sleep disorders.

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J Gerontol A Biol Sci Med Sci

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. 2023 Oct 28;78(11):2127-2135.

doi: 10.1093/gerona/glad125.

Frailty, an Independent Risk Factor in Progression Trajectory of Cardiometabolic Multimorbidity: A Prospective Study of UK Biobank

[Tianqi Ma](#)^{1,2}, [Lingfang He](#)^{1,2}, [Yi Luo](#)^{1,2}, [Dihan Fu](#)^{1,2}, [Jiaqi Huang](#)^{3,4}, [Guogang Zhang](#)⁵, [Xunjie Cheng](#)^{1,2}, [Yongping Bai](#)^{1,2}

Affiliations expand

- PMID: 37170845
- DOI: [10.1093/gerona/glad125](https://doi.org/10.1093/gerona/glad125)

Abstract

Background: Although frailty was associated with cardiometabolic diseases (CMDs, including coronary heart disease, stroke, and diabetes here), there was no systematic analyses estimating its role in incidence, progression, and prognosis of cardiometabolic multimorbidity (CMM).

Methods: We included 351 205 participants without CMDs at baseline in UK Biobank. Occurrences of first CMD, CMM, and death were recorded. We used multistate models to assess transition-specific role of baseline frailty measured by frailty phenotype and frailty index in CMM progression trajectory from no disease to single CMD, CMM, and death. Association between changes in frailty and outcomes was investigated among 17 264 participants.

Results: Among 351 205 participants (44.0% male, mean age 56.55 years), 8 190 (2.3%) had frail phenotype, and 13 615 (3.9%) were moderate/severe frail according to the frailty index. During median follow-up of 13.11 years, 41 558 participants experienced ≥ 1 CMD, 4 952 had CMM, and 20 670 died. In multistate models, frail phenotype-related hazard ratios were 1.94 and 2.69 for transitions from no CMD to single disease and death, 1.63 and 1.67 for transitions from single CMD to CMM and death, and 1.57 for transitions from CMM to death (all $p < .001$). Consistent results were observed for frailty index. Improvement of frailty reduced the risk of CMD progression and death.

Conclusions: Frailty is an independent risk factor for all transitions of CMM progression trajectory. Frailty-targeted management is a potential strategy for primary and secondary prevention of CMM beyond chronological age.

Keywords: Cardiometabolic diseases; Multistate model; UK Biobank.

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J Formos Med Assoc



. 2023 Nov;122(11):1111-1116.

doi: 10.1016/j.jfma.2023.03.009. Epub 2023 Mar 27.

[Multimorbidity and prior falls correlate with risk of 30-day hospital readmission in aged 80+: A prospective cohort study](#)

[Yu-Chieh Tsai](#)¹, [Yung-Ming Chen](#)², [Chiung-Jung Wen](#)³, [Meng-Chen Wu](#)⁴, [Yi-Chun Chou](#)³, [Jen-Hau Chen](#)², [Kun-Pei Lin](#)², [Ding-Cheng Chan](#)², [Feng-Ping Lu](#)⁵

Affiliations expand

- PMID: 36990860

- DOI: [10.1016/j.jfma.2023.03.009](https://doi.org/10.1016/j.jfma.2023.03.009)

Free article

Abstract

Background/purpose: Thirty-day hospital readmission rate significantly raised with advanced age. The performance of existing predictive models for readmission risk remained uncertain in the oldest population. We aimed to examine the effect of geriatric conditions and multimorbidity on readmission risk among older adults aged 80 and over.

Methods: This prospective cohort study enrolled patients aged 80 and older discharged from a geriatric ward at a tertiary hospital, with phone follow-up for 12 months. Demographics, multimorbidity, and geriatric conditions were assessed before hospital discharge. Logistic regression models were conducted to analyse risk factors for 30-day readmission.

Results: Patients readmitted had higher Charlson comorbidity index scores, and were more likely to have falls, frailty, and longer hospital stay, compared to those without 30-day readmission. Multivariate analysis revealed that higher Charlson comorbidity index score was associated with readmission risk. Older patients with a fall history within 12 months had a near 4-fold increase in readmission risk. Severe frailty status before index admission was associated with a higher 30-day readmission risk. Functional status at discharge was not associated with readmission risk.

Conclusion: In addition to multimorbidity, history of falls and frailty were associated with higher hospital readmission risk in the oldest.

Keywords: Aged; Falls; Frailty; Hospital readmissions; Multimorbidity.

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Conflict of interest statement

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

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Child Care Health Dev



. 2023 Nov;49(6):972-984.

doi: 10.1111/cch.13108. Epub 2023 Feb 28.

[A cross-sectional study of the association between family conflicts and children's health: Lolland-Falster Health Study](#)

[Elisabeth Søndergaard](#)¹, [Susanne Reventlow](#)¹, [Volkert Siersma](#)¹, [Dagny Ros Nicolaisdottir](#)¹, [Randi Jepsen](#)², [Knud Rasmussen](#)³, [Anne Møller](#)¹

Affiliations expand

- PMID: 36805605
- DOI: [10.1111/cch.13108](https://doi.org/10.1111/cch.13108)

Abstract

Background: Few family interaction processes are more detrimental to children's health than family conflicts. Conflictual relationships in childhood predict a host of adverse health outcomes across the life course. The current study examines associations between household conflicts and the health of children aged 6-12 years and explores to which extent this may vary by socioeconomic status (SES) and multimorbidity (MM) in the household.

Methods: Cross-sectional study using questionnaire data gathered between 2016 and 2020 as part of the Lolland-Falster Health Study (LOFUS) combined with routine register data on health care use and socio-demography from the Danish nationwide administrative databases. The study sample consisted of 1065 children 6-12 years old, who answered LOFUS4 or LOFUS11, from 777 households for which at least one adult answered LOFUS18.

Main outcome was children's health complaints, defined as headache, abdominal pain, back pain, and sleep difficulties. Covariates included MM, SES, and conflicts, all three measured at household level. Multivariable logistic regression models were used.

Results: Conflicts were negatively associated with children's health. This was most pronounced for general conflicts in the household, with increased complaints of abdominal pain, back pain, and sleep difficulties. The associations varied when we stratified the households according to MM and SES. Significant associations were found within households without MM for abdominal pain, and within households with MM and low SES, and without MM and with high SES for sleep difficulties. While the higher level of abdominal pain for the above indicated households were found for both internal and external conflicts in the household, the higher level in sleep difficulties was mostly driven by internal conflicts.

Conclusion: Children reporting frequent health complaints have a higher future health care use compared with children without such complaints. Our results indicate that growing up in a household with a high conflict level might be a predisposing factor.

Trial registration: ClinicalTrials.gov [NCT02482896](https://clinicaltrials.gov/ct2/show/study/NCT02482896).

Keywords: child public health; cross-sectional study; family functioning; parental illness; socio-economic status.

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- [63 references](#)

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Publication types, MeSH terms, Associated dataexpand

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Eur Child Adolesc Psychiatry

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. 2023 Nov;32(11):2129-2138.

doi: 10.1007/s00787-022-02041-3. Epub 2022 Aug 4.

The association between early childhood onset epilepsy and attention-deficit hyperactivity disorder (ADHD) in 3237 children and adolescents with Autism Spectrum Disorder (ASD): a historical longitudinal cohort data linkage study

[Lauren Carson](#)¹, [Valeria Parlatini](#)², [Tara Safa](#)³, [Benjamin Baig](#)⁴, [Hitesh Shetty](#)³, [Jacqueline Phillips-Owen](#)⁴, [Vibhore Prasad](#)^{#5}, [Johnny Downs](#)^{#4,3}

Affiliations expand

- PMID: 35927526
- PMCID: [PMC10576710](#)
- DOI: [10.1007/s00787-022-02041-3](#)

Free PMC article

Abstract

Children and young people with Autism Spectrum Disorder (ASD) have an increased risk of comorbidities, such as epilepsy and Attention-Deficit/Hyperactivity Disorder (ADHD). However, little is known about the relationship between early childhood epilepsy (below age 7) and later ADHD diagnosis (at age 7 or above) in ASD. In this historical cohort study, we examined this relationship using an innovative data source, which included linked data from routinely collected acute hospital paediatric records and childhood community and inpatient psychiatric records. In a large sample of children and young people with ASD (N

= 3237), we conducted a longitudinal analysis to examine early childhood epilepsy as a risk factor for ADHD diagnosis while adjusting for potential confounders, including socio-demographic characteristics, intellectual disability, family history of epilepsy and associated physical conditions. We found that ASD children and young people diagnosed with early childhood epilepsy had nearly a twofold increase in risk of developing ADHD later in life, an association which persisted after adjusting for potential confounders (adjusted OR = 1.72, CI95% = 1.13-2.62). This study suggests that sensitive monitoring of ADHD symptoms in children with ASD who have a history of childhood epilepsy may be important to promote early detection and treatment. It also highlights how linked electronic health records can be used to examine potential risk factors over time for multimorbidity in neurodevelopmental conditions.

Keywords: ADHD; ASD; Childhood epilepsy; Data Linkage.

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Conflict of interest statement

Authors have no competing interests to declare.

Comment in

- [Ripples of Hyperexcitability in Epilepsy, Autism, and Inattention.](#) Salpekar JA. *Epilepsy Curr.* 2023 Jan 23;23(2):97-98. doi: 10.1177/15357597221147351. eCollection 2023 Mar-Apr. PMID: 37122401 **Free PMC article.** No abstract available.
- [Cited by 2 articles](#)
- [47 references](#)
- [1 figure](#)

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

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. 2023 Nov;15(8):1315-1323.

doi: 10.1037/tra0001271. Epub 2022 Jun 2.

The transition to civilian life: Impact of comorbid PTSD, chronic pain, and sleep disturbance on veterans' social functioning and suicidal ideation

[Rachel Shor](#)¹, [Shelby Borowski](#)¹, [Rachel L Zelkowitz](#)¹, [Suzanne L Pineles](#)¹, [Laurel A Copeland](#)², [Erin P Finley](#)³, [Daniel F Perkins](#)⁴, [Dawne Vogt](#)¹

Affiliations expand

- PMID: 35653743
- PMCID: PMC10231656 (available on 2024-11-01)
- DOI: [10.1037/tra0001271](https://doi.org/10.1037/tra0001271)

Abstract

Objective: Trauma-exposed veterans may be more likely to experience posttraumatic stress disorder (PTSD), chronic pain, and sleep disturbance together rather than in isolation. Although these conditions are independently associated with distress and impairment, how they relate to social functioning and suicidal ideation (SI) when experienced comorbidly is not clear.

Method: Using longitudinal data on 5,461 trauma-exposed U.S. veterans from The Veterans Metrics Initiative study and self-reported disorders, we assessed (a) the extent to which PTSD co-occurs with sleep disturbance and chronic pain (CP); (b) the relationship of PTSD in conjunction with sleep disturbance and chronic pain with later social functioning

and SI; and (c) the extent to which social functioning mediates the impact of multimorbidity on SI.

Results: At approximately 15 months postseparation, 90.5% of veterans with probable PTSD also reported sleep disturbance and/or CP. Relative to veterans without probable PTSD, veterans with all 3 conditions ($n = 907$) experienced the poorest social functioning ($B = -.56, p < .001$) and had greater risk for SI ($OR = 3.78, p < .001$); Social functioning partially mediated the relationship between multimorbidity and SI. However, relative to those with PTSD alone, sleep disturbance and CP did not confer greater risk for SI.

Conclusions: Although these findings underscore the impact of PTSD on functioning and SI, they also highlight the complexity of multimorbidity and the importance of bolstering social functioning for veterans. (PsycInfo Database Record (c) 2023 APA, all rights reserved).

- [Cited by 1 article](#)
- [46 references](#)

SUPPLEMENTARY INFO

MeSH terms, Grants and funding expand

FULL TEXT LINKS



(premature birth OR "Premature Birth"[Mesh])

Sci Rep

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. 2023 Nov 3;13(1):18990.

doi: 10.1038/s41598-023-46271-0.

[Effects of heavy metal exposure during pregnancy on birth outcomes](#)

[Sabrina Shafi Zinia](#)¹, [Ki-Hyeok Yang](#)¹, [Eun Ju Lee](#)¹, [Myoung-Nam Lim](#)¹, [Jeeyoung Kim](#)¹, [Woo Jin Kim](#)²; [Ko-CHENS Study group](#)

Collaborators, Affiliations expand

- PMID: 37923810
- DOI: [10.1038/s41598-023-46271-0](https://doi.org/10.1038/s41598-023-46271-0)

Abstract

Exposure to heavy metals such as lead, cadmium, and mercury poses serious health risks to pregnant women because of their high toxicity. In this study, we investigated the associations of heavy metal exposure with birth outcomes of Korean infants. Data of 5,215 women between 2015 and 2019 were analyzed. This study was part of the Korean Children's Environmental Health (Ko-CHENS) study. Linear regression and logistic regression analyses were used to examine effects of concentrations of lead, cadmium, and mercury on birth weight, small for gestational age, and large for gestational age after adjusting for maternal age groups, parity, infant sex, education, income, smoking, drinking, body mass index, stillbirth, premature birth, diabetes, hypertension, and gestational diabetes. Besides adjusting for these covariates, each metal was mutually adjusted to estimate birth weight and large for gestational age status. Maternal cadmium concentrations during early pregnancy ($\beta = -39.96$; 95% confidence interval (CI): -63.76, -16.17) and late pregnancy ($\beta = -37.24$; 95% CI -61.63, -12.84) were significantly associated with birth weight. Cadmium levels during early pregnancy (adjusted OR = 0.637; 95% CI 0.444, 0.912) were also associated with large for gestational age status. Our findings suggest that prenatal cadmium exposure, even at a low level of exposure, is significantly associated with low birth weight.

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- [49 references](#)

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Review

Arch Gynecol Obstet

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. 2023 Nov 3.

doi: 10.1007/s00404-023-07259-3. Online ahead of print.

Impact of Sjögren's syndrome on maternal and fetal outcomes following pregnancy: a systematic review and meta-analysis of studies published between years 2007–2022

[Yang Yang](#)¹, [Xin-Xiang Huang](#)¹, [Rong-Xiu Huo](#)¹, [Jin-Ying Lin](#)²

Affiliations expand

- PMID: 37921880
- DOI: [10.1007/s00404-023-07259-3](https://doi.org/10.1007/s00404-023-07259-3)

Abstract

Objective: To show the impact of Sjögren's syndrome (SS) on maternal and fetal outcomes following pregnancy.

Methods: We performed a literature search based on PubMed, Web of science, Wan fang, China National Knowledge Infrastructure and ProQuest databases from 1 January 2007 to 6 November 2022. Grading of Recommendations, Assessment, Development, and Evaluations approach was used to assess the certainty of the evidence. Systematic reviews and meta-analyses were performed using RevMan 5.3 software. Pooled odds ratio (OR)

and 95% confidence interval (CI) were calculated using a random-effect, generic inverse variance method of DerSimonian and Laird. Trial sequential analyses were performed by TSA 0.9.

Results: Nine studies with 2341 patients and 2472 pregnancies with SS were included in our analysis. This current analysis showed pregnancy hypertension and preeclampsia/eclampsia to be significantly higher in pregnant women with SS compared to pregnant women without SS (OR: 1.65, 95% CI: 1.04-2.63; P = 0.03), (OR: 2.06, 95% CI: 1.16-3.65; P = 0.01) respectively. Cesarean section, thromboembolic disease, premature rupture of membranes, and spontaneous abortion were also significantly higher in the SS women with OR: 2.07, 95% CI: 1.48-2.88; P < 0.0001, OR: 9.45, 95% CI: 1.99-44.87; P = 0.005, OR: 1.36, 95% CI: 1.13-1.64; P = 0.001, OR: 9.30, 95% CI: 4.13-20.93; P < 0.00001, respectively. Significantly higher premature births were observed with infants who were born from SS mothers (OR: 2.19, 95% CI: 1.54-3.12; P < 0.0001). Infants defined as 'small for gestational age/intrauterine growth restriction' and 'weighing < 2500 g' were also significantly higher in patients suffering from SS (OR: 2.26, 95% CI: 1.38-3.70; P = 0.001), (OR: 3.84, 95% CI: 1.39-10.61; P = 0.009) respectively. In addition, live birth significantly favored infants who were born from mothers without SS (OR: 21.53, 95% CI: 8.36-55.44; P < 0.00001). Subgroup analysis by sample size revealed that pregnancy hypertension risk has significantly increased in small cohort (OR: 2.74, 95%CI: 1.45-5.18), and a slight increase was found in population-based studies (OR: 1.14, 95%CI: 0.91-1.43). In both small cohorts and population-based researches, cesarean section was significantly higher in SS (OR: 2.13, 95% CI: 1.29, 3.52; OR: 1.85, 95% CI: 1.29-2.64, respectively). The number of infants with intrauterine growth restriction did not grow in the population-based researches (OR: 2.07, 95%CI: 0.92-4.66) although there has been an increase in small reports (OR: 2.53, 95%CI: 1.16-5.51). Subgroup analysis was conducted on the basis of study location (not Asian vs. Asian countries) indicated that cesarean section was significantly higher in SS in both countries (OR: 1.69, 95% CI: 1.31-2.18; OR: 3.37, 95% CI: 2.39-4.77, respectively).

Conclusion: This meta-analysis has shown SS to have a high impact on maternal and fetal outcomes following pregnancy.

Keywords: Fetal outcomes; Maternal outcomes; Meta-analysis; Pregnancy outcome; Sjögren's syndrome.

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JAMA Netw Open



. 2023 Nov 1;6(11):e2341033.

doi: 10.1001/jamanetworkopen.2023.41033.

[Use of Dexmedetomidine and Opioids in Hospitalized Preterm Infants](#)

[Samantha Curtis](#)¹, [Ryan Kilpatrick](#)^{1,2}, [Zeenia C Billimoria](#)³, [Kanecia Zimmerman](#)^{1,2}, [Veeral Tolia](#)⁴, [Reese Clark](#)⁵, [Rachel G Greenberg](#)^{1,2}, [Mihai Puia-Dumitrescu](#)³

Affiliations expand

- PMID: 37921767
- PMCID: [PMC10625033](#)
- DOI: [10.1001/jamanetworkopen.2023.41033](#)

Abstract

Importance: Dexmedetomidine, an α 2-adrenergic agonist, is not approved by the Food and Drug Administration for use in premature infants. However, the off-label use of dexmedetomidine in premature infants has increased 50-fold in the past decade. Currently, there are no large studies characterizing dexmedetomidine use in US neonatal intensive care units (NICUs) or comparing the use of dexmedetomidine vs opioids in infants.

Objectives: To describe dexmedetomidine use patterns in the NICU and examine the association between dexmedetomidine and opioid use in premature infants.

Design, setting, and participants: A multicenter, observational cohort study was conducted from November 11, 2022, to April 4, 2023. Participants were inborn infants born between 22 weeks, 0 days, and 36 weeks, 6 days, of gestation at 1 of 383 Pediatrix Medical Group NICUs across the US between calendar years 2010 and 2020.

Main outcome and measure: Exposure to medications of interest defined as total days of exposure, timing of use, and changes over time.

Results: A total of 395 122 infants were included in the analysis. Median gestational age was 34 (IQR, 32-35) weeks, and median birth weight was 2040 (IQR, 1606-2440) g. There were 384 infants (0.1% of total; 58.9% male) who received dexmedetomidine. Infants who received dexmedetomidine were born more immature, had lower birth weight, longer length of hospitalization, more opioid exposure, and more days of mechanical ventilation. Dexmedetomidine use increased from 0.003% in 2010 to 0.185% in 2020 ($P < .001$ for trend), while overall opioid exposure decreased from 8.5% in 2010 to 7.2% in 2020 ($P < .001$ for trend). The median postmenstrual age at first dexmedetomidine exposure was 31 (IQR, 27-36) weeks, and the median postnatal age at first dexmedetomidine exposure was 3 (IQR, 1-35) days. The median duration of dexmedetomidine receipt was 6 (IQR, 2-14) days.

Conclusion and relevance: The findings of this multicenter cohort study of premature infants suggest that dexmedetomidine use increased significantly between 2010 and 2020, while overall opioid exposure decreased. Future studies are required to further examine the short- and long-term effects of dexmedetomidine in premature and critically ill infants.

Conflict of interest statement

Conflict of Interest Disclosures: Dr Zimmerman reported receiving grants from the National Institutes of Health during the conduct of the study and personal fees from National Medical Association for speaking engagements outside the submitted work. Dr Greenberg reported receiving consulting fees from Provepharm Inc and Tellus Therapeutics outside the submitted work. No other disclosures were reported.

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

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J Mother Child



. 2023 Nov 3;27(1):158-167.

doi: 10.34763/jmotherandchild.20232701.d-23-00056. eCollection 2023 Jun 1.

[The Involvement of Neonatal Intensive Care Unit and Other Perinatal Factors in Postpartum PTSD After Cesarean Section](#)

[Eirini Orovou](#)^{1,2}, [Panagiotis Eskitzis](#)², [Irina Mrvoljak-Theodoropoulou](#)³, [Maria Tzitiridou-Chatzopoulou](#)², [Christiana Arampatzi](#)², [Nikolaos Rigas](#)¹, [Ermioni Palaska](#)¹, [Maria Dagla](#)¹, [Maria Iliadou](#)¹, [Evangelia Antoniou](#)¹

Affiliations expand

- PMID: 37920113
- PMCID: [PMC10623112](#)
- DOI: [10.34763/jmotherandchild.20232701.d-23-00056](#)

Abstract

Background: The experience of a neonate hospitalised in the Neonatal Intensive Care Unit (NICU) is an understandably traumatic experience for the parents, especially, for the mothers of neonates. This mental distress resulting from preterm birth and/or NICU hospitalisation can be understood as post-traumatic symptomatology, according to the Diagnostic and Statistical Manual-5 version. The aim of this study is to investigate the impact of the admission of a neonate to the NICU (from any reason) on the development

of postpartum post-traumatic stress disorder (PTSD) in a sample of women after cesarean sections.

Material and methods: A total of 469 women who gave birth with cesarean section from July 2019 to June 2020 participated in this study, from the original sample of 490 women who consented to participate. Data were obtained from the researcher's socio-demographic questionnaire, the past traumatic Life Events Checklist, the perinatal stressor Criterion A, and the Post-Traumatic Stress Checklist from the Diagnostic and Statistical Manual-5 version.

Results: A percentage of 46.64% of sample experienced postpartum PTSD. Factors associated with PTSD were placenta previa type4, abruption, bleeding ($\beta = .07$, $p = .049$), premature contractions ($\beta = .08$, $p = .039$), heavy medical history or previous gynecological history and preeclampsia ($\beta = .08$, $p = .034$), abnormal heart rate, premature rupture of membrane, premature contractions, infections ($\beta = .14$, $p = .004$), life of child in danger ($\beta = .12$, $p = .025$), complications involving child ($\beta = .15$, $p = .002$), complications involving both (child and mother) ($\beta = .12$, $p = .011$), traumatic cesarean section ($\beta = .041$, $p < .001$) and prematurity ($\beta = .12$, $p = .022$).

Conclusions: Additional measures must be taken for mothers of children who have been admitted to the NICU with psychological support interventions and reassessment of their mental state.

Keywords: NICU; Neonatal intensive care unit; birth trauma; cesarean section; hospitalised neonate; postpartum PTSD; traumatic birth experience.

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- [48 references](#)

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J Mother Child

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. 2023 Nov 3;27(1):168-175.

doi: 10.34763/jmotherandchild.20222601.d-23-00017. eCollection 2023 Jun 1.

Placental Findings in Infants Gestational Age < 34 Weeks and Impact on Short-Term Outcomes

[Krešimir Šantić](#)^{1,2}, [Borna Biljan](#)^{1,2}, [Martina Kos](#)^{1,2}, [Ivana Serdarušić](#)^{1,2}, [Jasmina Rajc](#)^{2,3}, [Darjan Kardum](#)^{2,4}

Affiliations expand

- PMID: 37920111
- PMCID: [PMC10623114](#)
- DOI: [10.34763/jmotherandchild.20222601.d-23-00017](#)

Abstract

Aim: To analyse placental changes in infants' gestational age < 34 weeks and its correlation to short-term respiratory outcomes or death until hospital discharge.

Material and methods: Information regarding all in-house born preterm infants born before 34 weeks gestation and born from January 2009 until December 2014 were collected and included among others, placental pathology and relevant data on demographics and outcomes of infants.

Results: Placental abnormalities was found in 157/253 (65.05%) cases. Acute placental inflammation was found to be the most common in both groups of premature neonates, followed by maternal vascular underperfusion. Maternal vascular underperfusion was significantly more common in GA \leq 27 weeks compared to infants GA 28-33 weeks (35.2% vs. 13.7%; $p = 0.018$). Similarly, chronic placental inflammation was more common in infants GA \leq 27 weeks compared to infants GA 28-33 weeks (14.3% vs. 3.3%; $p = 0.014$). Infants with placental pathology had a lower median birth weight (1460g vs. 1754g; $p = 0.001$, and were of shorter median GA at birth (31 vs. 32; $p = 0.001$). Infants with any placental disease had higher rates of death until hospital discharge (10.2% vs. 3.1%; $p = 0.039$) and higher rates of any stage of bronchopulmonary dysplasia (41.4% vs. 26.0%; $p =$

0.013). There were no significant differences in mechanical ventilation rates, duration of mechanical ventilation and duration of supplemental oxygen therapy.

Conclusion: Identifiable placental abnormalities were found in most infants born < 34 weeks gestation. Placental pathology is associated with increased rates of bronchopulmonary dysplasia and death until hospital discharge.

Keywords: bronchopulmonary dysplasia; death until discharge; neonatal; oxygen therapy; placenta; premature neonates.

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Conflict of interest statement

Conflicts of interest
Nothing to declare.

- [50 references](#)

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BMJ Glob Health

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. 2023 Nov;8(11):e012413.

doi: 10.1136/bmjgh-2023-012413.

[Occupational health hazards of bidi workers and their families in India: a scoping review](#)

[Jyoti Tyagi](#)¹, [Deepti Beri](#)², [Samiksha Ingale](#)³, [Praveen Sinha](#)⁴, [Soumyadeep Bhaumik](#)^{1,3}

Affiliations expand

- PMID: 37918876
- DOI: [10.1136/bmjgh-2023-012413](https://doi.org/10.1136/bmjgh-2023-012413)

Free article

Abstract

Background: Bidi workers and their families are exposed to harmful substances during bidi rolling, thereby jeopardising their health. We aimed to assess existing evidence on health conditions of bidi workers and their families in India.

Methods: We searched nine databases and relevant websites, and conducted citation screening to identify primary studies assessing occupational health hazards of bidi workers and their families. Two authors independently conducted screening and data extraction. We synthesised the findings narratively in a structured fashion.

Results: We found 3842 studies, out of which 95 studies met our eligibility criteria. High prevalence of disease conditions across all organ systems of the body was reported in bidi workers. Studies on female bidi workers showed decreased fertility (n=2), increased frequency of miscarriages (n=1) and higher risk of cervical cancer (n=1). Pregnant bidi workers were at an increased risk of anaemia and pregnancy-induced hypertension (n=2), higher frequency of neonatal deaths (n=1), stillbirths (n=1) and premature births (n=1) in comparison with non-bidi workers. Babies born to bidi workers reported low birth weight (n=5). Evidence from cohort studies suggests causal nature of the exposure to the disease condition.

Conclusion: Our review shows that bidi rolling leads to numerous occupational health hazards in bidi workers and their family members. It is essential to provide alternative livelihoods, and safe and protective working environment, and cover bidi workers under various social security provisions to alleviate the deleterious effect of bidi making at home. It is also important to shift bidi making away from home and strengthen existing regulations and promulgation of new provisions, including India's Occupational Safety, Health, and Working Conditions Code 2020.

Keywords: Health systems; Public Health; Systematic review.

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Conflict of interest statement

Competing interests: None declared.

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Ultrasound Q

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. 2023 Nov 1.

doi: 10.1097/RUQ.0000000000000658. Online ahead of print.

[The Right Ventricular Fetal Tricuspid Annular Plane Systolic Excursion Index Is a New Index for Evaluating Fetal Cardiac Function of Gestational Hypertension](#)

[Shao-Zheng He](#)¹, [Fang-Ping Lai](#)¹, [Piao-Yi Zeng](#)¹, [Shi-Jie Zhang](#)¹, [Guo-Rong Lyu](#)¹

Affiliations expand

- PMID: 37918115
- DOI: [10.1097/RUQ.0000000000000658](https://doi.org/10.1097/RUQ.0000000000000658)

Abstract

The right ventricular fetal tricuspid annular plane systolic excursion index (FTI) can be used to evaluate right ventricular systolic function. The purpose of this study was to establish

the reference range of the FTI in normal fetuses and evaluate its diagnostic value in hypertensive disorders during pregnancy. In this prospective observational study, the right ventricular FTI was measured in 208 normal single-gestation fetuses between 20 and 40 weeks. With the increase in gestational age, the right ventricular FTI did not significantly fluctuate. With the increase in the severity of HDCP, the right ventricular FTI decreased gradually. Compared with the normal group, the low right ventricular FTI group had a higher incidence of premature delivery and emergency delivery due to continuous abnormal fetal heart monitoring, but there were no significant differences in low birth weight, new born Apgar score less than 7 in 5 minutes, or admission to the neonatal intensive care unit. The FTI of the right ventricle of normal fetuses is relatively constant at different gestational weeks. The right ventricular FTI can be used to evaluate fetal cardiac function changes in pregnant women with HDCP.

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Conflict of interest statement

The authors declare no conflicts of interest.

- [22 references](#)

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Curationis

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. 2023 Oct 26;46(1):e1-e8.

doi: 10.4102/curationis.v46i1.2409.

[Support needs of parents with preterm infants at resource-limited neonatal](#)

units in Limpopo province: A qualitative study

[Thendo Mahwasane¹](#), [Khathutshelo G Netshisaulu](#), [Thivhulawi N Malwela](#), [Maria S Maputle](#)

Affiliations expand

- PMID: 37916665
- PMCID: [PMC10623485](#)
- DOI: [10.4102/curationis.v46i1.2409](#)

Abstract

Background: Preterm birth is often unexpected and life-threatening for the baby and/or the mother. When admitted to the hospital, midwives need to provide informational, instrumental, psycho-cultural and emotional support to enhance post-discharge care.

Objectives: This study aimed to explore and describe the support provided to parents of preterm infants in preparing for post-discharge care. The study was conducted in three district hospitals in the Mopani district, South Africa.

Method: A qualitative approach wherein explorative, descriptive and contextual designs were used. A non-probability, convenience sampling was used to select 23 midwives who were working in the maternity unit for at least 2 years. Data were collected through in-depth individual semi-structured interviews until data saturation was reached. The data were analysed through Tesch's open coding method. Trustworthiness was ensured through credibility, transferability and confirmability. Ethical principles adhered to were: informed consent, beneficence, right to self-determination, confidentiality and anonymity.

Results: The findings revealed that parents need informational, instrumental direct supervision, and psycho-cultural and emotional support during preparation for discharge.

Conclusion: Parents were unsure of their ability to care for the preterm infants after discharge and manage their own needs. The provision of informational, instrumental, psycho-cultural and emotional support needs would play a vital role in their ability to cope with their parental roles and the relationship with their infant. Contribution: The support provided to parents could build parental confidence and act as an integral part of neonatal follow-up programmes.

Keywords: discharge plan; midwives; neonatal unit; preterm infants; support needs.

Conflict of interest statement

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

- [30 references](#)

SUPPLEMENTARY INFO

MeSH termsexpand

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Eur Arch Otorhinolaryngol

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. 2023 Nov 2.

doi: 10.1007/s00405-023-08254-9. Online ahead of print.

[Profiling the clinical characteristics and surgical efficacy of laryngomalacia in children](#)

[Ling Xiao](#)¹²³, [Yang Yang](#)¹²³, [Ling Ding](#)¹²³, [Zihai Zhang](#)¹²³, [Xuelei Li](#)¹²³, [Hongbing Yao](#)¹²³, [Xinye Tang](#)⁴⁵⁶

Affiliations expand

- PMID: 37914898

- DOI: [10.1007/s00405-023-08254-9](https://doi.org/10.1007/s00405-023-08254-9)

Abstract

Objective: To analyze the clinical characteristics of laryngomalacia in Chinese children and explore the surgical efficacy and factors influencing severe laryngomalacia.

Methods: Children (0-18 years) diagnosed with laryngomalacia in our hospital from January 2016 to January 2022 were enrolled in this study. Clinical data of patients, including general conditions, clinical symptoms, grading and classification, medical comorbidities, surgical efficacy, and the risk factors influencing severe laryngomalacia were retrospectively analyzed.

Results: A total of 1810 children were enrolled (male:female; 2.02:1), among which most were infants under 1 year (77.18%). Inspiratory laryngeal stridor (69.56%) was the most common symptom. Most patients had mild laryngomalacia (79.28%), with type IV laryngomalacia being the most common classification (52.27%). Congenital heart disease (37.85%) was the most common medical comorbidity. A total of 168 severe laryngomalacia cases were treated via supraglottoplasty with an effective rate of 83.93%. Notably, preterm birth (OR = 3.868, 95% CI 1.340 ~ 11.168), low birth weight (OR = 4.517, 95% CI 1.477 ~ 13.819) and medical comorbidities (OR = 7.219, 95% CI 2.534 ~ 20.564) were independent risk factors for poor prognosis ($P < 0.05$).

Conclusion: Laryngomalacia is common among infants under the age of one, and it is mostly characterized by inspiratory laryngeal stridor with various medical comorbidity. Supraglottoplasty is the first treatment choice for severe laryngomalacia cases with high success rates. However, premature delivery, low birth weight, and medical comorbidities significantly affect the efficacy of surgery.

Keywords: Children; Inspiratory stridor; Laryngomalacia; Supraglottoplasty.

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- [27 references](#)

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Fertil Steril



. 2023 Oct 30:S0015-0282(23)01950-7.

doi: 10.1016/j.fertnstert.2023.10.028. Online ahead of print.

[Thick endometrium is associated with hypertensive disorders of pregnancy in programmed frozen-thawed embryo transfers: a retrospective analysis of 2275 singleton deliveries](#)

[Yue Meng](#)¹, [Huikun Chen](#)¹, [Xiya Zhang](#)¹, [Xiaoqi Lin](#)¹, [Jianping Ou](#)¹, [Weijie Xing](#)²

Affiliations expand

- PMID: 37914068
- DOI: [10.1016/j.fertnstert.2023.10.028](https://doi.org/10.1016/j.fertnstert.2023.10.028)

Abstract

Objective: To investigate whether endometrial thickness (EMT) acts as a contributing factor to adverse perinatal outcomes in programmed frozen-thawed embryo transfer (FET) cycles.

Design: Retrospective cohort study.

Setting: University-based reproductive medical center.

Subject: The study included singleton live births resulting from programmed FET cycles that took place between January 2017 and April 2022 (N=2275 cycles).

Exposure: The EMT measurement conducted on the day of progesterone initiation was utilized. Programmed FET cycles with EMT less than 7 mm were excluded from consideration. All included subjects were divided into four groups based on the 10th, 50th, and 90th percentiles of EMT: group I (EMT \leq 8 mm, n = 193), group II (EMT = 8.1-10 mm, n = 1261), group III (EMT = 10.1-12 mm, n = 615), and group IV (EMT \geq 12 mm, n = 206). After adjusting for patient demographics and FET parameters, logistic regression analysis and restricted cubic spline (RCS) were used to investigate the relationship between EMT and perinatal outcomes. The group II (EMT = 8.1-10 mm) served as reference.

Main outcome measure(s): The primary outcome measure was the hypertensive disorders of pregnancy (HDP). Secondary outcomes included gestational diabetes mellitus, caesarean delivery, placenta previa, premature rupture of membrane, birthweight, preterm birth, low birthweight, macrosomia, small for gestational age, large for gestational age and neonatal morbidity.

Results(s): The incidence of HDP was substantially elevated in group IV when compared to the other groups (5.7% vs. 4.1% vs. 5.7% vs. 9.7% for groups I -IV, respectively). Additionally, group I displayed a higher incidence of caesarean deliveries, whereas both group I and group IV exhibited an elevated prevalence of placenta previa. After adjusting for confounding factors, patients in group IV exhibited a significantly increased risk of HDP (adjusted odds ratio [OR] = 2.03, 95% confidence interval [CI] 1.13-3.67) as compared to patients in the reference group. In addition, the RCS model revealed a nonlinear association between EMT and the odds of HDP on continuous scales. In comparison to women with an EMT of 9.5 mm, there was no significant change in the risk of HDP in women with EMT between 7 and 11 mm, as indicated by adjusted ORs of 1.37 (95% CI 0.41-4.52), 1.34 (95% CI 0.73-2.47), 1.13 (95% CI 0.79-1.62), 1.04 (95% CI 0.87-1.25), and 1.46 (95% CI 0.81-2.65), respectively. However, the risk of HDP was significantly higher in women with EMT ranging from 12 to 15 mm, with adjusted ORs of 1.86 (95% CI 1.03-3.35), 2.33 (95% CI 1.32-4.12), 2.92 (95% CI 1.52-5.64), and 3.62 (95% CI 1.63-8.04), respectively.

Conclusion(s): This study demonstrated a noteworthy association between EMT and adverse perinatal outcomes during the programmed FET cycles. Specifically, a thick endometrium (EMT >12 mm) was independently associated with an increased risk of developing HDP, while the optimal EMT for reducing risk of HDP was at around 9-10 mm.

Keywords: endometrial thickness; hypertensive disorders of pregnancy; programmed frozen-thawed embryo transfer cycles.

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Am J Perinatol

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. 2023 Nov 1.

doi: 10.1055/s-0043-1776416. Online ahead of print.

[Intratracheal Instillation of Budesonide-Surfactant for Prevention of Bronchopulmonary Dysplasia in Extremely Premature Infants](#)

[Kalsang Dolma](#)¹, [Michael Zayek](#)¹, [Aayushka Gurung](#)¹, [Fabien Eyal](#)¹

Affiliations expand

- PMID: 37913780
- DOI: [10.1055/s-0043-1776416](https://doi.org/10.1055/s-0043-1776416)

Abstract

Objective: This study aimed to determine the effect of intratracheal instillation of a budesonide-surfactant combination on the incidence of bronchopulmonary dysplasia (BPD) or death compared with surfactant alone in extremely preterm infants.

Study design: In this retrospective, single-center study, we included extremely preterm infants (<28 weeks' gestation) who received surfactant for respiratory distress in the first 3 days of life. We compared infants who received budesonide-surfactant combination

(intervention group: infants born between February 2016 and October 2021) with surfactant alone (control group: infants born from January 2010 through January 2016). The primary outcome was a composite of BPD grade 2 or 3 (as defined by Jensen et al, 2019) or death before 36 weeks' postmenstrual age (PMA).

Results: We included 966 extremely preterm infants (528 in the control group and 438 in the intervention group). While the incidence of death/BPD grade 2 or 3 at 36 weeks of PMA was not different between the two groups (66% in the intervention group vs. 63% in the control group; adjusted relative risk [aRR], 0.99; 95% confidence interval [CI], 0.90-1.07; *p*-value = 0.69), budesonide was associated with a reduction in the primary outcome only in a subgroup of infants with birth weight \geq 750 grams (36.8 vs. 43.5%, respectively; aRR 0.75; 95% CI, 0.57-0.98). Primary and secondary outcomes did not differ between the two groups within the subgroup of infants weighing <750 grams.

Conclusion: In extremely preterm infants, the budesonide-surfactant combination therapy reduced the rates of BPD or death in infants weighing \geq 750 grams; however, this beneficial effect was not seen in infants weighing <750 grams. Further investigation of this treatment may be indicated before it is considered a standard approach to management.

Key points: · Intratracheal budesonide-surfactant therapy reduces BPD in preterm infants weighing \geq 750 grams.. · Intratracheal budesonide-surfactant therapy does not affect BPD in preterm infants weighing <750 grams.. · Intratracheal budesonide-surfactant therapy does not affect the mortality rate in preterm infants..

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Conflict of interest statement

None declared.

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Expert Rev Vaccines

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. 2023 Nov 1.

doi: 10.1080/14760584.2023.2275712. Online ahead of print.

Public health impact and return on investment of the pediatric immunization program in Poland

[Claire E Mellott](#)¹, [Rafal Jaworski](#)², [Justin Carrico](#)¹, [Sandra E Talbird](#)¹, [Iwona Dobrowolska](#)³, [Dominik Golicki](#)⁴, [Goran Bencina](#)⁵, [Micah Clinkscates](#)¹, [Eugenia Karamousouli](#)⁶, [Amanda L Eiden](#)⁷, [Ugne Sabale](#)⁸

Affiliations expand

- PMID: 37909887
- DOI: [10.1080/14760584.2023.2275712](https://doi.org/10.1080/14760584.2023.2275712)

Free article

Abstract

Background: This study aimed to evaluate the epidemiological impact and return on investment of the pediatric immunization program (PIP) in Poland from the healthcare-sector and societal perspectives.

Research design and methods: A health-economic model was developed focusing on the 9 vaccines, targeting 11 pathogens, recommended by public health authorities for children aged 0-6 years in Poland. The 2019 birth cohort (388,178) was followed over their lifetime, with the model estimating discounted health outcomes, life-years gained, quality-adjusted life-years, and direct and indirect costs with and without the PIP based on current and pre-vaccine - era disease incidence estimates, respectively.

Results: Across 11 targeted pathogens, the Polish PIP prevented more than 452,300 cases of disease, 1,600 deaths 37,900 life-years lost, and 38,800 quality-adjusted life-years lost. The PIP was associated with vaccination costs of €54 million. Pediatric immunization averted €65 million from a healthcare-sector perspective (benefit-cost ratio [BCR], 2.2) and averted €358 million from a societal perspective (BCR, 7.6). BCRs from both perspectives remained > 1.0 in scenario analyses.

Conclusions: The Polish PIP, which has not previously been systematically assessed, brings large-scale prevention of disease-related morbidity, premature mortality, and associated costs. This analysis highlights the value of continued investment in pediatric immunization in Poland.

Keywords: Vaccination; benefit-cost ratio; model; pediatric; return on investment.

FULL TEXT LINKS



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BMC Med

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. 2023 Oct 31;21(1):413.

doi: 10.1186/s12916-023-03125-w.

[Association between antenatal corticosteroid treatment and severe adverse events in pregnant women](#)

[Hui-Ju Tsai](#)^{1,2}, [Beth I Wallace](#)^{3,4,5}, [Akbar K Waljee](#)^{3,4,5}, [Xiumei Hong](#)⁶, [Sheng-Mao Chang](#)⁷, [Yi-Fen Tsai](#)¹, [Mei-Leng Cheong](#)^{2,8}, [Ann Chen Wu](#)⁹, [Tsung-Chieh Yao](#)^{10,11}

Affiliations [expand](#)

- PMID: 37907932
- PMCID: [PMC10617183](#)

- DOI: [10.1186/s12916-023-03125-w](https://doi.org/10.1186/s12916-023-03125-w)

Free PMC article

Abstract

Background: Antenatal corticosteroids are considered the standard of care for pregnant women at risk for preterm birth, but studies examining their potential risks are scarce. We aimed to estimate the associations of antenatal corticosteroids with three severe adverse events: sepsis, heart failure, and gastrointestinal bleeding, in pregnant women.

Methods: Of 2,157,321 pregnant women, 52,119 at 24 weeks 0/7 days to 36 weeks 6/7 days of gestation were included in this self-controlled case series study during the study period of 2009-2018. We estimated incidence rates of three severe adverse events: sepsis, heart failure, and gastrointestinal bleeding. Conditional Poisson regression was used to calculate incidence rate ratios (IRRs) for comparing incidence rates of the adverse events in each post-treatment period compared to those during the baseline period among pregnant women exposed to a single course of antenatal corticosteroid treatment.

Results: Among 52,119 eligible participants who received antenatal corticosteroid treatment, the estimated incidence rates per 1000 person-years were 0.76 (95% confidence interval (CI): 0.69-0.83) for sepsis, 0.31 (95% CI: 0.27-0.36) for heart failure, and 11.57 (95% CI: 11.27-11.87) for gastrointestinal bleeding. The IRRs at 5 ~ 60 days after administration of antenatal corticosteroids were 5.91 (95% CI: 3.10-11.30) for sepsis and 4.45 (95% CI: 2.63-7.55) for heart failure, and 1.26 (95% CI: 1.02-1.55) for gastrointestinal bleeding; and the IRRs for days 61 ~ 180 were 2.00 (95% CI: 1.01-3.96) for sepsis, 3.65 (95% CI: 2.14-6.22) for heart failure, and 1.81 (95% CI: 1.56-2.10) for gastrointestinal bleeding.

Conclusions: This nationwide population-based study suggests that a single course of antenatal corticosteroids is significantly associated with a 1.3- to 5.9-fold increased risk of sepsis, heart failure, and gastrointestinal bleeding in pregnant women. Maternal health considerations, including recommendations for adverse event monitoring, should be included in future guidelines for antenatal corticosteroid treatment.

Keywords: Antenatal; Corticosteroids; Gastrointestinal bleeding; Heart failure; Sepsis.

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Conflict of interest statement

The authors declare that they have no competing interests.

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

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Reprod Health

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. 2023 Oct 31;20(1):161.

doi: 10.1186/s12978-023-01704-x.

[Associations between maternal occupational exposures and pregnancy outcomes among Chinese nurses: a nationwide study](#)

[Zhaoqiang Jiang](#)¹, [Junfei Chen](#)¹, [Lingfang Feng](#)¹, [Mingying Jin](#)¹, [Shuang Liu](#)¹, [Lina Wang](#)², [Jing Wang](#)¹, [Changyan Yu](#)³, [Jianhong Zhou](#)⁴, [Yan Ye](#)⁵, [Liangying Mei](#)⁶, [Wenlan Yu](#)³, [Xing Zhang](#)¹, [Jianlin Lou](#)^{7,8}

Affiliations expand

- PMID: 37907929
- PMCID: [PMC10617240](#)

- DOI: [10.1186/s12978-023-01704-x](https://doi.org/10.1186/s12978-023-01704-x)

Free PMC article

Abstract

Background: Several studies have provided evidence about adverse pregnancy outcomes of nurses involved in occupational exposure. However, the pregnancy outcomes among nurses in middle-income countries are not well demonstrated. The main aim of this study is to present the prevalence and influencing factors of pregnancy outcomes among female nurses in China.

Methods: We included 2243 non-nurse health care workers, and 4230 nurses in this national cross-sectional study in China. Information on occupational exposures and pregnancy outcomes was collected using a face-to-face investigation. Odds ratios (ORs) were estimated through logistic regression.

Results: The proportion of threatened abortion, spontaneous abortion, and stillbirth of female nurses was 2.6%, 7%, and 2.1%, respectively. We found an increased risk of threatened abortion among nurses with overtime work (OR = 1.719, 95% CI 1.158-2.550). The risk of threatened abortion and spontaneous abortion was elevated among nurses handling disinfectant (OR = 2.293 and 1.63, respectively). We found a nearly twofold increased risk of premature birth (OR = 2.169, 95% CI 1.36-3.459) among nurses handling anti-cancer drugs.

Conclusions: Our findings suggested that maternal occupational exposures might be associated with the risk of adverse pregnancy outcomes among female nurses in China. We recommend that policy-makers and hospital managers work together to reduce exposure to occupational hazards and improve pregnancy outcomes among female nurses.

Keywords: Female; Nurses; Occupational exposure; Pregnancy outcome.

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Conflict of interest statement

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

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

SUPPLEMENTARY INFO

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

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Neoreviews

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. 2023 Nov 1;24(11):e748-e752.

doi: 10.1542/neo.24-11-e748.

[Preterm Infant with Bruising and Discoloration of Upper Extremity after Birth](#)

[Karen Stadd](#)¹, [Alexander Gall](#)¹, [Michael J Kochan](#)¹

Affiliations expand

- PMID: 37907404
- DOI: [10.1542/neo.24-11-e748](https://doi.org/10.1542/neo.24-11-e748)

No abstract available

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS



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Horm Metab Res



. 2023 Nov;55(11):758-764.

doi: 10.1055/a-2183-8683. Epub 2023 Oct 30.

[The Associations of Maternal Blood Hemoglobin and Serum Triglyceride Levels and the Risk of Preterm Delivery](#)

[Xia Song](#)¹, [Jiujing Lin](#)², [Xiaoxiao Dong](#)³, [Mengyun Li](#)¹, [Xiangsheng Xue](#)², [Chenyang Hou](#)⁴, [Huichen Yao](#)⁵, [Qingzhi Hou](#)²

Affiliations expand

- PMID: 37903496
- DOI: [10.1055/a-2183-8683](https://doi.org/10.1055/a-2183-8683)

Abstract

The abnormal hemoglobin (HGB) and serum lipid concentrations during pregnancy will increase the risk of preterm delivery. Our study aimed to explore the correlation between prenatal HGB and serum lipid levels and preterm delivery. We enrolled 215 mother-infant pairs in a pilot cohort study. The logistic regression model and Restricted Cubic Spline model (RCS) were used to investigate the levels of prenatal blood HGB and serum lipid such as triglyceride (TG), total cholesterol, high-density lipoprotein, low density lipoprotein and preterm delivery. The results showed that moderate levels of prenatal blood HGB (OR=0.28; 95%CI: 0.10, 0.75, p-trend=0.018) and high level of serum TG (OR=0.29; 95%CI: 0.10, 0.84, p-trend=0.022) level were negatively associated with the risk of preterm delivery. The joint effect results showed that compared with lower level of prenatal blood

HGB (≤ 123.13 g/l) and TG (≤ 3.7 mmol/l), we found that high levels prenatal blood HGB and serum TG (OR=0.32, 95%CI: 0.12, 0.89) had a negative association with the risk of preterm delivery. Moreover, prenatal blood HGB and serum TG levels had negative linear dose-effect relationships with the risk of preterm delivery in overall and girl group ($p < 0.05$). Moderate levels of prenatal blood HGB and high level of serum TG were negatively associated with the risk of preterm delivery. The joint effect of high levels prenatal HGB and prenatal serum TG in the normal range were negatively correlated with preterm delivery. Moreover, the underlying mechanisms should be clarified in future studies.

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Conflict of interest statement

The authors declare that they have no conflict of interest.

SUPPLEMENTARY INFO

MeSH terms, Substances expand

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Curr Opin Endocrinol Diabetes Obes

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. 2023 Oct 31.

doi: 10.1097/MED.0000000000000842. Online ahead of print.

Adherence to pharmacotherapy: sine qua non for reducing cumulative risk of

premature coronary disease in familial hypercholesterolemia

[Jing Pang](#)¹, [Frank M Sanfilippo](#)², [Dick C Chan](#)¹, [Gerald F Watts](#)^{1,3}

Affiliations expand

- PMID: 37902122
- DOI: [10.1097/MED.0000000000000842](https://doi.org/10.1097/MED.0000000000000842)

Abstract

Purpose of review: Familial hypercholesterolemia (FH) is a dominant and highly penetrant monogenic disorder present from birth that markedly elevates plasma low-density lipoprotein (LDL)-cholesterol concentration and, if untreated, leads to atherosclerotic cardiovascular disease (ASCVD). The risk of ASCVD can be substantially reduced with lipid-lowering treatment (LLT). However, adherence to LLT remains a major challenge in FH patients and an under-recognized issue. We review several barriers to treatment adherence and implementation strategies for improving adherence in patients with FH.

Recent findings: Barriers that negatively affect patient adherence to treatment include the misunderstanding of perceived and actual risk of FH and the benefits of LLT, inadequate knowledge, lack of standardization of treatment, insufficient monitoring of LDL-cholesterol level, and inequalities in healthcare resources. Education of patients, carers and healthcare providers, guideline-directed treatment goals, regular monitoring, medication regimen simplification and greater access to established and new drugs are crucial enablers for improving adherence to treatment. However, given FH is present from birth, strategies for life-long adherence from childhood or young adulthood is critically important and requires further study. To be effective, strategies should be multifaceted, targeted and patient-centred involving a multidisciplinary-team with support from family, communities and peer groups.

Summary: FH confers a significant risk for ASCVD from a young age. Achieving better medication adherence is foundational for improving clinical outcomes and reducing the burden of atherosclerosis over a lifetime. Identification of key barriers and enablers are critical for implementing better adherence to treatment across the life-course of patients with FH.

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J Dent Res

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. 2023 Oct 29:220345231200788.

doi: 10.1177/00220345231200788. Online ahead of print.

[Gestational Serum Retinol Deficiency Is Associated with Enamel Hypoplasia](#)

[S R Samuel](#)¹, [C W M Lai](#)², [M M Khan](#)³, [M G Mathew](#)⁴, [M S Kramer](#)^{5,6}, [C-Y S Hsu](#)²

Affiliations expand

- PMID: 37899507
- DOI: [10.1177/00220345231200788](https://doi.org/10.1177/00220345231200788)

Abstract

Enamel hypoplasia (EH) is a prevalent developmental defect of teeth that can result from various insults, including prenatal nutrient deficiencies. This study aimed to evaluate the association between prenatal serum retinol deficiency and EH in the deciduous teeth of offspring at 2-y of age. A cohort of 1,450 pregnant women was enrolled, and their prenatal nutritional status was assessed between 12 and 14 wk of gestation. Maternal serum retinol, serum 25-hydroxyvitamin D (25OHD), hemoglobin, body mass index, and birth outcomes, infant feeding practices, family socioeconomic status, and demographic information were recorded. Oral health examinations were conducted for the children semiannually, and EH was diagnosed using the Modified DDE index on all the surfaces of erupted teeth. A

modified Poisson regression analysis was used to assess the cumulative risk of EH over a period of 2-y. A total of 920 (63.4%) mother-child pairs completed the study, and the cumulative EH prevalence among offspring after 2-y of follow-up was 16.5% ($N = 152$; 87/1,114 children in the first year and 132/920 in the second year, with 20/920 having EH only in the first year). After adjusting for potential confounders, maternal serum retinol deficiency significantly increased the risk of deciduous EH (risk ratio [RR], 2.0; 95% confidence interval [CI], 1.1-3.7). In addition, deficient serum 25OHD (RR, 6.5; 95% CI, 4.0-10.7), caesarean delivery (RR, 1.6; 95% CI, 1.0-2.4), Muslim (RR, 2.9; 95% CI, 2.0-4.1) and Christian (RR, 2.4; 95% CI, 1.6-3.5) versus Hindu religions, and very preterm birth (RR, 1.7; 95% CI, 1.1-2.9) increased the risk of EH. Children presenting with EH had 2 or more teeth affected, and the maxillary incisors were the most frequently affected, followed by the first primary molars and canines. In conclusion, maternal serum retinol deficiency during the 12 to 14 wk of gestation may increase the risk of deciduous EH, besides the well-established 25OHD deficiency.

Keywords: cohort studies; deciduous dentition; nutrition during pregnancy; pregnancy outcomes, tooth abnormalities; premature birth; religion.

Conflict of interest statement

Declaration of Conflicting InterestsThe authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Reprod Biol Endocrinol

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. 2023 Oct 27;21(1):101.

doi: 10.1186/s12958-023-01154-x.

Letrozole-stimulated endometrial preparation protocol is a superior alternative to hormone replacement treatment for frozen embryo transfer in women with polycystic ovary syndrome, a cohort study

Xiaojuan Wang^{#1 2}, Yuan Li^{#2}, Hongzhan Tan¹, Sufen Cai², Shujuan Ma², Yangqin Peng², Hui Guo², Xiaofeng Li², Yi Tang², Shunji Zhang², Ge Lin^{2 3}, Fei Gong^{4 5}

Affiliations expand

- PMID: 37891650
- PMCID: [PMC10605334](#)
- DOI: [10.1186/s12958-023-01154-x](#)

Free PMC article

Abstract

Background: The current routine endometrial preparation protocol for women with polycystic ovary syndrome (PCOS) is hormone replacement treatment (HRT). Letrozole is rarely used in frozen embryo cycles. Evidence confirming whether letrozole-stimulated (LS) protocol is suitable for frozen embryo transfer in patients with PCOS and for whom is suitable remains lacking.

Methods: This was a retrospective cohort study involving all frozen embryo transfer cycles with LS and HRT for PCOS during the period from Jan 2019 to December 2020 at a tertiary care center. Multivariate Logistic regression was used to analyze the differences in clinical pregnancy rate, live birth rate, miscarriage rate, the incidence of other pregnancy and obstetric outcomes between LS and HRT protocols after adjusting for possible confounding factors. Subgroup analysis was used to explore the population for which LS protocol was suitable.

Results: The results of multivariate logistic regression showed that LS was significantly associated with a higher clinical pregnancy rate (70.9% vs. 64.4%; aOR: 1.41, 95%CI: 1.18, 1.68), live birth rate (60.5% vs. 51.4% aOR: 1.49, 95%CI: 1.27, 1.76), and a lower risk of miscarriage (14.7% vs. 20.1% aOR: 0.68, 95%CI: 0.53, 0.89), hypertensive disorders of pregnancy (6.7% vs. 8.9% aOR: 0.63, 95%CI: 0.42, 0.95), and gestational diabetes mellitus (16.7% vs. 20.7% aOR: 0.71, 95%CI: 0.53, 0.93) than HRT. There were no significant differences in other outcomes such as preterm birth, cesarean delivery, small for gestational age, or large for gestational age between the two endometrial preparation protocols. Subgroup analysis showed that LS had higher live birth rates than HRT in most of the subgroups; in the three subgroups of maternal age ≥ 35 years, menstrual cycle < 35 days, and no insulin resistance, the live birth rates of the two endometrial preparation protocols were comparable.

Conclusions: LS protocol could improve the live birth rate and reduce the incidence of miscarriage, hypertensive disorders of pregnancy and gestational diabetes mellitus in patients with PCOS. LS protocol is suitable for all types of patients with PCOS. LS should be considered the preferred endometrial preparation protocol for women with PCOS.

Keywords: Endometrial preparation; Frozen embryo transfer; Hormone replacement treatment; Letrozole; Polycystic ovary syndrome.

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Conflict of interest statement

The author(s) declare(s) that they have no competing interests.

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

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. 2023 Nov;5(11):e798-e811.

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Effect of telehealth-integrated antenatal care on pregnancy outcomes in Australia: an interrupted time-series analysis

[Karthikayinie Thirugnanasundralingam¹](#), [Miranda Davies-Tuck²](#), [Daniel L Rolnik³](#), [Maya Reddy³](#), [Ben W Mol⁴](#), [Ryan Hodges³](#), [Kirsten R Palmer⁵](#)

Affiliations expand

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- DOI: [10.1016/S2589-7500\(23\)00151-6](https://doi.org/10.1016/S2589-7500(23)00151-6)

Free article

Abstract

Background: During the COVID-19 pandemic, rapid integration of telehealth into antenatal care occurred to support ongoing maternity care. A programme of this scale had not been previously implemented. We evaluated whether telehealth-integrated antenatal care in an Australian public health system could achieve pregnancy outcomes comparable to those of conventional care to assess its safety and efficacy.

Methods: Routinely collected data for individuals who gave birth at Monash Health (Melbourne, VIC, Australia) during a conventional care period (Jan 1, 2018, to March 22, 2020) and telehealth-integrated period (April 20, 2020, to April 25, 2021) were analysed. We included all births that occurred at 20 weeks' gestation or later or with a birthweight of at least 400 g (if duration of gestation was unknown). We excluded multiple births, births for which private antenatal care was received, and births to individuals transferred from other hospitals or who had no antenatal care. Baseline demographics, telehealth uptake,

and pregnancy complications (related to pre-eclampsia, fetal growth restriction [FGR], gestational diabetes, stillbirth, neonatal intensive care [NICU] admission, and preterm birth [<37 weeks' gestation]) were compared using comparative statistics and an interrupted time-series analysis. Results were stratified by care stream, with high-risk models consisting of obstetric specialist-led care, and all other streams categorised as low-risk models. The impact of the integrated period on outcomes was also assessed with stratification by parity.

Findings: 17 873 births occurred in the conventional period and 8131 in the integrated period. Compared with the conventional period, women giving birth during the integrated period were slightly older (30.63 years vs 30.88 years) and had slightly higher BMI (25.52 kg/m² vs 26.14 kg/m²), and more Australian-born women gave birth during the integrated period (37.37% vs 39.79%). There were no significant differences in smoking status or parity between the two groups. 107 (0.08%) of 129 514 antenatal consultations in the conventional period and 34 444 (45.94%) of 74 982 in the integrated period were delivered by telehealth. No significant differences between the conventional and integrated periods were seen in median gestational age at pre-eclampsia diagnosis (low-risk models 37.4 weeks in the conventional period vs 37.1 weeks in the integrated period, difference -0.3 weeks [-0.7 to 0.1]; high-risk models 35.5 weeks vs 36.3 weeks, difference 0.3 weeks [-0.3 to 1.1]), incidence of FGR below the 3rd birthweight percentile (low-risk models 1.62% vs 1.74%, difference 0.12 percentage points [-0.26 to 0.50]; high-risk 4.04% vs 4.13%, difference 0.089 percentage points [-1.08 to 1.26]), and incidence of preterm birth (low-risk models 4.99% vs 5.01%, difference 0.02% [-0.62 to 0.66]; high-risk models 15.76% vs 14.43%, difference -1.33% [-3.42 to 0.77]). Parity did not affect these findings. Interrupted time-series analysis showed a significant reduction in induction of labour for singletons with suspected FGR among women in low-risk models during the integrated period (-0.04% change per week [95% CI -0.07 to -0.01], $p=0.0040$), and NICU admission declined after telehealth integration (low-risk models -0.02% change per week [-0.03 to -0.003], $p=0.018$; high-risk models -0.10% change per week, -0.19 to -0.001; $p=0.047$). No significant differences in stillbirth rates were observed. The proportion of women diagnosed with gestational diabetes was significantly higher in the integrated period compared with the conventional period for both low-risk care models (22.28% vs 25.13%, difference 2.85 percentage points [1.60 to 4.11]) and high-risk care models (28.70% vs 34.02%, difference 5.32 percentage points [2.57 to 8.07]). However overall, when compared with the conventional period, there was no significant difference in proportion of women with gestational diabetes requiring insulin therapy (low-risk models 8.08% vs 7.73%, difference -0.35 percentage points [-1.13 vs 0.44]; high-risk models 14.81% vs 15.71%, difference 0.89 percentage points [-1.23 to 3.02]), or proportion of women with gestational diabetes who gave birth to a baby with macrosomia in the integrated period (low-risk models 3.16% vs 2.33%, difference -0.83 percentage points [-1.77 to 0.12]; high-risk models 5.58% vs 4.81%, difference -0.77 percentage points [-3.06 to 1.52]).

Interpretation: Telehealth-integrated antenatal care replaced around 46% of in-person consultations without compromising pregnancy outcomes. It might be associated with a reduction in labour induction for suspected FGR, particularly for women in low-risk models,

without compromising FGR detection or perinatal morbidity. These findings support the ongoing use of telehealth in providing flexible antenatal care.

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Conflict of interest statement

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SUPPLEMENTARY INFO

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J Dev Orig Health Dis

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. 2023 Oct 27:1-8.

doi: 10.1017/S2040174423000296. Online ahead of print.

Preterm birth, birthweight, and subsequent risk for depression

[Neha Rahalkar](#)^{#1}, [Aaron Holman-Vittone](#)^{#1}, [Christian Daniele](#)¹, [Rachel Wacks](#)¹, [Autumn Gagnon](#)¹, [Amy D'Agata](#)², [Nazmus Saquib](#)³, [Peter F Schnatz](#)⁴, [Mary C Sullivan](#)⁴, [Robert Wallace](#)⁵, [Cassandra N Spracklen](#)¹

Affiliations expand

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- DOI: [10.1017/S2040174423000296](https://doi.org/10.1017/S2040174423000296)

Abstract

An individual's birthweight, a marker of *in utero* exposures, was recently associated with certain psychiatric conditions. However, studies investigating the relationship between an individual's preterm birth status and/or birthweight and risk for depression during adulthood are sparse; we used data from the Women's Health Initiative (WHI) to investigate these potential associations. At study entry, 86,925 postmenopausal women reported their birthweight by category (<6 lbs., 6-7 lbs. 15 oz., 8-9 lbs. 15 oz., or ≥10 lbs.) and their preterm birth status (full-term or ≥4 weeks premature). Women also completed the Burnham screen for depression and were asked to self-report if: (a) they had ever been diagnosed with depression, or (b) if they were taking antidepressant medications. Linear and logistic regression models were used to estimate unadjusted and adjusted effect estimates. Compared to those born weighing between 6 and 7 lbs. 15 oz., individuals born weighing <6 lbs. ($\beta_{\text{adj}} = 0.007$, $P < 0.0001$) and ≥10 lbs. ($\beta_{\text{adj}} = 0.006$, $P = 0.02$) had significantly higher Burnham scores. Individuals born weighing <6 lbs. were also more likely to have depression (adjOR 1.21, 95% CI 1.11-1.31). Individuals born preterm were also more likely to have depression (adjOR 1.18, 95% CI 1.02-1.35); while attenuated, this association remained in analyses limited to only those reportedly born weighing <6 lbs. Our research supports the role of early life exposures on health risks across the life course. Individuals born at low or high birthweights and those born preterm may benefit from early evaluation and long-term follow-up for the prevention and treatment of mental health outcomes.

Keywords: CES-D; barker hypothesis; burnham screen; depression; low birthweight; postmenopausal women; preterm birth.

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BMC Pediatr



. 2023 Oct 26;23(1):533.

doi: 10.1186/s12887-023-04361-y.

[Impact of early-onset fetal growth restriction on the neurodevelopmental outcome of very preterm infants at 24 months: a retrospective cohort study](#)

[Mariana Cortez Ferreira](#)¹, [Joana Mafra](#)², [Ana Dias](#)³, [Isabel Santos Silva](#)², [Adelaide Taborda](#)³

Affiliations expand

- PMID: 37884935
- PMCID: [PMC10601105](#)
- DOI: [10.1186/s12887-023-04361-y](#)

Free PMC article

Abstract

Background: The association between fetal growth restriction (FGR) and childhood neurodevelopmental delay is unclear and the evidence available to the present date shows conflicting results. Our aim was to analyse the impact of early-onset FGR on the neurodevelopmental outcome at 24 months of corrected age in very preterm infants.

Methods: Retrospective cohort study of very preterm infants (≤ 32 weeks' gestation) admitted to a neonatal intensive care unit between 1 January 2013-31 December 2019. The control group comprised appropriate for gestational age (AGA) newborns. Griffiths III Mental Development Scale was performed at 24 months of corrected age.

Results: 132 infants were included: 44 FGR and 88 AGA. Mean Global Development Quotient (GDQ) was lower for FGR infants ($p = 0.004$) even after adjusting for maternal and perinatal factors ($\beta_{\text{adjusted}} -16.703$; $p = 0.009$). The average scores for the neurodevelopmental domains were highest for personal-social-emotional skills (107.02 ± 16.34), followed by eye/hand coordination (105.61 ± 14.20) and foundation of learning skills (102.23 ± 13.74) and were lowest for gross motor (97.90 ± 11.88) and language/communication skills (96.39 ± 18.88). FGR had a significant negative impact on all domains except for gross motor skills. After adjustment, FGR continued to have a significant adverse impact on language/communication ($\beta_{\text{adjusted}} -21.924$; $p = 0.013$), eye/hand coordination ($\beta_{\text{adjusted}} -15.446$; $p = 0.015$) and foundation of learning skills ($\beta_{\text{adjusted}} -15.211$; $p = 0.013$).

Conclusions: In very preterm infants, FGR was associated with a significantly increased risk of poor neurodevelopmental outcome at 24 months of corrected age compared to age-matched AGA infants.

Keywords: Children; Fetal growth restriction; Neonates; Neurodevelopmental disorder, Preterm infants.

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Conflict of interest statement

The authors declare that they have no competing interests.

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

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MeSH termsexpand

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J Matern Fetal Neonatal Med



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doi: 10.1080/14767058.2023.2271623. Epub 2023 Oct 26.

The interaction effect of pre-pregnancy body mass index and maternal age on the risk of pregnancy complications in twin pregnancies after assisted reproductive technology

[Shenglan Chen](#)¹, [Yu Zhou](#)¹, [Qin Mu](#)², [Yina Wang](#)³

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- PMID: 37884444
- DOI: [10.1080/14767058.2023.2271623](https://doi.org/10.1080/14767058.2023.2271623)

Free article

Abstract

Objective: The widespread use of assisted reproductive technology (ART) has led to an increased twin pregnancy rate and increased risk of pregnancy complications. Pre-pregnancy body mass index (BMI) and maternal age are both risk factors for pregnancy complications. This study aimed to explore whether there is an interaction effect between pre-pregnancy BMI and maternal age on pregnancy complications in women with twin pregnancies after ART.

Methods: Data of 445,750 women with twin pregnancies after ART were extracted from the National Vital Statistics System (NVSS) database in 2016-2021 in this retrospective cohort study. Univariate and multivariate logistic regression analyses were used to explore (1) the associations between pre-pregnancy BMI, maternal age, and total pregnancy

complications; (2) interaction effect between pre-pregnancy BMI and maternal age on total pregnancy complications; and (3) this interaction effect in parity, race, gestational weight gain (GWG), and preterm birth subgroups. The evaluation indexes were odds ratios (ORs), relative excess risk of interaction (RERI), attributable proportions of interaction (AP), and synergy index (S) with 95% confidence intervals (CIs).

Results: A total of 6,827 women had pregnancy complications. After adjusting for the covariates, compared with women had non-AMA and pre-pregnancy BMI <25 kg/m², higher maternal age combined with higher pre-pregnancy BMI was associated with higher odds of total pregnancy complications [OR = 2.16, 95%CI: (1.98-2.36)]. The RERI (95% CI) was 0.22 (0.04-0.41), AP (95% CI) was 0.10 (0.02-0.19), and S (95% CI) was 1.24 (1.03-1.49). Subgroup analysis results indicated that the potential additive effect between pre-pregnancy BMI and maternal age on total pregnancy complications was also found in women with different race, multipara/unipara, GWG levels, or preterm births/non-preterm births (all *p* < 0.05).

Conclusion: Pre-pregnancy BMI and maternal age may have an additive effect on the odds of pregnancy-related complications in women with twin pregnancy after ART.

Keywords: ART; NVSS; Pre-pregnancy BMI; interaction effect; maternal age; twin pregnancy.

SUPPLEMENTARY INFO

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J Matern Fetal Neonatal Med

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. 2023 Dec;36(2):2272577.

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Omeprazole activates aryl hydrocarbon receptor to reduce hyperoxia-induced oxidative stress in the peripheral blood mononuclear cells from premature infants

[Xi Yang](#)^{1,2,3}, [Zhengrong Bao](#)^{1,2,3}, [Xiaoping Lei](#)^{1,2,3}, [Xia Wang](#)^{1,2,3}, [Shuai Zhao](#)^{1,2,3}, [Fengling Du](#)^{1,2,3}, [Xingling Liu](#)^{1,2,3}, [Wenbin Dong](#)^{1,2,3}

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- PMID: 37884440
- DOI: [10.1080/14767058.2023.2272577](https://doi.org/10.1080/14767058.2023.2272577)

Free article

Abstract

Objective: To investigate the correlation between the aryl hydrocarbon receptor (AhR) and reactive oxygen species (ROS) in peripheral blood mononuclear cells (PBMCs) of premature infants, to demonstrate the protective role of AhR against hyperoxia-induced oxidative stress in premature infants and to provide a rational basis for the use of omeprazole (OM) as a new treatment for bronchopulmonary dysplasia (BPD).

Methods: From January 2021 to June 2021, 1-3 ml of discarded peripheral blood was collected from premature infants of gestational age less than 32 weeks who were not taking inhaled oxygen and were admitted to the Department of Neonatology of the Affiliated Hospital of Southwest Medical University. Using a random number table, the PBMCs were randomly assigned to each of the following groups: the control group, air + OM group, hyperoxia group, and hyperoxia + OM group. After 48 h of *in vitro* modeling and culture, PBMCs and the culture medium of each group were collected. Immunofluorescence analysis was used to examine ROS levels in PBMCs. A full-spectrum spectrophotometer was used to examine malondialdehyde (MDA) levels in the culture medium. Enzyme-linked immunosorbent assay (ELISA) was used to examine monocyte chemoattractant protein 1 (MCP-1) levels in culture medium. Immunofluorescence analysis was used to examine the intracellular localization of AhR. Western blotting was used to examine the expression level of AhR in PBMCs.

Results: Compared with those in the control group, the levels of ROS, MDA, and MCP-1 and the cytoplasm-nuclear translocation rate of AhR in the air + OM group did not change significantly ($p > 0.05$), but the expression level of AhR increased significantly ($p < 0.05$). The levels of ROS, MDA, and MCP-1 and the cytoplasm-nuclear translocation rate of AhR significantly increased in the hyperoxia group ($p < 0.05$), and the expression level of AhR was significantly reduced ($p < 0.05$). Compared with those in the hyperoxia group, the levels of ROS, MDA, and MCP-1 in the hyperoxia + OM group were significantly reduced ($p < 0.05$), and the cytoplasm-nuclear translocation rate of AhR and the expression level of AhR were significantly increased ($p < 0.05$), but did not reach the level of the control group ($p < 0.05$).

Conclusion: OM can activate AhR to inhibit hyperoxia-induced oxidative stress in the PBMCs from premature infants.

Keywords: AhR; Omeprazole; ROS; oxidative stress; premature infants.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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PLoS One

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. 2023 Oct 26;18(10):e0292665.

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[Association between gestational weight gain and adverse neonatal outcomes in women conceiving with assisted](#)

reproductive technology: Evidence from the NVSS 2019–2021

[Feifei Jiang](#)¹, [Yanan Li](#)², [Lipeng Sun](#)²

Affiliations expand

- PMID: 37883382
- PMCID: [PMC10602326](#)
- DOI: [10.1371/journal.pone.0292665](#)

Free PMC article

Abstract

Objective: To evaluate the association between gestational weight gain (GWG) and adverse neonatal outcomes in women who conceived using assisted reproductive technology (ART).

Methods: The National Vital Statistics System (NVSS) 2019–2021 provided data for this retrospective cohort study. Adverse neonatal outcomes included premature birth, small for gestational age (SGA), large for gestational age (LGA), macrosomia, low birth weight (LBW), and other abnormal conditions. Any adverse outcome was defined as at least one of the above six outcomes. Multivariate logistic regression analysis was employed to evaluate the associations between GWG and different outcomes, after adjusting for confounding factors. These associations were further assessed in subgroups of maternal age at delivery, paternal age at delivery, preconception body mass index (BMI), gestational age, maternal race, parity, gestational diabetes, and gestational hypertension.

Results: Totally 108201 women were included, with 22282 in the insufficient GWG group, 38034 in the sufficient GWG group, and 47885 in the excessive GWG group. Women with insufficient GWG [odds ratios (OR) = 1.11, 95%CI: 1.07–1.16, $P < 0.001$] and excessive GWG (OR = 1.14, 95%CI: 1.10–1.18, $P < 0.001$) had significantly greater risks of any adverse outcome than those with sufficient GWG. In contrast to sufficient GWG, insufficient GWG was associated with significantly elevated risks of premature birth (OR = 1.42, 95%CI: 1.35–1.48, $P < 0.001$), SGA (OR = 1.45, 95%CI: 1.37–1.53, $P < 0.001$), LBW (OR = 1.47, 95%CI: 1.37–1.58, $P < 0.001$), and other abnormal conditions (OR = 1.32, 95%CI: 1.27–1.39, $P < 0.001$), and excessive GWG was associated with significantly lower risks of premature birth (OR = 0.86,

95%CI: 0.83-0.90, $P < 0.001$), SGA (OR = 0.79, 95%CI: 0.75-0.83, $P < 0.001$), LBW (OR = 0.85, 95%CI: 0.79-0.91, $P < 0.001$), and other abnormal conditions (OR = 0.92, 95%CI: 0.88-0.96, $P < 0.001$). Infants born to women with insufficient GWG had significantly decreased risks of LGA (OR = 0.71, 95%CI: 0.66-0.75, $P < 0.001$) and macrosomia (OR = 0.68, 95%CI: 0.63-0.74, $P < 0.001$), and infants born to women with excessive GWG had significantly increased risks of LGA (OR = 1.50, 95%CI: 1.44-1.56, $P < 0.001$) and macrosomia (OR = 1.60, 95%CI: 1.51-1.69, $P < 0.001$).

Conclusion: Insufficient GWG and excessive GWG were associated with increased risks of any adverse outcome than sufficient GWG in women who conceived with ART, indicating the applicability of recommended GWG by the Institute of Medicine (IOM) in this population.

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Conflict of interest statement

The authors have declared that no competing interests exist.

- [26 references](#)
- [12 figures](#)

SUPPLEMENTARY INFO

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

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J Perinat Med

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. 2023 Oct 26.

The impact of the COVID-19 pandemic on antenatal care provision and associated mental health, obstetric and neonatal outcomes

[Anousha Woods](#)¹, [Emma Ballard](#)², [Sailesh Kumar](#)³, [Tracey Mackle](#)⁴, [Leonie Callaway](#)¹, [Alka Kothari](#)⁵, [Susan De Jersey](#)^{1,6}, [Elizabeth Bennett](#)⁴, [Katie Foxcroft](#)⁷, [Meg Willis](#)¹, [Akwasi Amoako](#)¹, [Christoph Lehner](#)¹

Affiliations expand

- PMID: 37883210
- DOI: [10.1515/jpm-2023-0196](https://doi.org/10.1515/jpm-2023-0196)

Abstract

Objectives: The COVID-19 pandemic imposed many challenges on pregnant women, including rapid changes to antenatal care aimed at reducing the societal spread of the virus. This study aimed to assess how the pandemic affected perinatal mental health and other pregnancy and neonatal outcomes in a tertiary unit in Queensland, Australia.

Methods: This was a retrospective cohort study of pregnant women booked for care between March 2019 - June 2019 and March 2020 - June 2020. A total of 1984 women were included with no confirmed cases of COVID-19. The primary outcome of this study was adverse maternal mental health defined as an Edinburgh Postnatal Depression Scale score of ≥ 13 or an affirmative response to 'EPDS Question 10'. Secondary outcomes were preterm birth <37 weeks and <32 weeks, mode of birth, low birth weight, malpresentation in labour, hypertensive disease, anaemia, iron/vitamin B12 deficiency, stillbirth and a composite of neonatal morbidity and mortality.

Results: There were no differences in the primary perinatal mental health outcomes. The rates of composite adverse neonatal outcomes (27 vs. 34 %, $p < 0.001$) during the pandemic were higher; however, there was no difference in perinatal mortality ($p = 1.0$), preterm birth ($p = 0.44$) or mode of delivery ($p = 0.38$).

Conclusions: Although there were no adverse consequences on maternal mental health during the pandemic, there was a concerning increase in neonatal morbidity potentially due to the altered model of maternity care implemented in the early COVID-19 pandemic.

Keywords: COVID-19; anxiety; depression; intensive care neonatal; pandemics; premature birth.

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JAMA Ophthalmol

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. 2023 Oct 26:e234787.

doi: 10.1001/jamaophthalmol.2023.4787. Online ahead of print.

[Neurodevelopmental Outcomes in Infants Screened for Retinopathy of Prematurity](#)

[Reem Karmouta](#)¹, [Jason C Strawbridge](#)¹, [Seth Langston](#)², [Marie Altendahl](#)³, [Monica Khitri](#)¹, [Alison Chu](#)³, [Irena Tsui](#)¹

Affiliations expand

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- PMID: PMC10603571 (available on 2024-10-26)

- DOI: [10.1001/jamaophthalmol.2023.4787](https://doi.org/10.1001/jamaophthalmol.2023.4787)

Abstract

Importance: Preterm infants screened for retinopathy of prematurity (ROP) are at risk for heterogeneous neurodevelopment outcomes that are difficult to predict.

Objective: To characterize the potential association between socioeconomic and clinical risk factors and neurodevelopmental outcomes in a diverse, multicenter cohort of premature neonates screened for ROP.

Design, setting, and participants: This was a retrospective cohort study using electronic medical records and US Census Bureau income data. This study was performed at academic (University of California, Los Angeles [UCLA] Mattel Children's Hospital and UCLA Santa Monica Hospital), community (Cedars-Sinai Medical Center), and LA county (Harbor-UCLA Medical Center) neonatal intensive care units. Participants included infants who met American Academy of Pediatrics guidelines for ROP screening and had records from at least 1 Bayley Scales of Infant and Toddler Development (BSID) neurodevelopment assessment between 0 and 36 months of adjusted age. Data analyses were conducted from January 1, 2011, to September 1, 2022.

Exposures: Demographic and clinical information, proxy household income, and health insurance type were collected as risk factors.

Main outcomes and measures: Neurodevelopmental outcomes in the cognitive, language, and motor domains measured via BSID were the primary outcomes.

Results: A total of 706 infants (mean [SD] age, 28.6 [2.4] weeks; 375 male [53.1%]) met inclusion criteria. In a multivariable model, which included adjustments for birth weight, sex, insurance type, intraventricular hemorrhage (IVH), and age at assessment, public health insurance was associated with a 4-fold increased risk of moderate to severe neurodevelopmental impairment (NDI) in cognitive and language domains (cognitive, odds ratio [OR], 3.65; 95% CI, 2.28-5.86; $P = 8.1 \times 10^{-8}$; language, OR, 3.96; 95% CI, 2.61-6.02; $P = 1.0 \times 10^{-10}$) and a 3-fold increased risk in the motor domain (motor, OR, 2.60; 95% CI, 1.59-4.24; $P = 1.4 \times 10^{-4}$). In this adjusted model, clinical factors that were associated with an increased risk of moderate to severe NDI included lower birth weight, diagnosis of IVH, male sex, and older age at time of Bayley assessment. In unadjusted analyses, infants who received either laser or anti-VEGF treatment, compared with infants without treatment-requiring ROP, had lower BSID scores in multiple domains at 0 to 12 months, 12 to 24 months, and 24 to 36 months (DATA). In the multivariable model, treatment type was no longer associated with worse neurodevelopmental outcomes in any domain.

Conclusions and relevance: Study results suggest an association between public insurance type and NDI in a diverse population screened for ROP, indicating the complexities of neurodevelopment. This study also supports the early neurodevelopmental

safety of anti-VEGF treatment, as anti-VEGF therapy was not found to be independently associated with worse NDI in any domain.

Conflict of interest statement

Conflict of Interest Disclosures: None reported.

- [28 references](#)

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Review

Cochrane Database Syst Rev

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. 2023 Oct 26;10(10):CD013158.

doi: 10.1002/14651858.CD013158.pub2.

[Surfactant therapy guided by tests for lung maturity in preterm infants at risk of respiratory distress syndrome](#)

[Greta Sibrecht](#)¹, [Colby R Kearn](#)², [Franciszek Borys](#)¹, [Mihai Morariu](#)³, [Matteo Bruschetti](#)^{4,5}, [Roger Soll](#)⁶

Affiliations expand

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Abstract

Background: Administration of various exogenous surfactant preparations has been shown to decrease lung injury and pneumothorax and improve survival in very preterm infants with respiratory distress syndrome (RDS). There is no consensus on the threshold for surfactant administration, to allow timely intervention and avoid over-treatment, also considering the invasiveness of the procedure and its cost. Rapid tests for lung maturity, which include the click test, lamellar body counts and stable microbubble test, might guide the identification of those infants needing surfactant administration.

Objectives: To assess the effects of surfactant treatment guided by rapid tests for surfactant deficiency in preterm infants at risk for or having RDS. Comparison 1: In preterm infants at risk for RDS, does surfactant treatment guided by rapid tests for surfactant deficiency compared to prophylactic surfactant administration to all high-risk infants minimize the need for surfactant treatment and prevent bronchopulmonary dysplasia and mortality? Comparison 2: In preterm infants who require early respiratory support, does surfactant treatment guided by rapid tests for surfactant deficiency compared to surfactant therapy provided to infants with RDS diagnosed on clinical and radiologic criteria minimize the need for surfactant treatment and prevent bronchopulmonary dysplasia and mortality?

Search methods: We searched in October 2022 CENTRAL, PubMed, Embase and three additional trial registries. We also screened the reference lists of included studies and related systematic reviews for studies not identified by the database searches.

Selection criteria: We included randomized controlled trials (RCTs) and quasi-RCTs evaluating rapid tests after birth for surfactant deficiency in infants at high risk of RDS or requiring respiratory support. We specified two comparisons: 1) surfactant treatment guided by rapid tests for surfactant deficiency versus prophylactic surfactant administration to all high-risk infants in extremely preterm (less than 28 weeks' gestation) and very preterm (28 to 32 weeks' gestation); 2) surfactant treatment guided by rapid tests for surfactant deficiency versus surfactant therapy provided to preterm infants (less than 37 weeks' gestation) with RDS diagnosed on clinical and radiologic criteria.

Data collection and analysis: We used standard Cochrane methods. We used the fixed-effect model with risk ratio (RR) and risk difference (RD), with their 95% confidence intervals (CIs) for dichotomous data. Our primary outcomes were: neonatal mortality, mortality prior to hospital discharge, bronchopulmonary dysplasia and the composite

outcome bronchopulmonary dysplasia or mortality. We used GRADE to assess the certainty of evidence.

Main results: We included three RCTs enrolling 562 newborn infants in this review. No studies compared surfactant treatment guided by rapid tests for surfactant deficiency versus prophylactic surfactant administration to all high-risk infants. Comparing surfactant therapy guided by rapid tests for surfactant deficiency versus surfactant therapy provided to infants with RDS diagnosed on clinical and radiologic criteria. No studies reported neonatal mortality. Compared with surfactant therapy provided to infants with RDS diagnosed on clinical and radiologic criteria, the evidence is very uncertain about the effect of surfactant treatment guided by rapid tests for surfactant deficiency on mortality prior to hospital discharge: RR 1.25, 95% CI 0.65 to 2.41, RD 0.01, 95% CI -0.03 to 0.05, 562 participants, 3 studies; I^2 for RR and RD = 75% and 43%, respectively; very low-certainty evidence. Surfactant treatment guided by rapid tests for surfactant deficiency may result in little to no difference in bronchopulmonary dysplasia: RR 0.90, 95% CI 0.61 to 1.32, RD -0.02, 95% CI -0.08 to 0.04, 562 participants, 3 studies; I^2 for RR and RD = 0%; low-certainty evidence. No studies reported the composite outcome bronchopulmonary dysplasia or mortality. Surfactant treatment guided by rapid tests for surfactant deficiency may result in little to no difference in surfactant utilization (RR 0.97, 95% CI 0.85 to 1.11, RD -0.02, 95% CI -0.10 to 0.06, 562 participants, 3 studies, I^2 for RR and RD = 63% and 65%, respectively, low-certainty evidence), and any pneumothorax (RR 0.53, 95% CI 0.15 to 1.92, RD -0.01, 95% CI -0.04 to 0.01, 506 participants, 2 studies, I^2 for RR and RD = 0%, low-certainty evidence) compared with surfactant therapy provided to infants with RDS diagnosed on clinical and radiologic criteria. No studies reported moderate to severe neurodevelopmental impairment. We identified two large ongoing RCTs.

Authors' conclusions: No studies compared surfactant treatment guided by rapid tests for surfactant deficiency to prophylactic surfactant administration to all high-risk infants. Low to very low-certainty evidence from three studies is available on surfactant therapy guided by rapid tests for surfactant deficiency versus surfactant therapy provided to infants with RDS diagnosed on clinical and radiologic criteria. No studies reported neonatal mortality, the composite outcome 'bronchopulmonary dysplasia or mortality', or neurodevelopmental outcomes. Compared with surfactant therapy provided to infants with RDS diagnosed on clinical and radiologic criteria, the evidence is very uncertain about the effect of surfactant treatment guided by rapid tests for surfactant deficiency on mortality prior to hospital discharge. Surfactant treatment guided by rapid tests for surfactant deficiency may result in little to no difference in bronchopulmonary dysplasia, surfactant utilization and any pneumothorax. The findings of the two large ongoing trials identified in this review are likely to have an important impact on establishing the effects of surfactant treatment guided by rapid tests for surfactant deficiency in preterm infants.

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Conflict of interest statement

GS has no relevant interests to declare.

CRK has no relevant interests to declare.

FB has no relevant interests to declare.

MM has no relevant interests to declare.

MB is an Associate Editor for Cochrane Neonatal. However, he had no involvement in the editorial processing of this review.

Roger Soll is the Co-ordinating Editor of Cochrane Neonatal (therefore the review was seen and edited by other members of the editorial team). He received a grant from the Gerber Foundation to update reviews on interventions for pain and discomfort.

Update of

- doi: 10.1002/14651858.CD013158

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SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Indian J Ophthalmol

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. 2023 Nov;71(11):3494-3500.

doi: 10.4103/IJO.IJO_889_23.

[The impact after 20 years of an early detection program for severe](#)

retinopathy of prematurity in a Latin American city

[Claudia Zuluaga-Botero](#)¹, [Erika Cantor](#)², [Francisco Bonilla](#)³, [Juan F Robayo-Velasquez](#)⁴, [Alexander M Martínez-Blanco](#)⁵

Affiliations expand

- PMID: 37870013
- DOI: [10.4103/IJO.IJO_889_23](https://doi.org/10.4103/IJO.IJO_889_23)

Free article

Abstract

Purpose: To evaluate the effects of long-standing early detection program in the incidence and trends of severe retinopathy of prematurity (ROP) in Cali, Colombia.

Methods: This was a retrospective cohort study of infants included in an ROP prevention, early detection, and prompt treatment program, from January 01, 2002, to December 31, 2021 (20 years). Infants with gestational age (GA) <37 weeks or birth weight (BW) <2000 g and those with known ROP risk factors were screened. The incidence of severe ROP was calculated, and the average annual percent change (AAPC) was estimated through a joinpoint model.

Results: 16,580 infants were screened, with an average GA and BW of 31.4 ± 2.8 weeks and 1526.5 ± 56.7 g, respectively. The incidence of severe ROP was 2.69% (446 cases, 95% confidence interval [95%CI]: 2.45%; 2.95%), with an average annual decrease of -14% (AAPC, 95%CI: -16.3%; -11.6%) from 13.6% in 2002 to 0.7% in 2021. In infants with GA <32 weeks, the incidence was 5.21%. A significant reduction in the risk of ROP was observed with increasing GA and BW ($P < 0.05$). Among the cases with severe ROP, 6.5% (29/446) had a GA ≥ 32 weeks with a maximum of 37 weeks; only 0.4% (2/446) of the detected infants had a BW >2000 g.

Conclusion: Awareness and screening as part of the early detection program to prevent ROP has shown a significant decline in the incidence of severe ROP over time. Screening infants with GA <32 weeks or BW <2000 g and preterm infants (<37 weeks) with risk factors may be a feasible decision for resource optimization.

Keywords: Birth weight; preterm infants; retinopathy of prematurity; screening program.

Conflict of interest statement

None

SUPPLEMENTARY INFO

MeSH termsexpand

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Indian J Ophthalmol

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. 2023 Nov;71(11):3484-3488.

doi: 10.4103/IJO.IJO_1158_23.

[Wide-field digital imaging system for assessing ocular anterior segment development in very preterm infants](#)

[Yu-Jing Wang](#)¹, [Min Ke](#)¹, [Ming Yan](#)¹

Affiliations expand

- PMID: 37870011
- DOI: [10.4103/IJO.IJO_1158_23](https://doi.org/10.4103/IJO.IJO_1158_23)

Free article

Abstract

Purpose: This study aims to longitudinally investigate developments of the anterior segment in very preterm infants who exhibit normal retinal development outcomes by utilizing a wide-field digital imaging system.

Methods: Between June 2021 and June 2022, neonates with a birth weight of <1500 g and/or a gestational age (GA) of less than 32 weeks were included in this study. The participants underwent regular ocular examinations, including sequential evaluations of the anterior segment and the retina, at intervals of 2-5 weeks, starting from birth and continuing until they reached a corrected GA of 48 weeks. Term neonates were selected as normal controls for the study. The study recorded the weight and GA of subjects at the time of examination, as well as indicators of abnormal development in the anterior segment.

Results: A total of 48 very preterm infants with normal retinal developmental outcomes were enrolled. The control group included 59 full-term infants. Common anterior segment eye abnormalities such as persistent hyperplasia of primary vitreous, persistent pupillary membranes, iris vessels, and anterior chamber angle vessels gradually subsided with the period in very preterm infants. The vascularity of the iris was substantially higher than in term controls ($P < 0.05$) at term gestation. The imaging of iris vessels and anterior chamber angle vessels in very preterm infants exhibited a decline at 46 and 47 weeks, respectively, which occurred slightly later compared to term infants.

Conclusion: In very preterm infants with normal outcomes, although the developmental process is delayed, they may form a normal anterior segment structure similar to that of full-term infants in the late stages, which is followed up by the wide-field digital imaging system.

Keywords: Anterior segment; glaucoma; normal development; very preterm birth; wide-field digital imaging system.

Conflict of interest statement

None

SUPPLEMENTARY INFO

MeSH termsexpand

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Observational Study

Indian J Ophthalmol

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. 2023 Nov;71(11):3478-3483.

doi: 10.4103/IJO.IJO_274_23.

[Role of fetal hemoglobin in the development and progression of retinopathy of prematurity in preterm infants](#)

[Nishi Prasad](#)¹, [Aditi Dubey](#)¹, [Kavita Kumar](#)¹, [Jyotsna Shrivastava](#)²

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- PMID: 37870010
- DOI: [10.4103/IJO.IJO_274_23](https://doi.org/10.4103/IJO.IJO_274_23)

Free article

Abstract

Purpose: The objective of this study was to find the association between fetal hemoglobin (HbF) concentration and retinopathy of prematurity (ROP) in preterm infants.

Methods: In this observational, prospective, longitudinal study, a total of 410 preterm infants with <36 gestational weeks and <2.5 kg birth weight, who were attending ROP clinic in a tertiary care hospital of central India for 1 year duration were included. Dilated

fundus examination was done as per ROP screening guidelines, and ROP was staged as per international classification for retinopathy of prematurity (ICROP) classification, 2021. HbF (%) was measured with high-performance liquid chromatography, and data was analyzed statistically. The relationship between HbF (%) and ROP was evaluated. Those infants who had ROP were further divided into treatment-requiring and non-treatment-requiring groups and HbF was compared in these groups at the first visit and after 1-month follow-up period. The outcome of ROP was studied with HbF levels.

Results: A total of 410 preterm infants were included, out of which 110 infants had ROP (26.8%). Infants with ROP had significantly lower percentage of HbF with gestational age groups and birth weight groups, compared to infants without ROP. Higher percentage of HbF was associated with a lower prevalence of ROP. Higher concentration of HbF was found in the ROP infants who regressed spontaneously without treatment and less concentration was found in those who progressed to a severe disease and those who required treatment. The predictive ability of HbF (%) was 0.976 for ROP.

Conclusion: Low fraction of HbF was found to be significantly associated with the development and progression of ROP.

Keywords: Fetal hemoglobin; preterm infants; protective; retinopathy of prematurity.

Conflict of interest statement

None

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Publication types, MeSH terms, Substancesexpand

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Observational Study

Indian J Ophthalmol

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. 2023 Nov;71(11):3473-3477.

doi: 10.4103/IJO.IJO_415_23.

Usefulness of Children's Hospital of Philadelphia ROP (CHOP ROP) model in the prediction of type 1 ROP

[Barkha Jain](#)¹, [Neha K Sethi](#)¹, [Amanpreet Sethi](#)², [Rhythm Arora](#)¹, [Twinkle Gupta](#)¹, [Harnoor Kaur](#)¹

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- DOI: [10.4103/IJO.IJO_415_23](https://doi.org/10.4103/IJO.IJO_415_23)

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Abstract

Purpose: Children's Hospital of Philadelphia retinopathy of prematurity (CHOP ROP) model can be used to predict ROP, a leading cause of childhood blindness, using risk factors such as postnatal weight gain, birth weight (BW), and gestation age (GA). The purpose of this study was to determine the usefulness of the CHOP ROP for the prediction of treatable ROP.

Methods: This was a prospective observational study. Babies <34 weeks of GA, BW <2000 grams, and GA 34-36 weeks with risk factors such as respiratory distress syndrome (RDS) were included; ROP screening, follow-up, and treatment were performed based on national guidelines. The average daily postnatal weight gain was measured, and the CHOP nomogram was plotted. Babies were categorized as high risk or low risk based on the "CHOP" alarm. The sensitivity and specificity of the CHOP ROP for the detection of treatable ROP were determined. In case of poor sensitivity, a new cutoff alarm level was planned using logistic regression analysis.

Results: Of 62 screened infants, 23 infants did not fulfill the criteria of the CHOP algorithm and were excluded. Thus, in the study on 39 infants, the predictive model with an alarm level of 0.014 had 100% specificity and 20% sensitivity. With the "new" alarm level (cutoff)

of 0.0003, the CHOP nomogram could detect all the infants who developed treatable ROP, that is, sensitivity increased to 100% but specificity decreased to 10.5%.

Conclusion: The CHOP ROP model with a cutoff point (0.014) performed poorly in predicting severe ROP in the study. Thus, there is a need to develop inclusive and more sensitive tailor-made algorithms.

Keywords: Blindness; infant; international classification of retinopathy of prematurity; preterm; retinopathy of prematurity; weight gain in infants; weight gain-based ROP prediction algorithm.

Conflict of interest statement

None

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Indian J Ophthalmol

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. 2023 Nov;71(11):3465-3472.

doi: 10.4103/IJO.IJO_3407_22.

[Early detection and correlation of tear fluid inflammatory factors that influence angiogenesis in premature](#)

infants with and without retinopathy of prematurity

[Anand Vinekar¹](#), [Archana Padmanabhan Nair²](#), [Shivani Sinha¹](#), [Tanuja Vaidya²](#), [Rohit Shetty³](#), [Arkasubhra Ghosh²](#), [Swaminathan Sethu²](#)

Affiliations expand

- PMID: 37870008
- DOI: [10.4103/IJO.IJO_3407_22](https://doi.org/10.4103/IJO.IJO_3407_22)

Free article

Abstract

Purpose: To measure the levels of inflammatory factors in tear fluid of pre-term infants with and without retinopathy of prematurity (ROP).

Methods: The cross-sectional pilot study included 29 pre-term infants undergoing routine ROP screening. Pre-term infants were grouped as those without ROP (no ROP; n = 14) and with ROP (ROP; n = 15). Sterile Schirmer's strips were used to collect the tear fluid from pre-term infants. Inflammatory factors such as interleukin (IL)-6, IL-8, MCP1 (Monocyte Chemoattractant Protein 1; CCL2), RANTES (Regulated on Activation, Normal T Cell Expressed and Secreted; CCL5), and soluble L-selectin (sL-selectin) were measured by cytometric bead array using a flow cytometer.

Results: Birth weight (BW) and gestation age (GA) were significantly ($P < 0.05$) lower in pre-term infants with ROP compared with those without ROP. Higher levels of RANTES ($P < 0.05$) and IL-8 ($P = 0.09$) were observed in the tear fluid of pre-term infants with ROP compared with those without ROP. Lower levels of tear fluid IL-6 ($P = 0.14$) and sL-selectin ($P = 0.18$) were measured in pre-term infants with ROP compared with those without ROP. IL-8 and RANTES were significantly ($P < 0.05$) higher in the tear fluid of pre-term infants with stage 3 ROP compared with those without ROP. Tear fluid RANTES level was observed to be inversely associated with GA and BW of pre-term infants with ROP and not in those without ROP. Furthermore, the area under the curve and odds ratio analysis demonstrated the relevance of RANTES/BW (AUC = 0.798; OR-7.2) and RANTES/MCP1 (AUC = 0.824; OR-6.8) ratios in ROP.

Conclusions: Distinct changes were observed in the levels of tear inflammatory factors in ROP infants. The status of RANTES in ROP suggests its possible role in pathobiology and warrants further mechanistic studies to harness it in ROP screening and management.

Keywords: Biomarker; IL-6; IL-8; RANTES; ROP; inflammatory factors; non-invasive; tear fluid.

Conflict of interest statement

None

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS



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Early Hum Dev

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. 2023 Nov;186:105873.

doi: 10.1016/j.earlhumdev.2023.105873. Epub 2023 Oct 11.

Neonatal outcomes of early preterm births according to the delivery indications

[Hyojeong Kim](#)¹, [Yu Mi Shin](#)¹, [Kyong-No Lee](#)¹, [Hyeon Ji Kim](#)¹, [Young Hwa Jung](#)², [Jee Yoon Park](#)³, [Kyung Joon Oh](#)¹, [Chang Won Choi](#)²

Affiliations expand

- PMID: 37844515

- DOI: [10.1016/j.earlhumdev.2023.105873](https://doi.org/10.1016/j.earlhumdev.2023.105873)

Free article

Abstract

Objective: To compare the neonatal outcomes of early preterm births according to delivery indications and determine the obstetric risk factors associated with adverse outcomes.

Methods: We retrospectively studied pregnancies delivered between 22 + 0 and 26 + 6 weeks at the tertiary center between April 2013 and April 2022. Stillbirths, elective termination of pregnancy, and multifetal pregnancies were excluded. Patients were classified into two groups according to delivery indications: spontaneous preterm birth (sPTB) due to premature rupture of membranes (PROM), preterm labor, or acute cervical insufficiency; and indicated preterm birth (IPTB). Obstetric and neonatal outcomes were compared between the groups.

Results: Of the 121 neonates, 73 % (88/121) underwent sPTB. The overall survival rates were 73 % and 49 % in the sPTB and IPTB groups, respectively ($p = 0.017$). Multivariate logistic regression analysis was performed with adjustment for gestational age at delivery, fetal growth restriction, cesarean section, histological chorioamnionitis, and funisitis. Moreover, in the 1-year follow-up, the proportion of body mass below the third percentile was significantly higher in the IPTB-group than in the sPTB-group (53 % vs. 20 %, $p = 0.019$). Furthermore, diagnoses of developmental delay and cerebral palsy were slightly higher in the IPTB-group (33 % and 20 %, respectively) than in the sPTB-group (27 % and 9 %, respectively); however, this difference was not statistically significant.

Conclusions: In early preterm births, IPTB was associated with a higher neonatal mortality than sPTB.

Keywords: Neonate; Preeclampsia; Preterm birth; Preterm labor; Previabile preterm birth.

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Conflict of interest statement

Declaration of competing interest The authors declare no conflicts of interest relevant to this work.

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Hosp Pediatr



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doi: 10.1542/hpeds.2022-007037.

Increasing Exclusive Nursery Care of Late Preterm and Low Birth Weight Infants

[Rakhi Gupta Basuray](#)^{1,2}, [Carrie Cacioppo](#)^{1,2}, [Vanessa Inuzuka](#)³, [Keri Cooper](#)³, [Charles Hardy](#)⁴, [Michael F Perry](#)²

Affiliations expand

- PMID: 37818615
- DOI: [10.1542/hpeds.2022-007037](https://doi.org/10.1542/hpeds.2022-007037)

Abstract

Background and objective: Late preterm (LPT) and low birth weight (LBW) infants are populations at increased risk for NICU admission, partly due to feeding-related conditions. This study was aimed to increase the percentage of LPT and LBW infants receiving exclusive nursery care using quality improvement methodologies.

Methods: A multidisciplinary team implemented interventions at a single academic center. Included infants were 35 to 36 weeks gestational age and term infants with birth weights <2500 g admitted from the delivery room to the nursery. Drivers of change included feeding protocol, knowledge, and care standardization. We used statistical process control charts to track data over time. The primary outcome was the percentage of infants receiving exclusive nursery care. Secondary outcomes included rates of hypoglycemia,

phototherapy, and average weight loss. Balancing measures were exclusive breast milk feeding rates and length of stay.

Results: Included infants totaled 1336. The percentage of LPT and LBW infants receiving exclusive nursery care increased from 83.9% to 88.8% with special cause variation starting 1 month into the postintervention period. Reduction in neonatal hypoglycemia, 51.7% to 45.1%, coincided. Among infants receiving exclusive nursery care, phototherapy, weight loss, exclusive breast milk feeding, and length of stay had no special cause variation.

Conclusions: Interventions involving a nursery feeding protocol, knowledge, and standardization of care for LPT and LBW infants were associated with increased exclusive nursery care (4.9%) and reduced rates of neonatal hypoglycemia (6.6%) without adverse effects. This quality initiative allowed for the preservation of the mother-infant dyad using high-value care.

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SUPPLEMENTARY INFO

MeSH termsexpand

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J Womens Health (Larchmt)

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. 2023 Nov;32(11):1208-1218.

doi: 10.1089/jwh.2023.0239. Epub 2023 Oct 10.

Pregnancy Complications Are Associated with Premature Coronary Artery Disease: Linking Three Cohorts

[Adeel Khoja](#)^{1,2,3}, [Prabha H Andraweera](#)^{1,2,3}, [Rosanna Tavella](#)^{1,4}, [Tiffany K Gill](#)¹, [Gustaaf A Dekker](#)^{1,2,5}, [Claire T Roberts](#)^{1,2,6}, [Suzanne Edwards](#)⁷, [Margaret A Arstall](#)^{3,8}

Affiliations expand

- PMID: 37815882
- DOI: [10.1089/jwh.2023.0239](https://doi.org/10.1089/jwh.2023.0239)

Abstract

Background: There is increasing evidence that women who experience placenta-mediated pregnancy complications and gestational diabetes mellitus (GDM) are at higher risk for the development of coronary artery disease (CAD) later in life. We hypothesized that there is an association between placenta-mediated pregnancy complications, GDM, and risk of premature CAD (PCAD). **Methods:** This research project involved a data linkage approach merging three databases of South Australian cohorts by using a retrospective, age-matched case-control study design. Cases ($n = 721$) were ascertained from the Coronary Angiogram Database of South Australia (CADOSA). Women <60 years from CADOSA were linked to South Australian Perinatal Statistics Collection (SAPSC) to ascertain their prior pregnancy outcomes. Controls ($n = 194$) were selected from North West Adelaide Health Study (NWAHS) and comprised women who were healthy or had other health conditions unrelated to CAD, age-matched to CADOSA (± 5 years), and linked to SAPSC to determine their pregnancy outcomes. PCAD was defined as $>50\%$ stenosis in one or more coronary arteries at coronary angiography. **Results:** Compared with women without a history of PCAD, women who were diagnosed with PCAD were more likely to have experienced the placenta-mediated pregnancy complications of preterm birth (adjusted odds ratio [OR] = 2.46, 95% confidence interval [CI]: 1.21-5.00) or low-birth weight (adjusted OR = 2.44, 95% CI: 1.22-4.88), or have been diagnosed with active asthma during pregnancy (adjusted OR = 3.52, 95% CI: 1.05-11.76). **Conclusion:** Placenta-mediated pregnancy complications should be recognized as clear risk markers for future PCAD.

Keywords: case-control study; data linkage; pregnancy complications; premature coronary artery disease; risk factors.

SUPPLEMENTARY INFO

MeSH termsexpand

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Clinical Trial

Clin Nutr

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. 2023 Nov;42(11):2229-2240.

doi: 10.1016/j.clnu.2023.09.005. Epub 2023 Sep 20.

[DHA, nutrient intake, and maternal characteristics as predictors of pregnancy outcomes in a randomised clinical trial of DHA supplementation](#)

[Yu Wang](#)¹, [Byron J Gajewski](#)¹, [Christina J Valentine](#)², [Sarah A Crawford](#)³, [Alexandra R Brown](#)¹, [Dinesh Pal Mudaranthakam](#)¹, [Juliana Teruel Camargo](#)³, [Susan E Carlson](#)⁴

Affiliations expand

- PMID: 37806075
- PMID: PMC10591724 (available on 2024-11-01)

- DOI: [10.1016/j.clnu.2023.09.005](https://doi.org/10.1016/j.clnu.2023.09.005)

Abstract

Purpose: To investigate the relationships among docosahexaenoic acid (DHA) intake, nutrient intake, and maternal characteristics on pregnancy outcomes in a phase III randomised clinical trial designed to determine the effect of a DHA dose of 1000 mg/day compared to 200 mg/day on early preterm birth (<34 weeks gestation).

Methods: A secondary aim of the phase III randomised trial was to explore the relationships among pregnancy outcomes (maternal red blood cell phospholipid (RBC-PL) DHA at delivery, preterm birth, gestational age at delivery, labor type, birth anthropometric measures, low birth weight, gestational diabetes, pre-eclampsia, and admission to a neonatal intensive care unit) in participants (n = 1100). We used Bayesian multiple imputation and linear and logistic regression models to conduct an analysis of five general classes of predictor variables collected during the trial: a) DHA intake, b) nutrient intake from food and supplements, c) environmental exposure to tobacco and alcohol, d) maternal demographics, and e) maternal medical history.

Results: DHA supplementation lowered the risk of preterm birth and NICU admission, and increased gestation and birth weight as observed in the primary analysis. Higher maternal RBC-PL-DHA at delivery was associated with DHA supplementation and formal education of a bachelor's degree or higher. DHA supplementation and maternal age were associated with a higher risk of gestational diabetes. Total vitamin A intake was associated with longer gestation, while fructose and intake of the long chain omega-6 fatty acid, arachidonic acid, were associated with shorter gestation. Risk of preterm birth was associated with a history of low birth weight, preterm birth, pre-eclampsia, and NICU admission.

Conclusion: Bayesian models provide a comprehensive approach to relationships among DHA intake, nutrient intake, maternal characteristics, and pregnancy outcomes. We observed previously unreported relationships between gestation duration and fructose, vitamin A, and arachidonic acid that could be the basis for future research.

Trial registration number and date: ClinicalTrials.gov ([NCT02626299](https://clinicaltrials.gov/ct2/show/study/NCT02626299)); December 10, 2015.

Keywords: Arachidonic acid; DHA; Fructose; Pregnancy; Preterm birth; Vitamin A.

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Conflict of interest statement

Conflicts of interest CJV, BJG and SEC were the principal investigators for the primary clinical trial. SEC has collaborated with DSM, the company that donated the capsules for the primary clinical trial but has no other conflicts of interest. All other authors have no

conflicts of interest. YW conducted the Bayesian analysis as partial fulfillment for her PhD dissertation in the Department of Biostatistics and Data Science. She also wrote the manuscript with the assistance of SEC and BJG.

- [47 references](#)

SUPPLEMENTARY INFO

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Menopause

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. 2023 Nov 1;30(11):1106-1113.

doi: 10.1097/GME.0000000000002258. Epub 2023 Oct 2.

[Sleep disturbances in women with early-onset menopausal transition: a population-based study](#)

[Satu A E Salin](#), [Susanna M Savukoski](#), [Paula R O Pesonen](#)¹, [Juha P Auvinen](#), [Maarit J Niinimäki](#)

Affiliations [expand](#)

- PMID: 37788421
- DOI: [10.1097/GME.0000000000002258](https://doi.org/10.1097/GME.0000000000002258)

Abstract

Objective: The aim of this study was to investigate sleep disturbances in 46-yr-old women and their association with early-onset menopausal transition.

Methods: The women of this cross-sectional birth cohort study were divided into climacteric (n = 359) and preclimacteric (n = 2,302) groups by their menopausal status, defined by follicle-stimulating hormone levels and menstrual history. Sleep disturbances were evaluated with Athens Insomnia Scale 5. We performed univariable and multivariable logistic regression models in which sleep parameters were dependent variables and climacteric status, hot flashes, smoking, and education level were independent variables. The use of hormone therapy was also evaluated in women suffering from sleeping disturbances.

Results: On the basis of the scale questions, climacteric women experienced significantly delayed sleep induction (12.2% vs 8.7%, $P = 0.047$), more problems with awakenings during the night (23.4% vs 14.6%, $P < 0.001$), earlier final awakening (13.8% vs 9.9%, $P = 0.039$), and more unsatisfying sleep quality (11.9% vs 7.9%, $P = 0.023$). Climacteric women who were experiencing hot flashes reported unsatisfactory sleep quality more frequently compared with climacteric women who did not experience hot flashes (17.0% vs 9.2%, $P = 0.047$). In the univariable and multivariable logistic regression models, being climacteric was independently associated with different impaired sleeping parameters. Most climacteric women who had a scale score of 4 or greater were not using hormone therapy, according to their medicine purchases over the past year.

Conclusions: Being climacteric was associated with sleep disturbances in women in their mid-40s. However, this association seemed to be particularly driven by hot flashes. Most climacteric women with clinically significant sleeping disturbances were not using hormone therapy.

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Conflict of interest statement

Financial disclosure/conflicts of interest: S.M.S. received a past grant from the Finnish Medical Foundation, a past grant from the Finnish Menopause Society, and a past grant from the Juho Vainio Foundation. The other authors have nothing to disclose.

- [46 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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J Allergy Clin Immunol Glob

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. 2023 Aug 3;2(4):100161.

doi: 10.1016/j.jacig.2023.100161. eCollection 2023 Nov.

[Respiratory-syncytial virus immunoprophylaxis on asthma symptoms development in prematurity with bronchopulmonary dysplasia](#)

[Li-Ching Fang](#)¹, [Jen-Yu Wang](#)², [Hsin-Hui Yu](#)³, [Li-Chieh Wang](#)³, [Bor-Luen Chiang](#)^{3 4 5}

Affiliations expand

- PMID: 37781666
- PMCID: [PMC10510012](#)
- DOI: [10.1016/j.jacig.2023.100161](#)

Free PMC article

Abstract

Background: Infants with respiratory-syncytial virus bronchiolitis hospitalization are more likely to develop wheezing and subsequent asthma. Reportedly, palivizumab prophylaxis

effectively prevents respiratory-syncytial virus hospitalization in high-risk children-such as premature infants or infants with bronchopulmonary dysplasia (BPD).

Objective: We sought to explore the effect of respiratory-syncytial virus immunoprophylaxis on the risk of asthma development in premature infants with BPD in subtropical areas.

Methods: This case-control study included preterm children with BPD born at Mackay Memorial Hospital, Taipei, Taiwan, from 1999 to 2015. Overall, medical records of 616 eligible participants were retrospectively collected from their birth to the time they attained an age of 5 to 20 years. The primary outcome was onset of active asthma.

Results: Overall, 576 consecutive cases met the inclusion criteria. Of these, 306 (53.2%) patients had palivizumab exposure and 191 (33.2%) were diagnosed with asthma. Patients with history of respiratory-syncytial virus bronchiolitis hospitalization had a higher risk of developing asthma in the future (adjusted odds ratio, 3.77; 95% CI, 2.30-6.20, $P < .001$; hazard ratio, 2.56; 95% CI, 1.81-3.62, $P < .001$). Palivizumab prophylaxis reduced future asthma development through the inhibition of respiratory-syncytial virus bronchiolitis hospitalization (coefficient, -0.021; 95% CI, -0.031 to -0.011, $P = .027$). Asthmatic children who received palivizumab immunoprophylaxis had a lesser active asthma duration than those who did not ($P = .005$).

Conclusions: Children with BPD with hospitalization for respiratory-syncytial virus bronchiolitis had higher risk of developing asthma compared with those without respiratory-syncytial virus infection. Prophylactic palivizumab might reduce later asthma development through inhibition of respiratory-syncytial virus bronchiolitis hospitalization. For those already developing asthma, palivizumab could reduce active asthma duration.

Keywords: Asthma; RSV bronchiolitis; bronchopulmonary dysplasia; palivizumab; prematurity.

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

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Randomized Controlled Trial

Obstet Gynecol

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. 2023 Nov 1;142(5):1179-1188.

doi: 10.1097/AOG.0000000000005386. Epub 2023 Sep 28.

Occipital Nerve Block Compared With Acetaminophen and Caffeine for Headache Treatment in Pregnancy: A Randomized Controlled Trial

[Elisa T Bushman](#)¹, [Christina T Blanchard](#), [Gabriella D Cozzi](#), [Allison M Davis](#), [Lorie Harper](#), [Lindsay S Robbins](#), [Benjamin Jones](#), [Jeff M Szychowski](#), [Kathleen B Digre](#), [Brian M Casey](#), [Alan T Tita](#), [Rachel G Sinkey](#)

Affiliations expand

- PMID: 37769308
- PMCID: [PMC10591891](#)
- DOI: [10.1097/AOG.0000000000005386](#)

Free PMC article

Abstract

Objective: To evaluate the efficacy of occipital nerve block compared with standard care , defined as acetaminophen with caffeine, for treatment of acute headache in pregnancy.

Methods: We conducted a single-center, unblinded, parallel, randomized controlled trial of pregnant patients with headache and pain score higher than 3 on the visual rating scale. Patients with secondary headache, preeclampsia, or allergy or contraindication to study medications were excluded. Participants were randomized to occipital nerve block or standard care (oral 650 mg acetaminophen and 200 mg caffeine). Crossover treatment was given at 2 hours and second-line treatment at 4 hours to those with worsening visual rating scale score or visual rating scale score higher than 3. The primary outcome was headache improvement to a visual rating scale score of 3 or lower within 2 hours of initial therapy. Secondary outcomes included serial visual rating scale scores, receipt of crossover or second-line therapy, patient satisfaction, and perinatal outcomes. Outcomes were assessed in an intention-to-treat analysis. We estimated that a sample of 62 would provide 80% power to detect a difference from 85% to 50% between groups.

Results: From February 2020 to May 2022, 62 participants were randomized to occipital nerve block (n=31) or standard care (n=31). Groups were similar except payer status. The primary outcome, headache improvement to visual rating scale score of 3 or lower, was not significantly different between groups (64.5% vs 51.6%, $P = .30$). The occipital nerve block group experienced lower median [interquartile range] visual rating scale scores at 1 hour (2 [0-5] vs 6 [2-7], $P = .014$), and more patients in the occipital nerve block group had visual rating scale scores of 3 or lower at 1 hour. Among patients receiving crossover treatment at 2 hours, the standard care group had a significantly lower visual rating scale score 1 hour after crossover to occipital nerve block than the occipital nerve block group receiving crossover to standard care ($P = .028$). There were no significant differences in second-line treatment, refractory headache, satisfaction, or complications. Patients receiving occipital nerve block delivered earlier (36.6 weeks vs 37.8 weeks), but preterm birth did not differ between groups.

Conclusion: Occipital nerve block is an effective and quick-acting treatment option for acute headache in pregnancy.

Clinical trial registration: ClinicalTrials.gov , [NCT03951649](https://clinicaltrials.gov/ct2/show/study/NCT03951649).

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Conflict of interest statement

Financial Disclosure Alan T. Tita disclosed that his institution received funding from Pfizer. Rachel G. Sinkey disclosed that her institution received funding from the NIH and AHA. The other authors did not report any potential conflicts of interest.

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

SUPPLEMENTARY INFO

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Meta-Analysis

Diabetes Care

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. 2023 Nov 1;46(11):2024-2034.

doi: 10.2337/dc23-1209.

[Ethnic Differences in the Association Between Age at Natural Menopause and Risk of Type 2 Diabetes Among Postmenopausal Women: A Pooled Analysis of Individual Data From 13 Cohort Studies](#)

[Hsin-Fang Chung](#)¹, [Annette J Dobson](#)¹, [Kunihiko Hayashi](#)², [Rebecca Hardy](#)³, [Diana Kuh](#)⁴, [Debra J Anderson](#)⁵, [Yvonne T van der Schouw](#)⁶, [Darren C Greenwood](#)⁷, [Janet E Cade](#)⁷, [Panayotes Demakakos](#)⁸, [Eric J Brunner](#)⁸, [Sophie V Eastwood](#)⁴, [Sven Sandin](#)^{9,10}, [Elisabete Weiderpass](#)¹¹, [Gita D Mishra](#)¹

Affiliations expand

- PMID: 37747341

- DOI: [10.2337/dc23-1209](https://doi.org/10.2337/dc23-1209)

Abstract

Objective: To investigate associations between age at natural menopause, particularly premature ovarian insufficiency (POI) (natural menopause before age 40 years), and incident type 2 diabetes (T2D) and identify any variations by ethnicity.

Research design and methods: We pooled individual-level data of 338,059 women from 13 cohort studies without T2D before menopause from six ethnic groups: White (n = 177,674), Chinese (n = 146,008), Japanese (n = 9,061), South/Southeast Asian (n = 2,228), Black (n = 1,838), and mixed/other (n = 1,250). Hazard ratios (HRs) of T2D associated with age at menopause were estimated in the overall sample and by ethnicity, with study as a random effect. For each ethnic group, we further stratified the association by birth year, education level, and BMI.

Results: Over 9 years of follow-up, 20,064 (5.9%) women developed T2D. Overall, POI (vs. menopause at age 50-51 years) was associated with an increased risk of T2D (HR 1.31; 95% CI 1.20-1.44), and there was an interaction between age at menopause and ethnicity ($P < 0.0001$). T2D risk associated with POI was higher in White (1.53; 1.36-1.73), Japanese (4.04; 1.97-8.27), and Chinese women born in 1950 or later (2.79; 2.11-3.70); although less precise, the risk estimates were consistent in women of South/Southeast Asian (1.46; 0.89-2.40), Black (1.72; 0.95-3.12), and mixed/other (2.16; 0.83-5.57) ethnic groups. A similar pattern, but with a smaller increased risk of T2D, was observed with early menopause overall (1.16; 1.10-1.23) and for White, Japanese, and Chinese women born in 1950 or later.

Conclusions: POI and early menopause are risk factors for T2D in postmenopausal women, with considerable variation across ethnic groups, and may need to be considered in risk assessments of T2D among women.

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Publication types, MeSH terms, Grants and fundingexpand

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J Viral Hepat

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. 2023 Nov;30(11):889-896.

doi: 10.1111/jvh.13878. Epub 2023 Sep 23.

Effects of hepatitis B virus infection on the treatment outcomes following in vitro fertilization/intracytoplasmic sperm injection: An analysis of 21,999 first embryo transfer cycles

[Ning-Zhao Ma¹](#), [Wei Dai¹](#), [Xiao Bao¹](#), [Zhi-Qin Bu¹](#), [Hao Shi¹](#), [Ying-Pu Sun¹](#)

Affiliations expand

- PMID: 37740608

- DOI: [10.1111/jvh.13878](https://doi.org/10.1111/jvh.13878)

Abstract

To investigate the effects of hepatitis B virus (HBV) infection on the outcomes of Chinese couples undergoing in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) and the clinical data of their neonates. A total of 21,999 first embryo transfer cycles were included. They were categorized into four groups based on the couple's hepatitis B surface antigen (HBsAg) result (Group A = female HBsAg⁻ and male HBsAg⁻; Group B = female HBsAg⁺ and male HBsAg⁻; Group C = female HBsAg⁻ and male HBsAg⁺; Group D = female HBsAg⁺ and male HBsAg⁺). The fertilization rate (FR), cleavage rate (CR), implantation rate (IPR), clinical pregnancy rate (CPR), live birth rate (LBR) and miscarriage rate (MCR) were analysed. Multilevel logistic regression was applied to evaluate the association. The total prevalence of HBV infection was 5.74% (2526/43998). There were no statistically significant differences in CRs (98.69%, 98.76%, 98.66%, 98.72%, $p > .05$), IPRs (45.86%, 47.33%,

45.19%, 39.61%, $p > .05$), CPRs (62.84%, 65.05%, 61.80%, 56.81%, $p > .05$), MCRs (12.70%, 11.99%, 12.58%, 4%, $p > .05$) and LBRs (53.43%, 55.38%, 52.70%, 54.54%, $p > .05$) among the four groups. However, there were significant differences in FRs (66.25%, 66.55%, 66.32%, 61.92%, $p < .05$). Group D had the lowest FR. After adjusting for confounders, the multilevel logistic regression showed that HBsAg⁺ had no impact on the LBR, CPR or MCR. We also analysed the data of 14,465 newborns, including 8593 singletons and 2936 twins. Among the four groups, no variables reached statistical significance, including neonatal birth weight (NBW), twin ratio, gestational age, premature birth, delivery type, fetal macrosomia or low birth weight ($p > .05$). Our study demonstrates that, although biparental HBV infection may affect the FR, neither single-parent infection nor biparental HBV infection affects IVF/ICSI outcomes or neonatal outcomes.

Keywords: HBsAg; IVF/ICSI; hepatitis B virus; neonatal outcomes; pregnancy outcomes.

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- [28 references](#)

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Acta Obstet Gynecol Scand

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. 2023 Nov;102(11):1541-1548.

doi: 10.1111/aogs.14683. Epub 2023 Sep 22.

Universal cervical length screening for preterm birth is not useful after 24 weeks of gestation

[Viola Seravalli](#)¹, [Isabella Abati](#)¹, [Noemi Strambi](#)¹, [Lorenzo Tofani](#)², [Claudia Tucci](#)¹, [Enrico Tartarotti](#)¹, [Mariasosaria Di Tommaso](#)¹

Affiliations expand

- PMID: 37737470
- PMCID: [PMC10577617](#)
- DOI: [10.1111/aogs.14683](#)

Free PMC article

Abstract

Introduction: Cervical length measurement using transvaginal sonography at 18⁺⁰ - 24⁺⁰ weeks of gestation is used to identify women at risk of preterm delivery, who may benefit from treatment with progesterone to prevent premature birth. Few and conflicting data exist regarding the predictive value of cervical length measurement performed at later gestational ages. The primary objective of this study was to evaluate the predictive accuracy for spontaneous preterm birth of a single cervical length measurement performed between 24 and 32 weeks of gestation in asymptomatic singleton pregnancies at low risk for spontaneous preterm birth. The secondary objective was to test the predictive accuracy of different cervical length thresholds in the same population.

Material and methods: This was a historical cohort study conducted in a tertiary referral hospital. A total of 2728 asymptomatic women with singleton pregnancy at low risk for spontaneous preterm birth were recruited. Of these women, 1548 had cervical length measured at 24⁺⁰ -27⁺⁶ weeks of gestation and 2191 women at 28⁺⁰ -32⁺⁰ weeks. In all, 1010 women were present in both gestational age windows. Maternal demographics, medical and obstetrical history, and pregnancy outcome were reviewed. The predictive value of cervical length for spontaneous preterm birth was evaluated through logistic regression analysis. Results were adjusted for confounding factors.

Results: Overall, spontaneous preterm birth occurred in 53/2728 women (1.9%). In both the 24⁺⁰ -27⁺⁶ and 28⁺⁰ -32⁺⁰ weeks groups, a shorter cervical length was significantly

associated with spontaneous preterm birth ($p < 0.01$), but it had a low predictive value, as shown by the receiver operating characteristics curve analysis (areas under the curve 0.62, 95% CI 0.50-0.74 for the 24⁺⁰ -27⁺⁶ weeks group, and 0.61, 95% CI 0.52-0.70 in the 28⁺⁰ - 32⁺⁰ weeks group). When the predictive accuracy for preterm delivery of different cervical length cut-offs was evaluated, the sensitivity and positive predictive value were low in both gestational age windows, irrespective of the threshold used.

Conclusions: In asymptomatic women with singleton pregnancy at low risk for spontaneous preterm birth, the predictive value of cervical length after 24⁺⁰ weeks of gestation is low. Therefore, cervical length screening in these women should be discouraged.

Keywords: cervical length; pregnancy; preterm birth; preterm delivery.

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Conflict of interest statement

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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

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Multicenter Study



Breastfeeding Behavior Within the Covid-19 Related Obstetric and Neonatal Outcome Study (CRONOS)

[Janine Zöllkau](#)¹, [Yvonne Heimann](#)¹, [Carsten Hagenbeck](#)², [Ulrich Pecks](#)³, [Michael Abou-Dakn](#)⁴, [Rolf Schlösser](#)⁵, [Anna Schohe](#)⁴, [Iris Dressler-Steinbach](#)⁶, [Maike Manz](#)⁷, [Constanze Banz-Jansen](#)⁸, [Edith Reuschel](#)⁹, [Antonella Iannaccone](#)¹⁰, [Michael K Bohlmann](#)¹¹, [Katrina Kraft](#)¹², [Sara Fill Malfertheiner](#)⁹, [Pauline Wimberger](#)¹³, [Thomas Kolben](#)¹⁴, [Catharina Bartmann](#)¹⁵, [Ann-Carolin Longardt](#)¹⁶

Affiliations [expand](#)

- PMID: 37712573
- DOI: [10.1177/08903344231190623](https://doi.org/10.1177/08903344231190623)

Abstract

Background: The SARS-CoV-2 pandemic and its influence on peripartum processes worldwide led to issues in breastfeeding support.

Research aim: The aim of this study was to describe breastfeeding behavior and peripartum in-hospital management during the pandemic in Germany and Austria.

Methods: This study was a descriptive study using a combination of secondary longitudinal data and a cross-sectional online survey. Registry data from the prospective multicenter COVID-19 Related Obstetric and Neonatal Outcome Study (CRONOS) cohort study (longitudinal, medical records of 1,815 parent-neonate pairs with confirmed SARS-CoV-2 infection during pregnancy) and a cross-sectional online survey of CRONOS hospitals' physicians ($N = 67$) were used for a descriptive comparison of feeding outcomes and postpartum management.

Results: In 93.7% ($n = 1700$) of the cases in which information on the neonate's diet was provided, feeding was with the mother's own milk. Among neonates not receiving their

mother's own milk, 24.3% ($n = 26$) reported SARS-CoV-2 infection as the reason. Peripartum maternal SARS-CoV-2 infection, severe maternal COVID-19 including the need for intensive care unit (ICU) treatment or invasive ventilation, preterm birth, mandatory delivery due to COVID-19, and neonatal ICU admission were associated with lower rates of breastfeeding. Rooming-in positively influenced breastfeeding without affecting neonatal SARS-CoV-2 frequency (4.2% vs. 5.6%). CRONOS hospitals reported that feeding an infant their mother's own milk continued to be supported during the pandemic. In cases of severe COVID-19, four of five hospitals encouraged breastfeeding.

Conclusion: Maintaining rooming-in and breastfeeding support services in the CRONOS hospitals during the pandemic resulted in high breastfeeding rates.

Keywords: Austria; COVID-19; CRONOS Registry; Germany; SARS-CoV-2; breastfeeding; lactation management; mother's milk feeding; pregnancy; prospective cohort.

Conflict of interest statement

Disclosures and Conflicts of InterestThe authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Pecks reports a grant from Krumme Stiftung and Deutsche Diabetes Gesellschaft, as well as non-financial support from Castor EDC and Deutsche Gesellschaft für Perinatale Medizin during the conduct of the study. All other authors have nothing to disclose.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Pediatr Pulmonol

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. 2023 Nov;58(11):3279-3292.

Peripheral airway dysfunction in prematurity-associated obstructive lung disease identified by oscillometry

[Michael Cousins](#)^{1,2}, [Kylie Hart](#)^{1,2}, [Bence L Radics](#)³, [A John Henderson](#)⁴, [Zoltán Hantos](#)⁵, [Peter D Sly](#)⁶, [Sailesh Kotecha](#)¹

Affiliations expand

- PMID: 37701982
- DOI: [10.1002/ppul.26658](https://doi.org/10.1002/ppul.26658)

Abstract

Introduction: Mechanisms underlying lung dysfunction after preterm birth are poorly understood. Studying phenotypes of prematurity-associated lung disease may aid understanding of underlying mechanisms. Preterm-born children with and without lung dysfunction and term controls were assessed using oscillometry before and after exercise, and after postexercise bronchodilation.

Methods: Preterm-born children, born at gestation of 34 weeks or less, were classified into those with prematurity-associated obstructive lung disease (POLD; $FEV_1 < LLN$, $FEV_1 / FVC < LLN$), prematurity-associated preserved ratio of impaired spirometry (pPRISm; $FEV_1 < LLN$, $FEV_1 / FVC \geq LLN$) and compared to preterm ($FEV_1 \geq LLN$) and term controls (%predicted $FEV_1 > 90\%$). All children underwent cardiopulmonary exercise, and oscillometry assessment at baseline, postexercise, and after postexercise bronchodilator administration.

Results: From 241 participants aged 7-12 years, complete data were available from 179: 15 children with POLD and 11 with pPRISm were compared with 93 preterm and 60 term controls. POLD group, when compared to both control groups, had impaired impedance, greater resistance, more negative (greater magnitude) reactance at low frequencies, and also had decreased compliance. pPRISm group demonstrated impaired reactance and compliance compared to term controls. No differences were noted between the preterm and term controls. Exercise had little impact on oscillometry values, but children with POLD had greatest improvements after postexercise bronchodilator administration, with decreased resistance and decreased magnitude of reactance, particularly at low frequencies.

Conclusion: Preterm-born children with obstructive airway disease had the greatest oscillometry impairments and the largest improvements after postexercise bronchodilator compared to control groups. Oscillometry can potentially be used to identify preterm-born children with lung disease to institute treatment.

Keywords: airway obstruction; albuterol; oscillometry; premature birth; respiratory mechanics.

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- [40 references](#)

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

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Am J Physiol Lung Cell Mol Physiol

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. 2023 Nov 1;325(5):L542-L551.

doi: 10.1152/ajplung.00008.2023. Epub 2023 Sep 12.

[Piezo channels in stretch effects on developing human airway smooth muscle](#)

[Brian Kelley](#)¹, [Emily Y Zhang](#)¹, [Latifa Khalfaoui](#)¹, [Marta Schiliro](#)¹, [Natalya Wells](#)¹, [Christina M Pabelick](#)^{1,2}, [Y S Prakash](#)^{1,2}, [Elizabeth R Vogel](#)¹

Affiliations expand

- PMID: 37697925
- DOI: [10.1152/ajplung.00008.2023](https://doi.org/10.1152/ajplung.00008.2023)

Abstract

The use of respiratory support strategies such as continuous positive airway pressure in premature infants can substantially stretch highly compliant perinatal airways, leading to airway hyperreactivity and remodeling in the long term. The mechanisms by which stretch detrimentally affects the airway are unknown. Airway smooth muscle cells play a critical role in contractility and remodeling. Using 18-22-wk gestation human fetal airway smooth muscle (fASM) as an in vitro model, we tested the hypothesis that mechanosensitive Piezo (PZ) channels contribute to stretch effects. We found that PZ1 and PZ2 channels are expressed in the smooth muscle of developing airways and that their expression is influenced by stretch. PZ activation via agonist Yoda1 or stretch results in significant $[Ca^{2+}]_i$ responses as well as increased extracellular matrix production. These data suggest that functional PZ channels may play a role in detrimental stretch-induced airway changes in the context of prematurity. **NEW & NOTEWORTHY** Piezo channels were first described just over a decade ago and their function in the lung is largely unknown. We found that piezo channels are present and functional in the developing airway and contribute to intracellular calcium responses and extracellular matrix remodeling in the setting of stretch. This may improve our understanding of the mechanisms behind development of chronic airway diseases, such as asthma, in former preterm infants exposed to respiratory support, such as continuous positive airway pressure (CPAP).

Keywords: asthma; contractility; extracellular matrix; lung; preterm birth.

SUPPLEMENTARY INFO

MeSH terms, Grants and funding expand

FULL TEXT LINKS



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. 2023 Nov:111:2-8.

doi: 10.1016/j.sleep.2023.08.030. Epub 2023 Sep 4.

Sleep disturbances are associated with feeding practices and age in preterm infants

[Karen Simon Rezende da Silveira](#)¹, [Junia Maria Serra-Negra](#)², [Ivana Meyer Prado](#)², [Lucas Guimarães Abreu](#)², [Thaliny Vitória Diniz Reis](#)², [Sheyla Marcia Aua](#)²

Affiliations expand

- PMID: 37696121
- DOI: [10.1016/j.sleep.2023.08.030](https://doi.org/10.1016/j.sleep.2023.08.030)

Abstract

Background: Preterm infants are under risk of several shortcomings including sleep disturbances (SD). This cross-sectional study evaluated factors associated with SD in preterm and low birth weight infants in a reference center for preterm children at a University Hospital, southeastern Brazil.

Methods: A hundred-four dyads of mothers-infants 0-3 years participated. Mothers answered an online questionnaire (Google Forms®) evaluating childbirth characteristics, gestational age, breastfeeding, bottle feeding, non-nutritive sucking habits and sociodemographic information. The Brazilian version of the Brief Infant Sleep Questionnaire (BISQ) evaluated SD. Bivariate and Logistic Regression analyses were performed ($p < 0.05$).

Results: SD was present in 45.2% of the sample. Multivariate Logistic Regression Model showed that infants breastfed ≥ 3 times at night had 5.006 more chances to have SD (CI 95% = 1.229-20.400) compared to those who did not breastfeed at night. Infants who were bottle-fed ≥ 3 times at night had 6.952 more chances to have SD (CI = 95% = 1.364-35.427) compared to those who were bottle fed less frequently. The chance of SD

decreased 6.6% (CI 95% = 0.889-0.982) for each increase of a month in infant's age, and infants from families with higher income had 3.535 more chances to have SD (CI 95% = 1.006-12.416).

Conclusion: The younger the child, a higher frequency of night feeding and belonging to higher income families were associated with SD. Recognizing the associated factors with SD in newborns and infants can aid families to better deal with this issue, promote better sleep quality and individualized counseling.

Keywords: Breastfeeding; Infant; Preterm; Sleep disturbances.

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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

MeSH termsexpand

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J Steroid Biochem Mol Biol

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. 2023 Nov;234:106397.

doi: 10.1016/j.jsbmb.2023.106397. Epub 2023 Sep 6.

Progesterone control of myometrial contractility

[Oksana Shynlova](#)¹, [Lubna Nadeem](#)², [Stephen Lye](#)³

Affiliations expand

- PMID: 37683774
- DOI: [10.1016/j.jsbmb.2023.106397](https://doi.org/10.1016/j.jsbmb.2023.106397)

Abstract

During pregnancy, the primary function of the uterus is to be quiescent and not contract, which allows the growing fetus to develop and mature. A uterine muscle layer, myometrium, is composed of smooth muscle cells (SMCs). Before the onset of labor contractions, the uterine SMCs experience a complex biochemical and molecular transformation involving the expression of contraction-associated proteins. Labor is initiated when genes in SMCs are activated in response to a combination of hormonal, inflammatory and mechanical signals. In this review, we provide an overview of molecular mechanisms regulating the process of parturition in humans, focusing on the hormonal control of the myometrium, particularly the steroid hormone progesterone. The primary reason for discussing the regulation of myometrial contractility by progesterone is the importance of the clinical problem of preterm birth. It is thought that the hormonal mechanisms regulating premature uterine contractions represent an untimely triggering of the normal events occurring during term parturition. Yet, our knowledge of the complex and redundant hormonal pathways controlling uterine contractile activity leading to delivery of the neonate remains incomplete. Finally, we introduce recent animal studies using a novel class of drugs, Selective Progesterone Receptor Modulators, targeting progesterone signaling to prevent premature myometrial contractions.

Keywords: Contractility; Myometrium; Physiologic inflammation; Preterm Birth; Progestin therapy; Transcriptional regulation; Uterus.

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Randomized Controlled Trial

J Hum Lact

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. 2023 Nov;39(4):656-665.

doi: 10.1177/08903344231192441. Epub 2023 Aug 31.

Inflammatory Markers in Mother's Own Milk and Infant Stool of Very Low Birthweight Infants

[Rebecca Hoban](#)¹, [Hadar Nir](#)^{1,2}, [Emily Somerset](#)³, [Jordan Lewis](#)^{4,5}, [Sharon Unger](#)^{1,6,7}, [Deborah L O'Connor](#)^{7,8}

Affiliations expand

- PMID: 37653641
- PMCID: [PMC10580668](#)
- DOI: [10.1177/08903344231192441](#)

Free PMC article

Abstract

Background: Mother's breastmilk is the gold standard for feeding preterm infants. Preterm delivery may be precipitated by inflammatory maternal states, but little is known about milk cytokine profiles and how they correlate with markers of infant gut inflammation (i.e., stool calprotectin) in this vulnerable population.

Research aim: To assess cytokines and inflammatory markers in milk from parents of very preterm infants over time as well as correlations between milk and infant's stool calprotectin.

Method: This is a secondary analysis of milk samples collected during OptiMoM, a triple-blind randomized clinical trial of infants born < 1250 g ([NCT02137473](#)). Longitudinally collected samples were analyzed for cytokines, choline, and inflammatory markers (C-reactive protein [CRP], IFN- γ , IL-10, IL-1 β , IL-1ra, IL-6, IL-8, TNF- α). Infant stools were collected for longitudinal calprotectin analysis. Generalized estimating equations quantified longitudinal profiles of milk markers and stool calprotectin, their associations, and the correlation between free choline and C-reactive protein over follow-up.

Result: Participants included 92 parents and infants (median weeks of gestation 27.3, median birth weight 845 g, and prevalence of male infants 45%). In all, 212 milk samples and 94 corresponding stool calprotectin levels were collected 1-11 weeks postpartum. C-reactive protein was present in much higher concentrations than other markers, and was highest in Week 1 postpartum. It decreased over time. IL-8 and free choline also changed over time while other markers did not. There was no correlation between any milk markers and stool calprotectin.

Conclusion: Milk from mothers of very preterm infants has detectable inflammatory markers, some of which change over time. Research is needed to determine if infant outcomes are associated with these markers.

Keywords: C reactive protein; breastfeeding; cytokines; human milk; inflammation; preterm infant; stool calprotectin.

Conflict of interest statement

Disclosures and Conflicts of InterestThe authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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

SUPPLEMENTARY INFO

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Pediatr Neurol



. 2023 Nov:148:8-13.

doi: 10.1016/j.pediatrneurol.2023.07.011. Epub 2023 Jul 20.

Brain Region Size Differences Associated With Dystonia in People With Cerebral Palsy Born Premature

[Keerthana Chintalapati](#)¹, [Toni S Pearson](#)², [Keisuke Ueda](#)¹, [Bhooma R Aravamathan](#)³

Affiliations expand

- PMID: 37633215
- DOI: [10.1016/j.pediatrneurol.2023.07.011](https://doi.org/10.1016/j.pediatrneurol.2023.07.011)

Abstract

Background: Dystonia in cerebral palsy (CP) is classically associated with deep gray matter injury at term gestation, but the patterns of injury associated with dystonia following premature birth are unclear. We examined whether there were brain regional size differences associated with dystonia in people with CP born premature.

Methods: In this retrospective cohort study, we identified subjects with CP born premature (<37 weeks gestational age) seen at a tertiary care CP center between February 1, 2017, to February 1, 2021, who had T1-weighted brain magnetic resonance imaging (MRI) done between ages one and five years available in the clinical record. We measured the following on these brain MRI images per the 2013 Kidokoro criteria: interhemispheric distance, biparietal width, lateral ventricle diameter, transcerebellar diameter, deep gray matter area, and corpus callosum thickness. We then compared the sizes of these

structures between those with and without dystonia correcting for gestational age at birth and gross motor functional ability (univariate general linear models).

Results: Fifty-five subjects met the inclusion and exclusion criteria. Interhemispheric distance was significantly greater in those with dystonia, suggesting decreased cortical volume ($P = 0.005$). There was no significant difference in the other measured structures between those with and without dystonia, including deep gray matter area.

Conclusions: Increased interhemispheric distance, not measures of deep gray matter size, correlate with the presence of dystonia in people with CP born premature.

Keywords: Cerebral palsy; Dystonia; Interhemispheric distance; Magnetic resonance imaging; Prematurity.

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Conflict of interest statement

Declaration of competing interest None of the authors of this article have any conflicts of interest. There are no financial, professional, or personal relationships from any of the authors that could influence this work.

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[Multicenter Study](#)

Chemosphere

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. 2023 Nov:340:139917.

doi: 10.1016/j.chemosphere.2023.139917. Epub 2023 Aug 21.

Residential greenspace counteracts PM_{2.5} on the risks of preterm birth subtypes: A multicenter study

[Wen Jiang](#)¹, [Cuiping Wang](#)², [Qingli Zhang](#)³, [Xiaojing Zeng](#)², [Haidong Kan](#)⁴, [Jun Zhang](#)⁵

Affiliations [expand](#)

- PMID: 37611762
- DOI: [10.1016/j.chemosphere.2023.139917](https://doi.org/10.1016/j.chemosphere.2023.139917)

Free article

Abstract

Background: The association between residential greenspace and preterm birth (PTB) risk remained inconclusive. The PTB subtypes have been ignored and the effect of co-exposure of PM_{2.5} on PTB risk is still unclear.

Objective: To investigate the independent, interactive, and mixed effects of residential greenspace and PM_{2.5} on the risk of PTB subtypes.

Methods: A total of 19,900 singleton births from 20 hospitals in Shanghai, China, from 2015 to 2017 were included. The Normalized Difference Vegetation Index (NDVI) within 500 m and 1000 m buffers of the maternal residence and a combined geoscience-statistical model-derived PM_{2.5} and its six components were used as the exposure measures. PTB (<37 completed weeks of gestation) were divided into early PTB (24-33 weeks) vs. late PTB (34-36 weeks) and into spontaneous PTB (sPTB), preterm premature rupture of the fetal membranes (PPROM), and iatrogenic PTB. Multivariable logistic regression models were applied to assess the independent and interactive effects of NDVI and PM_{2.5} on PTB in each trimester. The quantile g-computation approach was employed to explore the mixture effect of PM_{2.5} components and greenspace across the pregnancy and to determine the main contributors.

Results: Levels of PM_{2.5} and greenspace were associated with increased [aOR (95%CI) ranging from 1.18 (1.07, 1.30) to 3.36 (2.45, 4.64)] and decreased risks [aORs (95%CI) ranging from 0.64 (0.53, 0.78) to 0.86 (0.73, 0.99)] of PTB subtypes, respectively. At the same PM_{2.5} level, higher residential greenspace was associated with lower risks, and vice versa. All these associations were more pronounced in late pregnancy. Early PTB and

PPROM were the main affected subtypes, and the main drivers in PM_{2.5} were black carbon and ammonium.

Conclusions: Residential greenspace may mitigate the PTB risks due to PM_{2.5} exposure during pregnancy.

Keywords: Fine particular matter; Greenspace; Iatrogenic preterm birth; Preterm birth; Preterm premature rupture of fetal membranes; Spontaneous preterm birth.

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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 types, MeSH terms, Substances, Supplementary conceptsexpand

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52

Int J Gynaecol Obstet

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. 2023 Nov;163(2):430-437.

doi: 10.1002/ijgo.15030. Epub 2023 Aug 22.

[Obstetric practice differences between Syrian refugees and non-Syrian](#)

nonrefugee gravidae: A retrospective cross-sectional study

[Mariz Kasoha¹](#), [Meletios P Nigdelis¹](#), [Leila Bishara¹](#), [Gudrun Wagenpfeil²](#), [Erich-Franz Solomayer¹](#), [Bashar Haj Hamoud¹](#)

Affiliations expand

- PMID: 37605949
- DOI: [10.1002/ijgo.15030](https://doi.org/10.1002/ijgo.15030)

Abstract

Objective: To assess differences in obstetric practices between Syrian war refugees (SRs) and non-Syrian nonrefugees (NSRs) in a tertiary care provider in Germany.

Methods: This was a retrospective study of SRs (n = 356) and NSRs (n = 5836) giving birth between January 2015 and December 2018. Data on medical history, birth mode, complications, and neonatal parameters was extracted. Group differences were evaluated using Mann-Whitney and χ^2 test. Logistic regression models were fitted to investigate the association of refugee status with mode of birth in conditions associated with increased risk of cesarean section (CS).

Results: SRs had higher rates of adolescent pregnancies (1.7% versus 0.6%, P = 0.020) but fewer maternal diseases compared with NSRs (1.7% versus 3.9%, P = 0.035). The rate of CS was higher in the NSR group (43.9% versus 36%, P = 0.003), as well as the rates of premature rupture of membranes (P = 0.006) and steroid administration for lung maturation (P = 0.012). Cases of umbilical artery pH ≤ 7.0 were more common in SRs (0.4% versus 1.1%, P = 0.027). Women with previous CS had similar odds of CS in the current pregnancy irrespective of study group (odds ratio, 0.94 [95% confidence interval, 0.50-1.75]).

Conclusion: SR women had lower rates of CS but higher rates of adolescent pregnancies and neonatal pH ≤ 7.0 at birth compared with NSR women.

Keywords: Syrian civil war; birth asphyxia; cesarean section; refugee; vaginal delivery.

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- [25 references](#)

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Acta Obstet Gynecol Scand



. 2023 Nov;102(11):1450-1458.

doi: 10.1111/aogs.14663. Epub 2023 Aug 21.

[Cerebral palsy in children born after assisted reproductive technology in Norway: Risk, prevalence, and clinical characteristics](#)

[Henriette Carlsen](#)¹, [Torstein Vik](#)¹, [Guro L Andersen](#)^{1,2}, [Kristine Stangenes](#)³, [Solveig Bjellmo](#)^{4,5}, [Kjersti Westvik-Johari](#)⁶, [Sandra Julsen Hollung](#)^{1,2}

Affiliations expand

- PMID: 37602751
- PMCID: [PMC10577620](#)
- DOI: [10.1111/aogs.14663](#)

Abstract

Introduction: The aim was to investigate the risk, prevalence, and clinical characteristics of cerebral palsy among children born after assisted reproductive technology (ART) in Norway.

Material and methods: All liveborn children from 2002 to 2015 were included. Information was collected from the Medical Birth Registry of Norway, linked to the Norwegian Quality and Surveillance Registry for Cerebral Palsy as of December 31, 2022. Logistic regression analyses were used to calculate the prevalence of cerebral palsy per 1000 live births after ART and natural conception with birth year as covariate, crude odds ratios (OR) for cerebral palsy among children born after ART using children born after natural conception as reference, and OR adjusted for potential confounders, with 95% confidence intervals (CI). Potential mediators of the association were studied in stratified analyses. Descriptive statistics were used to compare proportions in clinical characteristics among children with cerebral palsy born after ART and natural conception.

Results: Among 833 645 livebirths, 23 645 children were born after ART and of the latter 97 were diagnosed with cerebral palsy. The overall prevalence of cerebral palsy after ART was 4.10 per 1000 live births (95% CI 3.36-5.00), decreasing from 7.79 per 1000 in 2002 to 3.55 in 2015. Compared with children born after natural conception, the OR for cerebral palsy was 2.01 (95% CI 1.63-2.47) adjusted for mother's age at birth, parity, and pre-pregnancy health. When restricted to singletons born at term, the adjusted OR for cerebral palsy was 1.13 (95% CI 0.76-1.69). The distribution of cerebral palsy subtypes and the severity of gross and fine motor function and associated impairments did not differ significantly between children with cerebral palsy born after ART and natural conception.

Conclusions: Children born after ART had a risk of cerebral palsy that was twice that of children born after natural conception. The increased risk of cerebral palsy after ART is likely attributed to multiple pregnancies and preterm births. The prevalence of cerebral palsy after ART decreased significantly during the study period, despite an increased use of ART in the population. The distribution of clinical characteristics did not differ between children with cerebral palsy born after ART and those born after a natural conception, suggesting that the risk factors for, and causes of cerebral palsy were similar.

Keywords: assisted reproductive technology; cerebral palsy; clinical characteristics; multiple pregnancy; preterm births.

Conflict of interest statement

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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

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MeSH termsexpand

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Multicenter Study

Acta Obstet Gynecol Scand

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. 2023 Nov;102(11):1459-1468.

doi: 10.1111/aogs.14659. Epub 2023 Aug 21.

[Association between socioeconomic status with pregnancy and neonatal outcomes: An international multicenter cohort](#)

[Gillian M Maher](#)^{1,2}, [Liam J Ward](#)^{3,4}, [Leah Hernandez](#)³, [Marius Kublickas](#)⁵, [Johannes J Duvekot](#)⁶, [Fergus P McCarthy](#)^{1,7}, [Ali S Khashan](#)^{1,2}, [Karolina Kublickiene](#)³

Affiliations expand

- PMID: 37602747
- PMCID: [PMC10577636](#)
- DOI: [10.1111/aogs.14659](#)

Free PMC article

Abstract

Introduction: Previous evidence examining the association between socioeconomic status and pregnancy complications are conflicted and often limited to using area-based measures of socioeconomic status. In this study, we aimed to examine the association between individual-level socioeconomic factors and a wide range of adverse pregnancy and neonatal outcomes using data from the IMPROVED birth cohort conducted in Sweden, the Netherlands and Republic of Ireland.

Material and methods: The study cohort consisted of women who participated in the IMPROVED birth cohort between 2013 and 2017. Data on socioeconomic factors were self-reported and obtained at 15 weeks' gestation, and included level of education, employment status, relationship status, and income. Data on pregnancy and neonatal outcomes included gestational hypertension, pre-eclampsia, gestational diabetes mellitus, emergency cesarean section, preterm birth, post term delivery, small for gestational age and Apgar score at 1 min. These data were obtained within 72 h following delivery and confirmed using medical records. Multivariable logistic regression examined the association between each socioeconomic variable and each outcome separately adjusting for maternal age, maternal body mass index, maternal smoking, maternal alcohol consumption and cohort center. We also examined the effect of exposure to any ≥ 2 risk factors compared to none.

Results: A total of 2879 participants were included. Adjusted results suggested that those with less than third level of education had an increased odds of gestational hypertension (OR: 1.74, 95% CI: 1.23-2.46), while those on a middle level of income had a reduced odds of emergency cesarean section (OR: 0.59, 95% CI: 0.42-0.84). No significant associations were observed between socioeconomic variables and neonatal outcomes. Exposure to any ≥ 2 socioeconomic risk factors was associated with an increased risk of preterm birth (OR: 1.75, 95% CI: 1.06-2.89).

Conclusions: We did not find strong evidence of associations between individual-level socioeconomic factors and pregnancy and neonatal outcomes in high-income settings overall, with only few significant associations observed among pregnancy outcomes.

Keywords: emergency cesarean section; gestational hypertension; neonatal outcomes; pregnancy outcomes; preterm birth; socioeconomic status.

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Conflict of interest statement

None.

- [24 references](#)

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

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Pediatr Pulmonol

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. 2023 Nov;58(11):3156-3170.

doi: 10.1002/ppul.26636. Epub 2023 Aug 18.

Lung function deficits and bronchodilator responsiveness at 12

years of age in children born very preterm compared with controls born at term

[Cecilia Hagman¹](#), [Lars J Björklund¹](#), [Leif Bjermer²](#), [Ingrid Hansen-Pupp¹](#), [Ellen Tufvesson²](#)

Affiliations expand

- PMID: 37594159
- DOI: [10.1002/ppul.26636](https://doi.org/10.1002/ppul.26636)

Abstract

Introduction: Very preterm birth is associated with lung function impairment later in life, but several aspects have not been studied. We aimed to comprehensively assess lung function at school age in very preterm infants and term controls, with special emphasis on bronchopulmonary dysplasia (BPD), sex, and bronchodilator response.

Methods: At 12 years of age, 136 children born very preterm (85 with and 51 without BPD) and 56 children born at term performed spirometry, body plethysmography, impulse oscillometry, measurement of diffusion capacity, and multiple breath washout, before and after bronchodilator inhalation.

Results: Airway symptoms and a diagnosis of asthma were more common in children born very preterm. These children had more airflow limitation, seen as lower forced expiratory volume in 1 s (FEV_1) ($p < .001$), FEV_1 /forced vital capacity (FVC) ($p = .011$), and mean forced expiratory flow between 25% and 75% of FVC ($p < .001$), and a higher total and peripheral airway resistance compared with term-born controls. There was no difference in total lung capacity but air trapping and lung clearance index were higher in children born very preterm. Diffusion capacity was lower in children born very preterm, especially in those with a diagnosis of BPD. In most other tests, the differences between preterm-born children with or without BPD were smaller than between children born preterm versus at term. Boys born preterm had more lung function deficits than preterm-born girls. In children born very preterm, airway obstruction was to a large extent reversible.

Conclusion: At 12 years of age, children born very preterm had lower lung function than children born at term in most aspects and there was only little difference between children with or without BPD. Airway obstruction improved markedly after bronchodilator inhalation.

Keywords: adolescence; airway obstruction; bronchopulmonary dysplasia; dysanapsis; sex.

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- [33 references](#)

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Pediatr Pulmonol

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. 2023 Nov;58(11):3054-3062.

doi: 10.1002/ppul.26620. Epub 2023 Aug 18.

[Reduced pulmonary oxygen diffusion at 36 weeks of postmenstrual age in small-for-gestational-age preterm infants of less than 32 weeks without bronchopulmonary dysplasia](#)

[Alessio Correani](#)^{1,2}, [Lucia Lanciotti](#)¹, [Chiara Giorgetti](#)², [Maria Laura Palazzi](#)², [Chiara Monachesi](#)¹, [Luca Antognoli](#)¹, [Ilaria Burattini](#)², [Paola Cogo](#)³, [Virgilio Carnielli](#)^{1,2}

Affiliations expand

- PMID: 37594147

- DOI: [10.1002/ppul.26620](https://doi.org/10.1002/ppul.26620)

Abstract

Background: Small-for-gestational-age (SGA) preterm infants are at increased risk of developing bronchopulmonary dysplasia (BPD). There is limited information on pulmonary oxygen diffusion of SGA preterm infants, particularly in those without BPD.

Objective: To compare the pulmonary oxygen diffusion of SGA to that of appropriate-for-gestational-age (AGA) preterm infants without BPD.

Study design: Preterm infants with a gestational age (GA) between 24.0 and 31.6 weeks were studied. The oxygen saturation (SpO_2), fraction to inspired oxygen (FiO_2), and the SpO_2 to FiO_2 ratio (SFR) were compared between SGA and AGA infants. The association between SGA and SFR at 36 weeks was assessed using a multiple regression analysis. In the subgroup without BPD, SGA were match-paired for GA and gender with AGA infants.

Results: We analyzed 1189 infants surviving at 36 weeks: 194 (16%) were SGA and 995 (84%) AGA. The incidence of BPD was significantly higher in SGA than AGA infants (32% vs. 13%; $p = .000$). Out of the 995 infants without BPD, 132 (13%) were SGA and 863 (87%) AGA. SGA was negatively associated with the SFR value at 36 weeks, independently from BPD. SGA infants without BPD had significantly higher (better) SFR at birth, but lower (worse) SpO_2 and SFR and from 33 to 36 weeks than their matched AGA counterpart. At 36 weeks, median SpO_2 and SFR values were 97.7 versus 98.4 ($p = .006$) and 465 versus 468 ($p = .010$) in match-paired SGA and AGA, respectively.

Conclusion: Among preterm infants of less than 32 weeks and without BPD, SGA infants had a reduced pulmonary oxygen diffusion at 36 weeks in comparison with AGA infants.

Keywords: appropriate-for-gestational-age; bronchopulmonary dysplasia; preterm infant; pulmonary oxygen diffusion; small-for-gestational-age.

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- [40 references](#)

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Observational Study

J Pediatr Gastroenterol Nutr



. 2023 Nov 1;77(5):597-602.

doi: 10.1097/MPG.0000000000003912. Epub 2023 Oct 27.

Antenatal Neuroprotective Magnesium Sulfate in Very Preterm Infants and Its Association With Feeding Intolerance

[Buse Ozer Bekmez¹](#), [Hayriye Gozde Kanmaz Kutman¹](#), [Yuksel Oguz²](#), [Dilek Uygur²](#), [Sarkhan Elbayiyev¹](#), [Fuat Emre Canpolat¹](#), [Serife Suna Oguz¹](#), [Cuneyt Tayman¹](#)

Affiliations expand

- PMID: 37580867
- DOI: [10.1097/MPG.0000000000003912](https://doi.org/10.1097/MPG.0000000000003912)

Abstract

Introduction/objective: Magnesium sulfate (MgSO₄) treatment is widely used for fetal neuroprotection despite the controversy concerning the side effects. There is limited data regarding the impact of various cumulative maternal doses and neonatal serum magnesium (Mg) levels on short-term neonatal morbidity and mortality. We opted to carry out a study to determine the impact of neonatal serum Mg levels on neonatal outcomes.

Method: We conducted this prospective observational study between 2017 and 2021. Antenatal MgSO₄ was used for neuroprotective purpose only during the study period. Inborn preterm infants delivered between 23 and 31 6/7 weeks of gestation were enrolled consecutively. Babies who underwent advanced resuscitation in the delivery room, inotropic treatment due to hemodynamic instability in the first 7 days of life, >12 hours since the discontinuation of maternal MgSO₄ treatment, severe anemia, and major congenital/chromosomal anomalies were excluded from the study. The subgroup of babies with serum Mg level at the 6th hour of life underwent an analysis. A neonatal Mg concentration of 2.5 mg/dL was used to classify MgSO₄-exposed patients into 2 groups (<2.5 mg/dL and ≥2.5 mg/dL). Another analysis was performed between babies whose mothers were exposed to MgSO₄ and those not exposed. Finally, the groups' neonatal outcomes were compared.

Results: Of the 584 babies, 310 received antenatal MgSO₄. The birth weights were significantly lower in the MgSO₄ exposed group (1113 ± 361 g vs 1202 ± 388 g, P = 0.005). Antenatal corticosteroid usage and intrauterine growth restriction were also noted to be higher. The MgSO₄ group was more likely to have bronchopulmonary dysplasia, prolonged invasive ventilation, necrotizing enterocolitis, delayed enteral nutrition, and feeding intolerance (P < 0.05). MgSO₄ treatment was shown as an independent risk factor for feeding intolerance when corrected for confounders (odds ratio 2.13, 95% confidence interval: 1.4-3.1, P = 0.001). Furthermore, serum Mg level significantly correlated with feeding intolerance (r = 0.21, P = 0.002).

Conclusion: This study highlighted the effect of MgSO₄ treatment and the potential superiority of serum Mg level as a predictor of immediate neonatal outcomes, particularly delayed enteral nutrition and feeding intolerance. Further studies are warranted to ascertain the optimal serum Mg concentration of preterm infants in early life to provide maximum benefit with minimal side effects.

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Conflict of interest statement

The authors report no conflicts of interest.

- [22 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

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J Obstet Gynaecol Res

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. 2023 Nov;49(11):2664-2670.

doi: 10.1111/jog.15771. Epub 2023 Aug 13.

[The initial number of fetuses in multiple pregnancy before reduction affects perinatal outcomes](#)

[Fatih Akkuş](#)¹, [Şükran Doğru](#)¹, [Aslı Altınordu Atcı](#)¹, [Yusuf Dal](#)², [Elifsenâ Canan Alp Arıcı](#)³, [Ali Acar](#)³

Affiliations expand

- PMID: 37574597
- DOI: [10.1111/jog.15771](https://doi.org/10.1111/jog.15771)

Abstract

Objective: In this study, we aimed to evaluate the perinatal outcomes of dichorionic diamniotic (DCDA) twin pregnancies reduced by the fetal reduction (FR) procedure and cases with continuing DCDA twin pregnancies without FR.

Materials and methods: FR performed in a university hospital in the last 10 years was evaluated. Pregnancies reduced to DCDA twin pregnancies by reduction from three or more pregnancies and pregnancies that started with DCDA twins and continued with DCDA twins were compared in terms of perinatal outcomes. In the subgroup analysis, those who were reduced from three-chorionic three-amniotic (TCTA) triplets to DCDA

twins and those who were reduced to DCDA twin pregnancies from four or more were compared in terms of perinatal outcomes.

Results: A total of 119 pregnant women were included in the study, 36 patients underwent FR, while 83 patients were DCDA twins who did not undergo FR. The groups were similar in terms of preterm delivery ($p = 0.370$). There was a higher rate of miscarriage (21.4% vs. 0.0%, $p = 0.019$) in the group that was reduced to DCDA twins from quadruplet and above pregnancies compared to the group that was reduced from TCTA triplets to DCDA twins. The gestational week at birth was lower in the group reduced to DCDA twins from quadruplets and above pregnancies (31.00 ± 4.31 vs. 34.64 ± 2.88 , $p = 0.019$).

Conclusion: The study's results show that the perinatal outcomes of multiple pregnancies with and without FR are the same. As the number of reduced fetuses increases, the rates of preterm birth and miscarriage also increase.

Keywords: fetal reduction; obstetric complications; premature labor; twin pregnancy.

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[Review](#)

Nutrition

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. 2023 Nov;115:112094.

doi: 10.1016/j.nut.2023.112094. Epub 2023 Jun 3.

Association between maternal anemia and stunting in infants and children aged 0–60 months: A systematic literature review

[Siti Rahayu Nadhiroh](#)¹, [Fedora Micheala](#)², [Serene En Hui Tung](#)³, [Theresia Chrisanthy Kustiawan](#)²

Affiliations expand

- PMID: 37572547
- DOI: [10.1016/j.nut.2023.112094](https://doi.org/10.1016/j.nut.2023.112094)

Abstract

Objectives: Maternal anemia is a worldwide health issue and a common pregnancy complication. It leads to consequences including infant mortality, low birth weight, preterm birth, unrecoverable or partially reversible neurobehavioral and cognitive deficits, and short birth length. However, the relationship between maternal anemia and stunting in children is not well defined. This systematic literature review sought to determine whether maternal anemia was associated with height or length and stunting conditions in infants and children ages 0-60 mo in cohort, case-control, and cross-sectional studies carried out in several countries.

Methods: A systematic review was performed on articles published from 2014-2021 related to maternal anemia and stunting. The electronic databases used were ScienceDirect, PubMed, Scopus, ProQuest, Google Search, and AJOG (American Journal of Obstetrics and Gynecology). The literature search was performed up to December 7, 2021.

Results: Twelve studies were included. Nine studies examined the correlation between maternal anemia and length or weight in children. Seven of the nine studies showed an association between maternal anemia and stunting in children; the others showed an association between maternal anemia and birth length. Three studies found no association between maternal anemia and stunting in children under age 5 y.

Conclusions: The current review emphasizes that stunting in children may be associated with maternal anemia, specifically in developing countries. This implies that it is crucial to prevent anemia in adolescent girls and women before and during pregnancy as a part of programs to eliminate stunting in children.

Keywords: Anemia; Children; Maternal; Stunting; Undernutrition.

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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 types, MeSH termsexpand

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J Perinatol

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. 2023 Nov;43(11):1420-1428.

doi: 10.1038/s41372-023-01748-8. Epub 2023 Aug 9.

Developmental consequences of short apneas and periodic breathing in preterm infants

[Alicia K Yee](#)¹, [Leon S Siriwardhana](#)¹, [Gillian M Nixon](#)^{1,2}, [Lisa M Walter](#)¹, [Flora Y Wong](#)^{1,3}, [Rosemary S C Horne](#)⁴

Affiliations expand

- PMID: 37558750
- PMCID: [PMC10615736](#)
- DOI: [10.1038/s41372-023-01748-8](#)

Free PMC article

Abstract

Objective: We investigated the relationship between respiratory events experienced before and after hospital discharge and developmental outcomes at 6 months corrected age (CA).

Study design: Preterm infants born between 28-32 weeks gestational age (GA) were studied at 32-36 weeks postmenstrual age (PMA), 36-40 weeks PMA, 3- and 6-months CA. Percentage total sleep time (%TST) with respiratory events (isolated apneas, sequential apneas and periodic breathing (PB)) at each study was calculated. Stepwise multiple linear regressions determined significant predictors of developmental outcomes at 6 months.

Result: %TST with respiratory events at term were significant predictors of language ($R^2 = 0.165$, $\beta = -0.416$) and motor ($R^2 = 0.180$, $\beta = -0.485$) composite scores of the Bayley Scales of Infant Development at 6 months, independent of GA, birth weight and sex.

Conclusions: In clinically stable very preterm infants at term equivalent age, time spent having respiratory events, was related to a reduction in language and motor outcomes at 6 months.

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Conflict of interest statement

The authors declare no competing interests.

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

SUPPLEMENTARY INFO

MeSH terms, Grants and fundingexpand

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J Perinatol



. 2023 Nov;43(11):1363-1367.

doi: 10.1038/s41372-023-01744-y. Epub 2023 Aug 7.

[Phototherapy: a new risk factor for necrotizing enterocolitis in very low birth weight preterm infants? a retrospective case-control study](#)

[Jie Li](#)¹, [Xiao-Yun Zhong](#)¹, [Li-Gang Zhou](#)¹, [Yan Wu](#)¹, [Li Wang](#)¹, [Si-Jie Song](#)²

Affiliations expand

- PMID: 37550528
- DOI: [10.1038/s41372-023-01744-y](https://doi.org/10.1038/s41372-023-01744-y)

Abstract

Objective: To investigate the association between phototherapy (PT) and the development of necrotizing enterocolitis (NEC) in very low birth weight (VLBW) infants.

Study design: A retrospective case-control study was conducted on VLBW infants with or without NEC (stage IIA or greater) born at ≤ 35 weeks' gestation in a tertiary hospital over 7 years. Sample size calculation, trend test, as well as univariate and multiple logistic regression analyses were employed.

Results: A total of 824 VLBW infants were reviewed, with 74 cases and 122 controls finally enrolled. The odds of NEC increased with the duration and number of PT sessions. Exposure to >120 h and >4 instances of PT were significantly associated with NEC in multivariate analysis.

Conclusion: This is the first study suggesting a potential association between PT and development of NEC in VLBW infants. This association needs further exploration.

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Multicenter Study

J Perinatol

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. 2023 Nov;43(11):1398-1405.

doi: 10.1038/s41372-023-01729-x. Epub 2023 Aug 4.

[Use of term reference infants in assessing the developmental outcome](#)

of extremely preterm infants: lessons learned in a multicenter study

[Charles E Green](#)¹, [Jon E Tyson](#)², [Roy J Heyne](#)³, [Susan R Hintz](#)⁴, [Betty R Vohr](#)⁵, [Carla M Bann](#)⁶, [Abhik Das](#)⁷, [Edward F Bell](#)⁸, [Sana Boral Debsareea](#)⁹, [Emily Stephens](#)², [Marie G Gantz](#)⁶, [Carolyn M Petrie Huitema](#)⁷, [Karen J Johnson](#)⁸, [Kristi L Watterberg](#)¹⁰, [Ricardo Mosquera](#)¹¹, [Myriam Peralta-Carcelen](#)¹², [Deanne E Wilson-Costello](#)¹³, [Tarah T Colaizy](#)⁸, [Nathalie L Maitre](#)¹⁴, [Stephanie L Merhar](#)¹⁵, [Ira Adams-Chapman](#)¹⁶, [Janell Fuller](#)¹⁷, [Michelle E Hartley-McAndrew](#)¹⁸, [William F Malcolm](#)¹⁹, [Sarah Winter](#)²⁰, [Andrea F Duncan](#)²¹, [Gary J Myer](#)²², [Stephen D Kicklighter](#)²³, [Myra H Wyckoff](#)³, [Sara B DeMauro](#)²⁴, [Anna Maria Hibbs](#)¹³, [Barbara J Stoll](#)², [Waldemar A Carlo](#)¹², [Krisa P Van Meurs](#)⁴, [Matthew A Rysavy](#)⁸, [Ravi M Patel](#)¹⁶, [Pablo J Sánchez](#)¹⁴, [Abbot R Lupton](#)⁵, [C Michael Cotten](#)¹⁹, [Carl T D'Angio](#)²³, [Michele C Walsh](#)²⁵; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network

Collaborators, Affiliations expand

- PMID: 37542155
- PMCID: [PMC10615749](#)
- DOI: [10.1038/s41372-023-01729-x](#)

Free PMC article

Abstract

Objective: Extremely preterm (EP) impairment rates are likely underestimated using the Bayley III norm-based thresholds scores and may be better assessed relative to concurrent healthy term reference (TR) infants born in the same hospital.

Study design: Blinded, certified examiners in the Neonatal Research Network (NRN) evaluated EP survivors and a sample of healthy TR infants recruited near the 2-year assessment age.

Results: We assessed 1452 EP infants and 183 TR infants. TR-based thresholds showed higher overall EP impairment than Bayley norm-based thresholds (O.R. = 1.86; [95% CI 1.56-2.23], especially for severe impairment (36% vs. 24%; $p \leq 0.001$). Difficulty recruiting TR patients at 2 years extended the study by 14 months and affected their demographics.

Conclusion: Impairment rates among EP infants appear to be substantially underestimated from Bayley III norms. These rates may be best assessed by comparison with healthy term infants followed with minimal attrition from birth in the same centers.

Gov id: Term Reference (under the Generic Database Study): [NCT00063063](#).

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Conflict of interest statement

The authors declare no competing interests.

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

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Randomized Controlled Trial

Acta Obstet Gynecol Scand

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. 2023 Nov;102(11):1575-1585.

doi: 10.1111/aogs.14628. Epub 2023 Aug 4.

How safe is the treatment of pregnant women with fear of childbirth using eye movement desensitization and reprocessing therapy? Obstetric outcomes of a multi-center randomized controlled trial

[Melanie A M Baas](#)^{1,2}, [Claire A I Stramrood](#)³, [Lea M Dijkman](#)⁴, [Joost W Vanhommerig](#)⁵, [Ad de Jongh](#)^{6,7}, [Mariëlle G van Pampus](#)¹

Affiliations expand

- PMID: 37540081
- PMCID: [PMC10577619](#)
- DOI: [10.1111/aogs.14628](#)

Free PMC article

Abstract

Introduction: Pregnant women with fear of childbirth display an elevated risk of a negative delivery experience, birth-related post-traumatic stress disorder, and adverse perinatal outcomes such as preterm birth, low birthweight, and postpartum depression. One of the therapies used to treat fear of childbirth is eye movement desensitization and reprocessing (EMDR) therapy. The purpose of the present study was to determine the obstetric safety and effectiveness of EMDR therapy applied to pregnant women with fear of childbirth.

Material and methods: A randomized controlled trial (the OptiMUM-study) was conducted in two teaching hospitals and five community midwifery practices in the Netherlands ([www.trialregister.nl](#), NTR5122). Pregnant women (n = 141) with a gestational age between 8 and 20 weeks and suffering from fear of childbirth (i.e. sum score on the Wijma Delivery Expectations Questionnaire ≥ 85) were randomly allocated to either EMDR therapy (n = 70) or care-as-usual (CAU) (n = 71). Outcomes were maternal and neonatal outcomes and patient satisfaction with pregnancy and childbirth.

Results: A high percentage of cesarean sections (37.2%) were performed, which did not differ between groups. However, women in the EMDR therapy group proved seven times less likely to request an induction of labor without medical indication than women in the CAU group. There were no other significant differences between the groups in maternal or neonatal outcomes, satisfaction, or childbirth experience.

Conclusions: EMDR therapy during pregnancy does not adversely affect pregnancy or the fetus. Therefore, therapists should not be reluctant to treat pregnant women with fear of childbirth using EMDR therapy.

Keywords: EMDR; childbirth; childbirth experience; eye movement desensitization and reprocessing therapy; fear of childbirth; pregnancy; tocophobia.

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Conflict of interest statement

AdJ has been a board member of the Dutch EMDR Association and EMDR Europe Association, and receives fees for courses and books about trauma and EMDR. The other authors have no potential conflicts of interest.

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

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Hum Brain Mapp

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. 2023 Nov;44(16):5372-5386.

doi: 10.1002/hbm.26442. Epub 2023 Aug 4.

Preterm-birth alters the development of nodal clustering and neural connection pattern in brain structural network at term-equivalent age

[Weihao Zheng](#)¹, [Xiaomin Wang](#)¹, [Tingting Liu](#)², [Bin Hu](#)^{1,3,4,5}, [Dan Wu](#)²

Affiliations expand

- PMID: 37539754
- PMCID: [PMC10543115](#)
- DOI: [10.1002/hbm.26442](#)

Free PMC article

Abstract

Preterm-born neonates are prone to impaired neurodevelopment that may be associated with disrupted whole-brain structural connectivity. The present study aimed to investigate the longitudinal developmental pattern of the structural network from preterm birth to term-equivalent age (TEA), and identify how prematurity influences the network topological organization and properties of local brain regions. Multi-shell diffusion-weighted MRI of 28 preterm-born scanned a short time after birth (PB-AB) and at TEA (PB-TEA), and 28 matched term-born (TB) neonates in the Developing Human Connectome Project (dHCP) were used to construct structural networks through constrained spherical deconvolution tractography. Structural network development from preterm birth to TEA showed reduced shortest path length, clustering coefficient, and modularity, and more "connector" hubs linking disparate communities. Furthermore, compared with TB newborns, premature birth significantly altered the nodal properties (i.e., clustering coefficient, within-module degree, and participation coefficient) in the limbic/paralimbic, default-mode, and subcortical systems but not global topology at TEA, and we were able

to distinguish the PB from TB neonates at TEA based on the nodal properties with 96.43% accuracy. Our findings demonstrated a topological reorganization of the structural network occurs during the perinatal period that may prioritize the optimization of global network organization to form a more efficient architecture; and local topology was more vulnerable to premature birth-related factors than global organization of the structural network, which may underlie the impaired cognition and behavior in PB infants.

Keywords: classification; graph theory; preterm; structural network; term-equivalent age.

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Conflict of interest statement

The authors declare no conflict of interest.

- [Cited by 1 article](#)
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[Review](#)

Acta Obstet Gynecol Scand

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. 2023 Nov;102(11):1558-1565.

doi: 10.1111/aogs.14595. Epub 2023 Aug 3.

Inpatient vs outpatient management of pregnancies with vasa previa: A historical cohort study

[Linda A Villani](#)¹, [Rashida Al-Torshi](#)¹, [Prakesh S Shah](#)², [John C Kingdom](#)¹, [Rohan D'Souza](#)^{1,3,4}, [Johannes Keunen](#)¹

Affiliations expand

- PMID: 37537788
- PMCID: [PMC10577631](#)
- DOI: [10.1111/aogs.14595](#)

Free PMC article

Abstract

Introduction: Vasa previa, a condition where unprotected fetal blood vessels lie in proximity to the internal cervical opening, is a potentially lethal obstetric complication. The precarious situation of these vessels increases the risk of fetal hemorrhage with spontaneous or artificial rupture of membranes, frequently causing fetal/neonatal demise or severe morbidity. As a result, in many centers, inpatient management forms the mainstay when vasa previa is diagnosed antenatally. This study aimed to determine whether a subpopulation of pregnancies diagnosed antenatally with vasa previa could be safely managed as outpatients.

Material and methods: We reviewed all cases of vasa previa in singleton pregnancies, with no fetal anomalies, diagnosed at Mount Sinai Hospital, Toronto, from January 2008 to December 2017. Cases were categorized into three arms for analysis: outpatients (OP), asymptomatic hospitalized (ASH) and symptomatic hospitalized (SH). The SH arm included patients admitted with any antepartum bleeding or suspicious fetal non-stress test. Those that presented with symptomatic uterine activity/threatened preterm labor and delivered within 7 days of diagnosis were excluded from the study. Records were analyzed for details on hospitalization, antenatal corticosteroid administration, cervical length measurements, and fetal/neonatal mortality and morbidity.

Results: Of the 84 antenatally-diagnosed cases of vasa previa, 47 fulfilled eligibility criteria. A total of 15 cases were managed as OP, 22 as ASH and 10 as SH. Unplanned cesareans

were highest in the SH arm (40% vs. 0% ASH vs. 13.3% OP). Those in the SH arm delivered earliest (median 33.8 weeks, interquartile range (IQR) 33.2-34.3 weeks). Of the asymptomatic patients, those in the ASH arm delivered earlier than those in the OP arm (35.3 [34.6-36.2] weeks vs. 36.7 [35.6-37.2] weeks, $p = 0.037$). There were no cases of fetal/neonatal death, anemia or severe neonatal morbidity and no significant differences between groups based on cervical length or antenatal corticosteroid administration.

Conclusions: Our study suggests that asymptomatic women with an antenatal diagnosis of vasa previa, singleton pregnancies, and at low risk for preterm birth may safely managed as outpatients, as long as they are able to access hospital promptly in the event of antepartum bleeding or early labor.

Keywords: antenatal corticosteroids; outpatient management; pregnancy; vasa previa.

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Conflict of interest statement

The authors report no conflict of interest.

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

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Ann Thorac Surg

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. 2023 Nov;116(5):995-996.

doi: 10.1016/j.athoracsur.2023.07.029. Epub 2023 Aug 1.

Shades of Uncertainty: Perspectives on Hypoplastic Left Heart Syndrome in Premature and Low-Birth-Weight Infants

[Ame M Bigelow](#)¹, [Tara Karamlou](#)²

Affiliations expand

- PMID: 37536487
- DOI: [10.1016/j.athoracsur.2023.07.029](https://doi.org/10.1016/j.athoracsur.2023.07.029)

No abstract available

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Randomized Controlled Trial

Pediatr Pulmonol

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. 2023 Nov;58(11):3063-3070.

doi: 10.1002/ppul.26624. Epub 2023 Aug 2.

Nonsynchronized nasal intermittent positive pressure ventilation versus continuous positive airway pressure as a primary mode of respiratory support in neonates (26–40 weeks) admitted in a tertiary care center: A randomized controlled trial

[Rakesh Dey](#)¹, [Syamal Kumar Sardar](#)¹, [Anindya Kumar Saha](#)¹, [Suchandra Mukherjee](#)¹

Affiliations expand

- PMID: 37530509
- DOI: [10.1002/ppul.26624](https://doi.org/10.1002/ppul.26624)

Abstract

Introduction: Continuous positive airway pressure (CPAP) is a standard respiratory care for neonates for last few decades but it too has a high failure rate. Nasal intermittent positive pressure ventilation (NIPPV) is proven to be superior to CPAP in maintaining higher mean airway pressure in neonates with Respiratory Distress Syndrome. The main objective of this study was to compare failure within 72 h of initiation of primary respiratory support between nonsynchronized NIPPV and CPAP in all causes of respiratory distress in newborn infants. Secondly feed intolerance, Necrotizing enterocolitis (NEC > stage II), hemodynamically significant patent ductus arteriosus, intraventricular hemorrhage (IVH > grade III), retinopathy of prematurity (ROP), bronchopulmonary dysplasia (BPD), duration of support and mortality were also compared.

Methods: This was a single center randomized controlled trial. Stratified randomization was done for 216 neonates, based on the gestational age in two subgroups 26-33 weeks and 34-40 weeks who presented with respiratory distress within 5 days of birth, to receive either NIPPV or CPAP. Primary and secondary outcomes were documented.

Results: Statistically significant difference was noted for primary outcome (RR 0.48 [confidence interval = 0.301-0.786], $p = 0.003$) but not for other secondary outcomes.

NIPPV appeared superior in respect to noninvasive ventilation days, BPD occurrence and hospitalization duration.

Conclusion: As a primary mode, nonsynchronized NIPPV was more efficacious than CPAP in preventing intubation within 72 h of initiation of respiratory support. Further multicenter studies are warranted to explore the benefits of this respiratory support.

Keywords: CPAP; nasal IPPV; neonate; primary mode; respiratory distress.

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- [24 references](#)

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Publication types, MeSH terms, Associated data expand

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Environ Res

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. 2023 Nov 1;236(Pt 2):116772.

doi: 10.1016/j.envres.2023.116772. Epub 2023 Jul 28.

[Associations between area-level arsenic exposure and adverse birth outcomes: An Echo-wide cohort analysis](#)

[Jonathan V Lewis](#)¹, [Emily A Knapp](#)¹, [Shivani Bakre](#)¹, [Aisha S Dickerson](#)¹, [Theresa M Bastain](#)², [Casper Bendixsen](#)³, [Deborah H Bennett](#)⁴, [Carlos A Camargo](#)⁵, [Andrea E Cassidy-Bushrow](#)⁶, [Elena Colicino](#)⁷, [Viren D'Sa](#)⁸, [Dana Dabelea](#)⁹, [Sean Deoni](#)¹⁰, [Anne L Dunlop](#)¹¹, [Amy J Elliott](#)¹², [Shohreh F Farzan](#)², [Assiamira Ferrara](#)¹³, [Rebecca C Fry](#)¹⁴, [Tina Hartert](#)¹⁵, [Caitlin G Howe](#)¹⁶, [Linda G Kahn](#)¹⁷, [Margaret R Karagas](#)¹⁶, [Teng-Fei Ma](#)¹⁸, [Daphne Koinis-Mitchell](#)⁸, [Debra MacKenzie](#)¹⁹, [Luis E Maldonado](#)², [Francheska M Merced-Nieves](#)²⁰, [Jenae M Neiderhiser](#)²¹, [Anne E Nigra](#)²², [Zhongzheng Niu](#)², [Sara S Nozadi](#)²³, [Zorimar Rivera-Núñez](#)²⁴, [Thomas G O'Connor](#)²⁵, [Sarah Osmundson](#)²⁶, [Amy M Padula](#)²⁷, [Alicia K Peterson](#)¹³, [Allison R Sherris](#)²⁸, [Anne Starling](#)²⁹, [Jennifer K Straughen](#)⁶, [Rosalind J Wright](#)⁷, [Qi Zhao](#)³⁰, [Amii M Kress](#)³¹

Affiliations expand

- PMID: 37517496
- PMCID: PMC10592196 (available on 2024-11-01)
- DOI: [10.1016/j.envres.2023.116772](https://doi.org/10.1016/j.envres.2023.116772)

Abstract

Background: Drinking water is a common source of exposure to inorganic arsenic. In the US, the Safe Drinking Water Act (SDWA) was enacted to protect consumers from exposure to contaminants, including arsenic, in public water systems (PWS). The reproductive effects of preconception and prenatal arsenic exposure in regions with low to moderate arsenic concentrations are not well understood.

Objectives: This study examined associations between preconception and prenatal exposure to arsenic violations in water, measured via residence in a county with an arsenic violation in a regulated PWS during pregnancy, and five birth outcomes: birth weight, gestational age at birth, preterm birth, small for gestational age (SGA), and large for gestational age (LGA).

Methods: Data for arsenic violations in PWS, defined as concentrations exceeding 10 parts per billion, were obtained from the Safe Drinking Water Information System. Participants of the Environmental influences on Child Health Outcomes Cohort Study were matched to arsenic violations by time and location based on residential history data. Multivariable, mixed effects regression models were used to assess the relationship between preconception and prenatal exposure to arsenic violations in drinking water and birth outcomes.

Results: Compared to unexposed infants, continuous exposure to arsenic from three months prior to conception through birth was associated with 88.8 g higher mean birth weight (95% CI: 8.2, 169.5), after adjusting for individual-level confounders. No statistically

significant associations were observed between any preconception or prenatal violations exposure and gestational age at birth, preterm birth, SGA, or LGA.

Conclusions: Our study did not identify associations between preconception and prenatal arsenic exposure, defined by drinking water exceedances, and adverse birth outcomes. Exposure to arsenic violations in drinking water was associated with higher birth weight. Future studies would benefit from more precise geodata of water system service areas, direct household drinking water measurements, and exposure biomarkers.

Keywords: Arsenic; Contamination; Drinking water; Public water systems; Reproductive health; Water violations.

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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.

- [52 references](#)

SUPPLEMENTARY INFO

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

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Acta Paediatr

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. 2023 Nov;112(11):2352-2358.

doi: 10.1111/apa.16924. Epub 2023 Aug 2.

Benefits of routine probiotic supplementation in preterm infants

C P Rath^{1,2}, G Athalye-Jape^{1,2}, E Nathan^{3,4}, D Doherty^{3,4}, S Rao^{2,5}, S Patole^{1,2}

Affiliations expand

- PMID: 37505925
- DOI: [10.1111/apa.16924](https://doi.org/10.1111/apa.16924)

Abstract

Aim: We introduced routine probiotic supplementation (RPS) of preterm infants in June 2012. We previously reported that RPS reduced the incidence of necrotising enterocolitis (NEC) and mortality in such infants. In this study, we assessed if the benefits of RPS were sustained for infants in the current era.

Method: We compared the outcomes of preterm infants in recent epoch 3 (RPS, 1st June 2014 to 31st December 2019) versus epoch 2 (RPS, 1st June 2012 to 31st May 2014) and epoch 1 (no RPS, 1st December 2008 to 30th November 2010). Multiple logistic and Cox regression models were used to compare the outcomes.

Results: There were 645 infants in epoch 1, 712 in epoch 2 and 1715 in epoch 3. Age at full feeds was significantly lower in epoch 3 vs. 2 and epoch 3 vs. 1 in infants <28 weeks of gestation. NEC and late-onset sepsis (LOS) were significantly lower in epoch 3 vs. 1 in infants <28 weeks. LOS and age at full feeds were significantly lower in epoch 3 vs. 2 and epoch 3 vs. 1 in infants with gestation 28 to 32 weeks.

Conclusion: The benefits associated with RPS were sustained during epoch 3.

Keywords: necrotising enterocolitis; preterm infants; probiotics; supplementation; very low birth weight.

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- [23 references](#)

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Fertil Steril

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. 2023 Nov;120(5):1013-1022.

doi: 10.1016/j.fertnstert.2023.07.011. Epub 2023 Jul 24.

[Elevated antimüllerian hormone levels are not associated with preterm delivery after in vitro fertilization or ovulation induction](#)

[Anne E Kim](#)¹, [Michael K Simoni](#)², [Ashni Nadgauda](#)³, [Nathanael Koelper](#)⁴, [Anuja Dokras](#)⁵

Affiliations expand

- PMID: 37495009
- DOI: [10.1016/j.fertnstert.2023.07.011](https://doi.org/10.1016/j.fertnstert.2023.07.011)

Abstract

Objective: To investigate the association between antimüllerian hormone (AMH) and preterm birth risk in a larger cohort of patients who underwent either in vitro fertilization or ovulation induction with intrauterine insemination at a US academic fertility center.

Design: Retrospective cohort study.

Setting: Single academic fertility center.

Patient(s): Live singleton births from patients who underwent in vitro fertilization or ovulation induction between 2016 and 2020 at a single academic fertility center were included in this study. Patients were excluded if they had a missing prepregnancy AMH level, a pregnancy using donor oocytes or a gestational carrier, multiple gestations, a delivery before 20 weeks gestation, or a cerclage in place.

Intervention(s): AMH level.

Main outcome measure(s): The primary outcome was the proportion of preterm delivery. Secondary outcomes included the rate of pregnancy-induced hypertension, gestational diabetes, and small for gestational age.

Result(s): In the entire cohort ($n = 875$), 8.4% of deliveries were preterm. The mean AMH values were similar between those with term and preterm births (3.9 vs. 4.2 ng/mL). Similar proportions of patients with term and preterm deliveries had AMH levels greater than the 75th percentile (25% vs. 21%). The odds of preterm birth were similar by AMH quartile after adjusting for the history of preterm birth. Similarly, in the polycystic ovary syndrome (PCOS) cohort, there was no difference between mean AMH values of term and preterm births ($n = 139$, 9.6 vs. 10.0 ng/mL). The proportions of patients with PCOS with AMH levels greater than the 75th percentile were similar between those with term and preterm deliveries (25% vs. 22%). The odds of preterm birth were similar by the AMH quartile after adjusting for the history of preterm birth.

Conclusion(s): Elevated AMH levels were not associated with an increased risk of preterm birth in patients who conceived after in vitro fertilization and ovulation induction, including patients with PCOS. Although studies suggest that AMH levels may help stratify the risk of preterm birth in this population, our findings indicate that further studies are needed before clinical application.

Keywords: Antimüllerian hormone; in vitro fertilization; ovulation induction; preterm birth; preterm delivery.

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Conflict of interest statement

Declaration of interests A.E.K. has nothing to disclose. M.K.S. has nothing to disclose. A.N. has nothing to disclose. N.K. has nothing to disclose. A.D. has nothing to disclose.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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71

Acta Obstet Gynecol Scand

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. 2023 Nov;102(11):1549-1557.

doi: 10.1111/aogs.14642. Epub 2023 Jul 25.

[Pregestational maternal risk factors for preterm and term preeclampsia: A population-based cohort study](#)

[Anne Kvie Sande](#)^{1,2}, [Ingvild Dalen](#)³, [Erik Andreas Torkildsen](#)^{1,2}, [Ragnar Kvie Sande](#)^{1,2}, [Nils-Halvdan Morken](#)^{2,4}

Affiliations expand

- PMID: 37491773
- PMCID: [PMC10577625](#)
- DOI: [10.1111/aogs.14642](#)

Free PMC article

Abstract

Introduction: Most studies on factors affecting the risk of preeclampsia have not separated preterm from term preeclampsia, and we still know little about whether the predisposing conditions have a differentiated effect on the risk of preterm and term preeclampsia. Our aim was to assess whether diabetes type 1 and 2, chronic kidney disease, asthma, epilepsy, rheumatoid arthritis and chronic hypertension were differentially associated with preterm and term preeclampsia.

Material and methods: This is a nationwide, population-based cohort study containing all births registered in the Medical Birth Registry of Norway from 1999 to 2016. Multinomial logistic regression analysis was used to estimate relative risk ratios (RRRs) with 95% confidence intervals (95% CIs), adjusting for maternal age, parity, multiple gestation and all other studied maternal risk factors.

Results: We registered 1 044 860 deliveries, of which 9533 (0.9%) women had preterm preeclampsia (<37 weeks) and 26 504 (2.5%) women had term preeclampsia (>37 weeks). Most of the assessed maternal risk factors were associated with increased risk for both preterm and term preeclampsia, with adjusted RRRs ranging from 1.2 to 10.5 (preterm vs no preeclampsia) and 0.9-5.7 (term vs no preeclampsia). Diabetes type 1 and 2 (RRR preterm vs term preeclampsia 2.89, 95% CI 2.46-3.39 and RRR 1.68, 95% CI 1.25-2.25, respectively), chronic kidney disease (RRR 1.55, 95% CI 1.11-2.17) and chronic hypertension (RRR 1.85, 95% CI 1.63-2.10) were more strongly associated with preterm than term preeclampsia in adjusted analyses. For asthma, epilepsy and rheumatoid arthritis, RRRs were closer to one and not significant when comparing risk of preterm and term preeclampsia. Main results were similar when using a diagnosis at <34 weeks to define preterm preeclampsia.

Conclusions: Diabetes type 1 and 2, chronic kidney disease and chronic hypertension were more strongly associated with preterm than term preeclampsia.

Keywords: epidemiology; preterm preeclampsia; risk factors; term preeclampsia.

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Conflict of interest statement

AKS, ID and EAT have no conflicts of interest to declare. RKS is at the board of the Nordic Federation of Societies of Obstetrics and Gynecology. Other than this, he has no conflicts of interest to declare. NHM is a former associate editor of AOGS. Other than this, he has no conflicts of interest to declare.

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

SUPPLEMENTARY INFO

MeSH terms, Grants and fundingexpand

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Environ Res

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. 2023 Nov 1;236(Pt 2):116712.

doi: 10.1016/j.envres.2023.116712. Epub 2023 Jul 22.

[Hair as an alternative matrix to assess exposure of premature neonates to phthalate and alternative plasticizers in the neonatal intensive care unit](#)

[Paulien Cleys](#)¹, [Lucas Panneel](#)², [Jasper Bombeke](#)³, [Catalina Dumitrascu](#)³, [Govindan Malarvannan](#)³, [Giulia Poma](#)³, [Antonius Mulder](#)⁴, [Philippe G Jorens](#)⁵, [Adrian Covaci](#)⁶

Affiliations expand

- PMID: 37482128
- DOI: [10.1016/j.envres.2023.116712](https://doi.org/10.1016/j.envres.2023.116712)

Abstract

Due to adverse health effects, di-(2-ethylhexyl) phthalate (DEHP), a plasticizer used to soften plastic medical devices (PMDs), was restricted, and gradually replaced by alternative plasticizers (APs). Up to this date, urine was the sole matrix studied for plasticizer exposure in neonates hospitalized in the neonatal intensive care unit (NICU), a population highly vulnerable to toxic effects of plasticizers. The primary aim of this study was to assess simultaneous measurement of phthalate and AP metabolites in neonatal scalp hair. In addition, we aimed to use this matrix to investigate exposure of premature neonates to plasticizers during their stay in the NICU. Hair samples in this study were collected from premature neonates and their mothers included in a prospective birth cohort study in a tertiary NICU at the Antwerp University Hospital (UZA), Belgium. Samples from premature neonates (n = 45) and their mothers (n = 107) as well as from control neonates (n = 24) and mothers (n = 29) were analyzed using liquid-chromatography coupled to tandem mass spectrometry. This is the first study reporting metabolites of phthalate and alternative plasticizers in neonatal hair samples as biomarkers for exposure to these plasticizers. Results showed that hair sampled from premature neonates after a NICU stay contained significantly higher metabolite concentrations of both phthalates (DEHP, DiBP, and DnBP; 9.0-2500, 9.3-2200, and 24.7-5300 ng/g), and alternative plasticizers (DEHA, DEHT, and TOTM; 38.8-3400, 127.5-5700, and 10.8-8700 ng/g) - when compared to healthy control neonates. Besides, DEHP and DEHT metabolite concentrations were significantly higher than in hair sampled from adult populations. In addition, prolonged NICU exposure to non-invasive respiratory support devices and gastric tubes was correlated with increased concentrations in hair samples, indicating accumulation of plasticizers in this alternative matrix. In conclusion, our data indicate that preterm neonates are still highly exposed to phthalate and alternative plasticizers during NICU stay, despite the EU Medical Devices Regulation.

Trial registration: ClinicalTrials.gov [NCT05404815](https://clinicaltrials.gov/ct2/show/study/NCT05404815).

Keywords: Biomonitoring; DEHP; Hair sampling; Harmful plastic additives; Neonatal intensive care unit; Plastic medical devices.

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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 types, MeSH terms, Substances, Associated dataexpand

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J Pediatr (Rio J)

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. 2023 Nov-Dec;99(6):529-530.

doi: 10.1016/j.jpmed.2023.07.001. Epub 2023 Jul 20.

[A few breaths at birth; a lifetime of health](#)

[Waldemar A Carlo](#)¹, [Vivek V Shukla](#)²

Affiliations expand

- PMID: 37482078
- PMCID: [PMC10594006](#)
- DOI: [10.1016/j.jpmed.2023.07.001](#)

Free PMC article

No abstract available

Conflict of interest statement

Conflicts of interest The authors declare no conflicts of interest.

- [9 references](#)

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS



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74

J Perinatol



. 2023 Nov;43(11):1429-1436.

doi: 10.1038/s41372-023-01727-z. Epub 2023 Jul 15.

[Preterm birth and early life environmental factors: neuropsychological profiles at adolescence and young adulthood](#)

[Lexuri Fernández de Gamarra-Oca](#)¹, [Leire Zubiaurre-Elorza](#)², [Ainara Gómez-Gastiasoro](#)³, [Marta Molins-Sauri](#)⁴, [Begoña Loureiro](#)⁵, [Javier Peña](#)¹, [M Acebo García-Guerrero](#)¹, [Naroa Ibarretxe-Bilbao](#)¹, [Olga Bruna](#)⁴, [Carme Junqué](#)^{6,7}, [Alfons Macaya](#)⁸, [Maria A Poca](#)⁹, [Natalia Ojeda](#)¹

Affiliations expand

- PMID: 37454175
- DOI: [10.1038/s41372-023-01727-z](https://doi.org/10.1038/s41372-023-01727-z)

Abstract

Objectives: To establish neuropsychological profiles after high- and low-risk preterm birth (i.e., with and without neonatal brain injury) during adolescence and young adulthood and to assess the potential role of early life environmental factors in cognition.

Study design: Participants (N = 177; M_{age} = 20.11 years) of both sexes were evaluated when adolescent or in young adulthood. They were grouped according to their birth status: 30 high-risk preterm, 83 low-risk preterm and 64 born at full term.

Results: Significant differences were found in several cognitive domains between groups. Furthermore, familial socioeconomic status (SES) moderated the relation between the degree of maturity/immaturity at birth and cognition ($F_{(5,171)} = 11.94, p < 0.001, R^2 = 0.26$).

Discussion: The findings showed different neuropsychological profiles during adolescence and young adulthood, with the high-risk preterm sample evidencing lower cognitive values. In addition, higher scores in the familial SES score in this study seem to have a protective effect on cognition.

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- [57 references](#)

SUPPLEMENTARY INFO

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nature portfolio 

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World J Pediatr

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. 2023 Nov;19(11):1104-1110.

doi: 10.1007/s12519-023-00742-6. Epub 2023 Jul 15.

Status of the neonatal follow-up system in China: survey and analysis

[Qi Zhou](#)¹, [Yun Cao](#)², [Lan Zhang](#)¹, [Nurya Erejep](#)³, [Wen-Long Xiu](#)⁴, [Jing-Yun Shi](#)⁵, [Rui Cheng](#)⁶, [Wen-Hao Zhou](#)¹, [Shoo K Lee](#)⁷

Affiliations expand

- PMID: 37452966
- PMCID: [PMC10533627](#)
- DOI: [10.1007/s12519-023-00742-6](#)

Free PMC article

Abstract

Background: There is little information about neonatal follow-up programs (NFUPs) in China. This study aimed to conduct a survey of hospitals participating in the Chinese Neonatal Network (CHNN) to determine the status of NFUPs, including resources available, criteria for enrollment, neurodevelopmental assessments, and duration of follow-up.

Methods: We conducted a descriptive study using an online survey of all 72 hospitals participating in CHNN in 2020. The survey included 15 questions that were developed based on the current literature and investigators' knowledge about follow-up practices in China.

Results: Sixty-four (89%) of the 72 hospitals responded to the survey, with an even distribution of children's (31%), maternity (33%) and general (36%) hospitals. All but one (98%) hospital had NFUPs, with 44 (70%) being established after 2010. Eligibility criteria for follow-up were variable, but common criteria included very preterm infants < 32 weeks or < 2000 g birth weight (100%), small for gestational age (97%), hypoxic ischemic encephalopathy (98%) and postsurgery (90%). The average follow-up rate was 70% (range: 7.5%-100%). Only 12% of hospitals followed up with patients for more than 24 months. There was significant variation in neurodevelopmental assessments, follow-up schedule, composition of staff, and clinic facilities and resources. None of the staff had received formal training, and only four hospitals had sent staff to foreign hospitals as observers.

Conclusions: There is significant variation in eligibility criteria, duration of follow-up, types of assessments, staffing, training and facilities available. Coordination and standardization are urgently needed.

Keywords: Follow-up; Neonate; Survey.

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Conflict of interest statement

No financial or non-financial benefits have been received or will be received from any party related directly or indirectly to the subject of this article. Authors Shoo K. Lee and Wen-Hao Zhou are members of the Editorial Board for World Journal of Pediatrics. The paper was handled by the other Editor and has undergone rigorous peer review process. Authors Shoo K. Lee and Wen-Hao Zhou were not involved in the journal's review of, or decisions related to, this manuscript.

- [24 references](#)

SUPPLEMENTARY INFO

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

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76

[Review](#)

Surv Ophthalmol

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. 2023 Nov-Dec;68(6):1153-1165.

doi: 10.1016/j.survophthal.2023.06.010. Epub 2023 Jul 7.

Insulin-like growth factor-1 and retinopathy of prematurity: A systemic review and meta-analysis

[Yanyan Fu](#)¹, [Chunyan Lei](#)¹, [Ran Qibo](#)¹, [Xi Huang](#)¹, [Yingying Chen](#)¹, [Miao Wang](#)¹, [Meixia Zhang](#)²

Affiliations expand

- PMID: 37423521
- DOI: [10.1016/j.survophthal.2023.06.010](https://doi.org/10.1016/j.survophthal.2023.06.010)

Abstract

The prevalence of retinopathy of prematurity (ROP) is rapidly increasing worldwide. Many researchers have explored the relationship between insulin-like growth factor-1 (IGF-1) and ROP; however, the results are controversial. This meta-analysis evaluates the correlation between IGF-1 and ROP systematically. We searched for PubMed, Web of Science, Embase, the Cochrane Central Register of Controlled Trials, Ovid MEDLINE, SinoMed, ClinicalTrials.gov, and 3 Chinese databases up to June 2022. Then, the meta-regression and subgroup analysis were carried out. Twelve articles with 912 neonates were included in this meta-analysis. The results revealed that 4 of 7 covariates account for significant heterogeneity: location, measurement method of IGF-1 levels, collection time of blood sample, and the severity of ROP. The pooled analysis showed that low IGF-1 levels could serve as a risk factor associated with the development and severity of ROP. Serum IGF-1 monitoring in preterm infants after birth will be helpful in the diagnosis and treatment of ROP, and the reference value of IGF-1 should be standardized according to the measurement of IGF-1 and the region, as well as the postmenstrual age of prematurity.

Keywords: IGF-1; Meta-analysis; ROP; Systemic review.

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Conflict of interest statement

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

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances expand

FULL TEXT LINKS



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77

Randomized Controlled Trial

Clin Nurs Res

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. 2023 Nov;32(8):1104-1114.

doi: 10.1177/10547738231184923. Epub 2023 Jul 5.

[Virtual Reality Headset Simulating a Nature Environment to Improve Health Outcomes in Pregnant Women: A Randomized-Controlled Trial](#)

[Süreyya Kılıç¹](#), [Sema Dereli Yılmaz²](#)

Affiliations expand

- PMID: 37408298
- DOI: [10.1177/10547738231184923](https://doi.org/10.1177/10547738231184923)

Abstract

The single-blind randomized-controlled experimental study aimed to determine the effects of watching nature images through virtual reality (VR) headset on stress, anxiety, and

attachment levels of pregnant women with preterm birth threats (PBTs). The participants were 131 primiparous pregnant women admitted to the perinatology clinic due to PBT between April 5, 2022 and July 20, 2022. The intervention group watched videos containing nature images accompanied by nature sounds in six sessions through VR headset three times daily for 2 days. Each session lasted for 5 min. The data were accumulated with the Information Form, Stress Subscale of Depression Anxiety Stress Scale-21, State Anxiety Inventory, Prenatal Attachment Inventory, and Information Form of Satisfaction Level of VR Headset. State anxiety and stress levels of pregnant women in intervention group were statistically significantly lower than those in controls. There was no difference in prenatal attachment levels concerning intragroup comparisons of intervention group.

Trial registration: ClinicalTrials.gov [NCT05352503](#) [NCT05312502](#).

Keywords: anxiety; attachment; preterm birth threat; stress; virtual reality.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Associated dataexpand

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Sage Journals 

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Cite

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78

CNS Neurosci Ther

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. 2023 Nov;29(11):3199-3211.

doi: 10.1111/cns.14320. Epub 2023 Jun 27.

[Altered gray-to-white matter tissue contrast in preterm-born adults](#)

[Benita Schmitz-Koep](#)^{1,2}, [Aurore Menegaux](#)^{1,2}, [Juliana Zimmermann](#)^{1,2}, [Melissa Thalhammer](#)^{1,2}, [Antonia Neubauer](#)^{1,2}, [Jil Wendt](#)^{1,2}, [David Schinz](#)^{1,2}, [Marcel Daamen](#)^{3,4}, [Henning](#)

[Boecker](#)³, [Claus Zimmer](#)^{1,2}, [Josef Priller](#)⁵, [Dieter Wolke](#)^{6,7}, [Peter Bartmann](#)⁴, [Christian Sorg](#)^{1,2,5}, [Dennis M Hedderich](#)^{1,2}

Affiliations expand

- PMID: 37365964
- PMCID: [PMC10580354](#)
- DOI: [10.1111/cns.14320](#)

Free PMC article

Abstract

Aims: To investigate cortical organization in brain magnetic resonance imaging (MRI) of preterm-born adults using percent contrast of gray-to-white matter signal intensities (GWPC), which is an in vivo proxy measure for cortical microstructure.

Methods: Using structural MRI, we analyzed GWPC at different percentile fractions across the cortex (0%, 10%, 20%, 30%, 40%, 50%, and 60%) in a large and prospectively collected cohort of 86 very preterm-born (<32 weeks of gestation and/or birth weight <1500 g, VP/VLBW) adults and 103 full-term controls at 26 years of age. Cognitive performance was assessed by full-scale intelligence quotient (IQ) using the Wechsler Adult Intelligence Scale.

Results: GWPC was significantly decreased in VP/VLBW adults in frontal, parietal, and temporal associative cortices, predominantly in the right hemisphere. Differences were pronounced at 20%, 30%, and 40%, hence, in middle cortical layers. GWPC was significantly increased in right paracentral lobule in VP/VLBW adults. GWPC in frontal and temporal cortices was positively correlated with birth weight, and negatively with duration of ventilation ($p < 0.05$). Furthermore, GWPC in right paracentral lobule was negatively correlated with IQ ($p < 0.05$).

Conclusions: Widespread aberrant gray-to-white matter contrast suggests lastingly altered cortical microstructure after preterm birth, mainly in middle cortical layers, with differential effects on associative and primary cortices.

Keywords: brain development; cerebral cortex; preterm birth; structural magnetic resonance imaging; tissue contrast.

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Conflict of interest statement

No potential conflicts of interest.

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

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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79

J Ultrasound Med

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. 2023 Nov;42(11):2583-2588.

doi: 10.1002/jum.16293. Epub 2023 Jun 19.

Intra-Sonographer Correlation Between Transabdominal and Transvaginal Cervical Length Measurements and Associated Patient Demographics

[Jessica A Peterson](#)¹, [Isaiah Smolar](#)¹, [Guillaume Stoffels](#)¹, [Angela Bianco](#)¹

Affiliations expand

- PMID: 37334907

- DOI: [10.1002/jum.16293](https://doi.org/10.1002/jum.16293)

Abstract

Objectives: To assess transvaginal (TV) and transabdominal (TA) cervical length (CL) measurements' variability and patient factors associated with TA CL accuracy. We hypothesized that patient factors would affect the accuracy of TA CL.

Methods: This was a prospective cohort study. During anatomy ultrasound, TA and TV CL measurements were obtained, distance from placental edge to internal cervical os assessed, and demographic questionnaires completed. Patients between 18 to 22 weeks and 6 days were included and those <18 year old or with a twin gestation were excluded. TA CL >0.5 cm different from TV length was considered inaccurate.

Results: A total of 530 patients were included. Exactly 18.7% had a prior cesarean, 9.8% a preterm birth, and 2.2% a cervical procedure. Mean age and BMI were 31.1 years and 27.8 kg/m². Median number of living children was one. Median TA and TV CL were 3.42 and 3.53 cm. Exactly 36% (95% CI: 32-40%) of TA CL measurements were inaccurate. CL of 3.4 cm corresponded to a mean difference of zero between TA and TV CL. TA ultrasound had a sensitivity of 25% and a specificity of 98.5% to detect TV CL <2.5 cm. On multivariable analyses, Hispanic ethnicity was associated with inaccurate TA measurement (OR 0.48, 95% CI: 0.24-0.96, P = .04).

Conclusions: On average, TA CL underestimates TV CL when TV CL >3.40 cm and overestimates TV CL when TV CL <3.40 cm. Additional co-variables did not impact accuracy. TA ultrasound has low sensitivity to predict short cervix. Relying solely on TA CL to identify those who need intervention may miss diagnoses. It may be reasonable to develop protocols in which TV CL is used for TA CL <3.4 cm.

Keywords: cervical length; cervix; placenta previa; transabdominal; transvaginal; ultrasound.

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- [10 references](#)

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MeSH termsexpand

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80

Br J Clin Pharmacol

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. 2023 Nov;89(11):3324-3329.

doi: 10.1111/bcp.15829. Epub 2023 Jul 10.

[Prospective evaluation of pregnancy outcomes after gestational exposure to prazosin](#)

[Natalie Zitoun](#)¹, [M Karen Campbell](#)^{1,2,3,4,5}, [Doreen Matsui](#)², [Facundo Garcia-Bournissen](#)^{1,2,4,5}

Affiliations expand

- PMID: 37323115
- DOI: [10.1111/bcp.15829](https://doi.org/10.1111/bcp.15829)

Abstract

Aims: Prazosin is an antihypertensive medication which can be used to help with post-traumatic stress disorder (PTSD) symptoms. Little data is currently available on its safety in pregnancy. The aim of this study was to assess the fetal and pregnancy safety associated with prazosin exposures in early pregnancy.

Methods: Subjects were 11 patients who took prazosin during pregnancy and were counselled at the FRAME clinic in London Health Sciences Centre (Ontario, Canada) between 1 January 2000 and 31 December 2021. Data on their other exposures and

pregnancy outcomes were collected from medical records and through telephone questionnaires.

Results: It was found that 6/11 (54.5%) subjects did not report any adverse outcomes and experienced uneventful pregnancies. There were two miscarriages. Birthweights were within the normal range for the remaining nine pregnancies. Adverse events reported were consistent with background population expectation, including: one postpartum haemorrhage, one case of preeclampsia, one preterm birth, two NICU admissions, and two caesarean sections.

Conclusions: For these 11 subjects, pregnancy outcomes after exposure to prazosin were consistent with typical outcomes from unexposed pregnancies. More data are needed to conclude that prazosin is safe for use in pregnant subjects. However, the lack of adverse effects above baseline is reassuring to future patients who may be unintentionally exposed to prazosin while pregnant. Therefore, this study contributes valuable data towards monitoring safety of prazosin in pregnancy.

Keywords: drug safety; post-traumatic stress disorder; prazosin; pregnancy; reproductive clinical pharmacology.

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81

Transfus Clin Biol

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. 2023 Nov;30(4):382-386.

doi: 10.1016/j.tracli.2023.06.001. Epub 2023 Jun 13.

Comparison of restrictive and liberal red blood cell suspension transfusion and analysis of influencing factors on prognosis of premature infants

Zhi Zeng¹, Yu-Dan Chen², Ming-Wei Yin³, Xue-Jun Chen¹, Ting Wang⁴, Jun Xu¹, Ji-Hua Ma¹

Affiliations expand

- PMID: 37321534
- DOI: [10.1016/j.tracli.2023.06.001](https://doi.org/10.1016/j.tracli.2023.06.001)

Abstract

Objective: To investigate the influence of restrictive and liberal red blood cell suspension (RBCs) transfusions on the prognosis of premature infants and to analyze the influencing factors to provide a reference for the transfusion strategy of preterm infants.

Methods: Retrospective analysis was conducted on 85 cases of anemic premature infants treated in our center, including 63 cases in the restrictive transfusion group and 22 in the liberal transfusion group.

Results: RBCs transfusions were effective in both groups, and there were no statistically significant differences in post-transfusion hemoglobin and hematocrit between the two groups ($P > 0.05$). The outcome events: the duration of ventilatory support was statistically longer in the restrictive group compared with the liberal group ($P < 0.001$); however, the differences in mortality, the increased weight before discharge, and length of stay in the hospital within the two groups were not statistically significant ($P = 0.237, 0.36$ and 0.771 , respectively). Univariate survival analysis showed that age, birth weight, Apgar 1 min and Apgar 10 min scores were the influencing factors for death, with P values of $0.035, 0.004, <0.001$, and 0.013 , respectively; COX regression analysis showed that Apgar 1 min score was an independent factor of the survival time of preterm infants ($P = 0.002$).

Conclusion: Compared with the restrictive transfusion group, liberal transfusion patients presented a shorter duration of ventilatory support, which is more beneficial to the prognosis of premature infants.

Keywords: Factors; Liberal transfusion; Premature infants; RBCs; Restrictive transfusion; Survival.

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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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BJOG

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. 2023 Nov;130(12):1491-1492.

doi: 10.1111/1471-0528.17569. Epub 2023 Jun 13.

[Can uteroplacental insufficiency explain the increased cardiovascular](#)

risk in women with a history of spontaneous preterm birth?

[Veronica Giorgione](#)^{1,2}

Affiliations expand

- PMID: 37311696
- DOI: [10.1111/1471-0528.17569](https://doi.org/10.1111/1471-0528.17569)

No abstract available

Comment on

- [Long-term maternal mortality risk following spontaneous preterm birth: A retrospective cohort study.](#)
Theilen LH, Hammad I, Meeks H, Fraser A, Manuck TA, Varner MW, Smith KR. *BJOG*. 2023 Nov;130(12):1483-1490. doi: 10.1111/1471-0528.17552. Epub 2023 May 22. PMID: 37212439

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS



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83

J Formos Med Assoc

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. 2023 Nov;122(11):1199-1207.

The effect of patient volume on mortality and morbidity of extremely low birth weight infants in Taiwan

[Chia-Ling Wu](#)¹, [Chia-Huei Chen](#)², [Jui-Hsing Chang](#)², [Chun-Chih Peng](#)², [Chyong-Hsin Hsu](#)³, [Chia-Ying Lin](#)³, [Wai-Tim Jim](#)², [Hung-Yang Chang](#)⁴, [Taiwan Premature Infant Follow-up Network](#)⁵

Affiliations expand

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- DOI: [10.1016/j.jfma.2023.05.024](https://doi.org/10.1016/j.jfma.2023.05.024)

Free article

Abstract

Background: To assess whether the number of extremely low birth weight (ELBW) infants treated annually in neonatal intensive care units (NICUs) in Taiwan affects the mortality and morbidity of this patient population.

Methods: This retrospective cohort study included preterm infants with ELBW (≤ 1000 g). NICUs were divided into three subgroups according to the annual admissions of ELBW infants (low, ≤ 10 ; medium, 11-25; and high, >25). Perinatal characteristics, mortality, and short-term morbidities were compared between groups.

Results: A total of 1945 ELBW infants from 17 NICUs were analyzed (low-volume, $n = 263$; medium-volume, $n = 420$; and high-volume, $n = 1262$). After risk adjustments, infants from NICUs with low patient volumes were at a higher risk of death. The risk-adjusted odds ratios (aOR) for mortality were 0.61 (95% CI, 0.43-0.86) in the high-volume NICUs and 0.65 (95% CI, 0.43-0.98) in medium-volume NICUs, compared with infants admitted to low-volume NICUs. Infants in medium-volume NICUs had the lowest incidence of prenatal steroid exposure (58.1%, $P < 0.001$) and were associated with the highest risk of necrotizing enterocolitis (aOR, 2.35 [95% CI, 1.48-3.72]), severe intraventricular hemorrhage (aOR, 1.55 [95% CI, 1.01-2.28]), and bronchopulmonary dysplasia (aOR, 1.61 [95% CI, 1.10-2.35]). However, survival without major morbidity did not differ between the groups.

Conclusion: The mortality risk was higher among ELBW infants admitted to NICUs with a low annual patient volume. This may emphasize the importance of systematically referring patients from these vulnerable populations to appropriate care settings.

Keywords: Extremely low birth weight; Infant mortality; Morbidity; Neonatal; Neonatal intensive care units.

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Conflict of interest statement

Declaration of competing interest None.

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Soc Psychiatry Psychiatr Epidemiol

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. 2023 Nov;58(11):1603-1624.

doi: 10.1007/s00127-023-02505-0. Epub 2023 Jun 4.

[Factors associated with new onset of father-to-infant bonding failure from 1 to 6 months postpartum: an adjunct study of the Japan environment and children's study](#)

[Taeko Suzuki](#) ^{#1,2}, [Toshie Nishigori](#) ^{#3}, [Taku Obara](#) ^{3,4,5}, [Miyuki Mori](#) ^{1,2}, [Kasumi Sakurai](#) ⁴, [Mami Ishikuro](#) ⁵, [Hirotaka Hamada](#) ⁶, [Masatoshi Saito](#) ⁶, [Junichi Sugawara](#) ^{4,5,7}, [Takahiro Arima](#) ⁴, [Hirohito Metoki](#) ⁸, [Shinichi Kuriyama](#) ^{4,5,9}, [Aya Goto](#) ¹⁰, [Nobuo Yaegashi](#) ^{4,5,6}, [Hidekazu Nishigori](#) ^{#11}

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- PMID: 37271773
- DOI: [10.1007/s00127-023-02505-0](https://doi.org/10.1007/s00127-023-02505-0)

Abstract

Purpose: This study aimed to determine the factors associated with new onset father-to-infant (paternal) bonding failure from 1 to 6 months postpartum.

Methods: This was a prospective birth-cohort study. Paternal bonding failure was evaluated using the Japanese version of the Mother-to-Infant Bonding Scale (MIBS-J) at 1 and 6 months postpartum. For cut-off scores, overall bonding failure, MIBS-J total scores ≥ 5 ; subscale for lack of affection, MIBS-J_LA scores ≥ 3 ; and subscale for anger/rejection, MIBS-J_AR scores ≥ 3 were used in this study. Multivariate regression analysis was performed to analyze relative variables.

Results: We analyzed 872 fathers. The frequency of new-onset overall bonding failure, lack of affection, and anger/rejection was 5.6%, 4.9%, and 6.3%, respectively. For new-onset overall bonding failure, significant associated factors were paternal childcare leave (adjusted odds ratio [AOR] 3.192; 95% confidence interval [CI] 1.203-8.469), paternal new-onset depression symptoms (AOR 3.181; 95% CI 1.311-7.716), and maternal new-onset overall bonding failure (AOR 4.595; 95% CI 1.119-18.866). For new-onset lack of affection, significant associated factors were preterm birth (AOR 4.189; 95% CI 1.473-11.913) and paternal new-onset depression symptoms (AOR 3.290; 95% CI 1.294-8.362). For new-onset anger and rejection, significant associated factors were paternal childcare leave (AOR 3.142; 95% CI 1.138-8.676), paternal new-onset depression symptoms (AOR 2.829; 95% CI 1.133-7.068), and maternal new-onset anger/rejection (AOR 7.064; 95% CI 2.300-21.700).

Conclusions: The factors associated with new-onset paternal bonding failure from 1 to 6 months postpartum were paternal childcare leave, preterm birth, paternal postpartum depression symptoms, and maternal bonding failure.

Keywords: Anger and rejection; Japanese version of the Mother-to-Infant Bonding Scale (MIBS-J); Lack of affection; New-onset father-to-infant bonding failure; Postpartum.

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J Perinat Med

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. 2023 May 30;51(8):1097-1103.

doi: 10.1515/jpm-2022-0547. Print 2023 Oct 26.

[German obstetrician's self-reported attitudes and handling in threatening preterm birth at the limits of viability](#)

[Katja Schneider](#)¹, [Johanna Müller](#)², [Ekkehard Schleußner](#)²

Affiliations expand

- PMID: 37256371
- DOI: [10.1515/jpm-2022-0547](https://doi.org/10.1515/jpm-2022-0547)

Abstract

Objectives: Antenatal treatment and information influences the course of pregnancy and parental decision-making in cases of threatened prematurity on the borderline of viability. Numerous studies have shown significant interprofessional differences in assessing ethical boundary decisions; hence, this study aimed to evaluate obstetricians attitudes, practices and antenatal parental counseling regarding threatened preterm birth in Germany.

Methods: An anonymous online questionnaire was administered to 543 obstetricians at tertiary perinatal centers and prenatal diagnostic centers in Germany. The survey contained questions on basic ethical issues assessed using the Likert scale and a case vignette regarding the practical procedures of an imminent extreme premature birth at 23 1/7 gestational weeks.

Results: In the case of unstoppable preterm birth, 15 % of clinicians said they would carry out a cesarean section; however, specialists from centers with a high number of very low birth weight infants would do so significantly more often. Among respondents, 29.8 % did not take any therapeutic measures without discussing the child's treatment options with their parents, 19.9 % refused to offer actionable advice to the parents, and 57 % said they would advise parents to seek intensive care treatment for the child with the option of changing treatment destination in the event of serious complications. Moreover, 84 % said they would provide information together with neonatologists.

Conclusions: Joint counseling with neonatologists is widely accepted. The size of the perinatal center significantly influences the practical approach to threatened preterm births. Respect for parents' decision-making autonomy regarding the child's treatment options is central and influences therapy initiation.

Keywords: borderline of viability; decision-making; ethics; parental counseling; perinatology.

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MeSH termsexpand

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. 2023 Nov;90(11):1089-1095.

doi: 10.1007/s12098-023-04604-x. Epub 2023 May 25.

Retinopathy of Prematurity and Glucose-6-Phosphate Dehydrogenase Activity: A Case-Control Study

[Rajarajan Paulpandian](#)¹, [Sourabh Dutta](#)², [Reena Das](#)³, [Deeksha Katoch](#)⁴, [Praveen Kumar](#)¹

Affiliations expand

- PMID: 37227582
- DOI: [10.1007/s12098-023-04604-x](https://doi.org/10.1007/s12098-023-04604-x)

Abstract

Objective: To determine whether red blood cell glucose-6-phosphate dehydrogenase (G6PD) activity is associated with retinopathy of prematurity (ROP).

Methods: This case-control study was conducted in a Level-3 neonatal unit. Subjects were inborn boys with birth weight <2000 g. "Cases" were consecutive subjects with ROP of any severity. "Controls" were consecutive unrelated subjects without ROP. Recipients of blood or exchange transfusions were excluded. Sixty cases (out of 98 screened) and 60 controls (out of 93 screened) were enrolled. G6PD activity (quantitative assay) as the candidate risk factor was evaluated.

Results: Sixty cases with 60 controls [mean (SD) gestation 28.80 (2.2) and 30.60 (2.2) wk respectively] were compared. "Cases" had a higher median (1st, 3rd quartile) G6PD activity compared to "controls" [7.39 (4.7, 11.5) vs. 6.28 (4.2, 8.8) U/g Hb, $p = 0.084$]. G6PD activity was highest among ROP requiring treatment [8.68 (4.7, 12.3)] followed by ROP not requiring treatment [6.91 (4.4, 11.0)], followed by controls ($p_{\text{linear trend}} = 0.06$). Gestation, birth weight, duration of oxygen, breastmilk feeding, and clinical sepsis were other variables associated with ROP on univariable analysis. On multivariable logistic regression, G6PD activity [Adjusted OR 1.14 (1.03, 1.25), $p = 0.01$] and gestation [Adjusted OR 0.74 (0.56, 0.97), $p = 0.03$] independently predicted ROP. C-statistic of the model was 0.76 (95% CI 0.67, 0.85).

Conclusions: Higher G6PD activity was independently associated with ROP after adjusting for confounders. Each 1 U/g Hb increase in G6PD increased the odds of ROP by 14%. Severer forms of ROP were associated with higher levels of G6PD activity.

Keywords: Anti-oxidant; Glucose-6-phosphate dehydrogenase; Neonate; Prematurity; Retinopathy.

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- [30 references](#)

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Review

J Perinat Med

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. 2023 May 22;51(8):1046-1051.

doi: 10.1515/jpm-2023-0074. Print 2023 Oct 26.

[Use, misuse, and overuse of antenatal corticosteroids. A retrospective cohort study](#)

[Livi Cojocaru](#)¹, [Shruti Chakravarthy](#)¹, [Hooman Tadbiri](#)², [Rishika Reddy](#)¹, [James Ducey](#)¹, [Gary Fruhman](#)¹

Affiliations expand

- PMID: 37216498
- DOI: [10.1515/jpm-2023-0074](https://doi.org/10.1515/jpm-2023-0074)

Abstract

Objectives: To evaluate the timing of antenatal corticosteroids (ACS) administration in relation to the delivery timing based on indications and risk factors for preterm delivery.

Methods: We conducted a retrospective cohort study to understand what factors predict the optimal timing of ACS administration (ACS administration within seven days). We reviewed consecutive charts of adult pregnant women receiving ACS from January 1, 2011, to December 31, 2019. We excluded pregnancies under 23 weeks, incomplete and duplicate records, and patients delivered outside our health system. The timing of ACS administration was categorized as optimal or suboptimal. These groups were analyzed regarding demographics, indications for ACS administration, risk factors for preterm delivery, and signs and symptoms of preterm labor.

Results: We identified 25,776 deliveries. ACS were administered to 531 pregnancies, of which 478 met the inclusion criteria. Of the 478 pregnancies included in the study, 266 (55.6 %) were delivered in the optimal timeframe. There was a higher proportion of patients receiving ACS for the indication of threatened preterm labor in the suboptimal group as compared to the optimal group (85.4 % vs. 63.5 %, $p < 0.001$). In addition, patients who delivered in the suboptimal timeframe had a higher proportion of short cervix (33 % vs. 6.4 %, $p < 0.001$) and positive fetal fibronectin (19.8 % vs. 1.1 %, $p < 0.001$) compared to those who delivered in the optimal timeframe.

Conclusions: More emphasis should be placed on the judicious use of ACS. Emphasis should be placed on clinical assessment rather than relying solely on imaging and laboratory tests. Re-appraisal of institutional practices and thoughtful ACS administration based on the risk-benefit ratio is warranted.

Keywords: antenatal diagnosis; corticosteroids; premature birth; prematurity; preterm labor.

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- [26 references](#)

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Publication types, MeSH terms, Substancesexpand

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BJOG

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. 2023 Nov;130(12):1483-1490.

doi: 10.1111/1471-0528.17552. Epub 2023 May 22.

[Long-term maternal mortality risk following spontaneous preterm birth: A retrospective cohort study](#)

[Lauren H Theilen](#)^{1,2}, [Ibrahim Hammad](#)^{1,2}, [Huong Meeks](#)³, [Alison Fraser](#)³, [Tracy A Manuck](#)^{1,4}, [Michael W Varner](#)^{1,2}, [Ken R Smith](#)³

Affiliations expand

- PMID: 37212439
- PMID: PMC10592573 (available on 2024-11-01)
- DOI: [10.1111/1471-0528.17552](https://doi.org/10.1111/1471-0528.17552)

Abstract

Objective: To determine whether women with spontaneous preterm birth (PTB) have increased risks for long-term mortality.

Design: Retrospective cohort.

Setting: Births in Utah between 1939 and 1977.

Population: We included women with a singleton live birth ≥ 20 weeks who survived at least 1 year following delivery. We excluded those who had never lived in Utah, had improbable birthweight/gestational age combinations, underwent induction (except for preterm membrane rupture) or had another diagnosis likely to cause PTB.

Methods: Exposed women had ≥ 1 spontaneous PTB between 20⁺⁰ weeks and 37⁺⁰ weeks. Women with > 1 spontaneous PTB were included only once. Unexposed women had all deliveries at or beyond 38⁺⁰ weeks. Exposed women were matched to unexposed women by birth year, infant sex, maternal age group and infant birth order. Included women were followed up to 39 years after index delivery.

Main outcome measures: Overall and cause-specific mortality risks were compared using Cox regression.

Results: We included 29 048 exposed and 57 992 matched unexposed women. There were 3551 deaths among exposed (12.2%) and 6013 deaths among unexposed women (10.4%). Spontaneous PTB was associated with all-cause mortality (adjusted hazard ratio [aHR] 1.26, 95% confidence interval [CI] 1.21-1.31), death from neoplasms (aHR 1.10, 95% CI 1.02-1.18), circulatory disease (aHR 1.35, 95% CI 1.25-1.46), respiratory disease (aHR 1.73, 95% CI 1.46-2.06), digestive disease (aHR 1.33, 95% CI 1.12-1.58), genito-urinary disease (aHR 1.60, 95% CI 1.15-2.23) and external causes (aHR 1.39, 95% CI 1.22-1.58).

Conclusions: Spontaneous PTB is associated with modestly increased risks for all-cause and some cause-specific mortality.

Keywords: follow-up studies; lifecourse; premature birth; retrospective studies; women's health.

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Conflict of interest statement

Disclosure of Interests

The authors report no relevant financial, personal, political, intellectual, or religious conflicts of interest.

Comment in

- [Can uteroplacental insufficiency explain the increased cardiovascular risk in women with a history of spontaneous preterm birth?](#)

Giorgione V.BJOG. 2023 Nov;130(12):1491-1492. doi: 10.1111/1471-0528.17569.

Epub 2023 Jun 13.PMID: 37311696 No abstract available.

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Clin Exp Pediatr

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. 2023 Nov;66(11):458-464.

doi: 10.3345/cep.2022.01235. Epub 2023 May 16.

[Spontaneous movements as prognostic tool of neurodevelopmental outcomes in preterm infants: a narrative review](#)

[Hyun lee Shin¹](#), [Myung Woo Park¹](#), [Woo Hyung Lee²](#)

Affiliations expand

- PMID: 37202346

- DOI: [10.3345/cep.2022.01235](#)

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Abstract

An estimated 15 million infants are born prematurely each year. Although the survival rate of preterm infants has increased with advances in perinatal and neonatal care, many still experience various complications. Since improving the neurodevelopmental outcomes of preterm births is a crucial topic, accurate evaluations should be performed to detect infants at high risk of cerebral palsy. General movements are spontaneous movements involving the whole body as the expression of neural activity and can be an excellent biomarker of neural dysfunction caused by brain impairment in preterm infants. The predictive value of general movements with respect to cerebral palsy increases with continuous observation. Automated approaches to examining general movements based on machine learning can help overcome the limited utilization of assessment tools owing to their qualitative or semiquantitative nature and high dependence on assessor skills and experience. This review covers each of these topics by summarizing normal and abnormal general movements as well as recent advances in automatic approaches based on infantile spontaneous movements.

Keywords: Cerebral palsy; General movements; Neurodevelopmental Disorders; Premature birth.

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Observational Study

Arch Dis Child Fetal Neonatal Ed

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. 2023 Nov;108(6):643-648.

doi: 10.1136/archdischild-2022-325245. Epub 2023 May 16.

Clinical usefulness of reintubation criteria in extremely preterm infants: a cohort study

[Tugba Alarcon-Martinez](#)^{1,2}, [Samantha Latremouille](#)¹, [Lajos Kovacs](#)³, [Robert E Kearney](#)⁴, [Guilherme M Sant'Anna](#)¹, [Wissam Shalish](#)⁵

Affiliations expand

- PMID: 37193586
- DOI: [10.1136/archdischild-2022-325245](https://doi.org/10.1136/archdischild-2022-325245)

Abstract

Objective: To describe the thresholds of instability used by clinicians at reintubation and evaluate the accuracy of different combinations of criteria in predicting reintubation decisions.

Design: Secondary analysis using data obtained from the prospective observational Automated Prediction of Extubation Readiness study ([NCT01909947](#)) between 2013 and 2018.

Setting: Multicentre (three neonatal intensive care units).

Patients: Infants with birth weight ≤ 1250 g, mechanically ventilated and undergoing their first planned extubation were included.

Interventions: After extubation, hourly O₂ requirements, blood gas values and occurrence of cardiorespiratory events requiring intervention were recorded for 14 days or until reintubation, whichever came first.

Main outcome measures: Thresholds at reintubation were described and grouped into four categories: increased O₂, respiratory acidosis, frequent cardiorespiratory events and severe cardiorespiratory events (requiring positive pressure ventilation). An automated algorithm was used to generate multiple combinations of criteria from the four categories and compute their accuracies in capturing reintubated infants (sensitivity) without including non-reintubated infants (specificity).

Results: 55 infants were reintubated (median gestational age 25.2 weeks (IQR 24.5-26.1 weeks), birth weight 750 g (IQR 640-880 g)), with highly variable thresholds at reintubation. After extubation, reintubated infants had significantly greater O₂ needs, lower pH, higher

pCO₂ and more frequent and severe cardiorespiratory events compared with non-reintubated infants. After evaluating 123 374 combinations of reintubation criteria, Youden indices ranged from 0 to 0.46, suggesting low accuracy. This was primarily attributable to the poor agreement between clinicians on the number of cardiorespiratory events at which to reintubate.

Conclusions: Criteria used for reintubation in clinical practice are highly variable, with no combination accurately predicting the decision to reintubate.

Keywords: Intensive Care Units, Neonatal; Neonatology.

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Conflict of interest statement

Competing interests: None declared.

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[Multicenter Study](#)

Arch Dis Child Fetal Neonatal Ed

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. 2023 Nov;108(6):599-606.

doi: 10.1136/archdischild-2022-325285. Epub 2023 Apr 26.

Neonatal outcomes following early fetal growth restriction: a subgroup analysis of the EVERREST study

[Ingran Lingam](#)^{1,2}, [Jade Okell](#)³, [Katarzyna Maksym](#)³, [Rebecca Spencer](#)^{3,4}, [Donald Peebles](#)^{5,6}, [Gina Buquis](#)³, [Gareth Ambler](#)⁷, [Eva Morsing](#)⁸, [David Ley](#)⁸, [Dominique Singer](#)⁹, [Violeta Tenorio](#)¹⁰, [Jade Dyer](#)³, [Yuval Ginsberg](#)^{3,11}, [Tal Weissbach](#)^{3,12}, [Angela Huertas-Ceballos](#)⁵, [Neil Marlow](#)³, [Anna David](#)³; [EVERREST consortium](#)

Collaborators, Affiliations expand

- PMID: 37185272
- DOI: [10.1136/archdischild-2022-325285](https://doi.org/10.1136/archdischild-2022-325285)

Free article

Abstract

Objective: To quantify the risks of mortality, morbidity and postnatal characteristics associated with extreme preterm fetal growth restriction (EP-FGR).

Design: The EVERREST (Do **e s v**ascular endothelial growth factor gene therapy saf **e l y** imp **r o v e** outcome in seve **r e e**arly-onset fetal growth re **st** riction?) prospective multicentre study of women diagnosed with EP-FGR (singleton, estimated fetal weight (EFW) <3rd percentile, <600 g, 20⁺⁰-26⁺⁶ weeks of gestation). The UK subgroup of EP-FGR infants (<36 weeks) were sex-matched and gestation-matched to appropriate for age (AGA) infants born in University College London Hospital (1:2 design, EFW 25th-75th percentile).

Setting: Four tertiary perinatal units (UK, Germany, Spain, Sweden).

Main outcomes: Antenatal and postnatal mortality, bronchopulmonary dysplasia (BPD), sepsis, surgically treated necrotising enterocolitis (NEC), treated retinopathy of prematurity (ROP).

Results: Of 135 mothers recruited with EP-FGR, 42 had a stillbirth or termination of pregnancy (31%) and 93 had live births (69%). Postnatal genetic abnormalities were identified in 7/93 (8%) live births. Mean gestational age at birth was 31.4 weeks (SD 4.6). 54 UK-born preterm EP-FGR infants (<36 weeks) were matched to AGA controls. EP-FGR was associated with increased BPD (43% vs 26%, OR 3.6, 95% CI 1.4 to 9.4, p=0.01), surgical NEC (6% vs 0%, p=0.036) and ROP treatment (11% vs 0%, p=0.001). Mortality was probably

higher among FGR infants (9% vs 2%, OR 5.0, 95% CI 1.0 to 25.8, $p=0.054$). FGR infants more frequently received invasive ventilation (65% vs 50%, OR 2.6, 95% CI 1.1 to 6.1, $p=0.03$), took longer to achieve full feeds and had longer neonatal stays (median difference 6.1 days, 95% CI 3.8 to 8.9 and 19 days, 95% CI 9 to 30 days, respectively, $p<0.0001$).

Conclusions: Mortality following diagnosis of EP-FGR is high. Survivors experience increased neonatal morbidity compared with AGA preterm infants.

Trial registration number: [NCT02097667](#).

Keywords: intensive care units, neonatal; neonatology; paediatrics.

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Conflict of interest statement

Competing interests: None declared.

- [Cited by 3 articles](#)

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Publication types, MeSH terms, Associated dataexpand

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. 2023 Nov-Dec;99(6):582-587.

doi: 10.1016/j.jpmed.2023.04.005. Epub 2023 May 10.

What the skin of 341 premature newborns says – a transversal study

[Danielle Arake Zanatta](#)¹, [Vânia Oliveira Carvalho](#)², [Regina Paula Guimarães Vieira Cavalcante da Silva](#)³

Affiliations expand

- PMID: 37172615
- PMCID: [PMC10594010](#)
- DOI: [10.1016/j.jpmed.2023.04.005](#)

Free PMC article

Abstract

Objectives: Determine the frequency of dermatological diagnoses in preterm newborns up to 28 days of life and associated perinatal factors.

Method: a cross-sectional analytical study with a convenience sample and prospective data collection, was conducted between November 2017 and August 2019. Overall, 341 preterm newborns who had been admitted to a University hospital - including those admitted to the Neonatal Intensive Care Unit - were evaluated.

Results: 61 (17.9%) had less than 32 weeks gestational age (GA), with a mean GA and birth weight of 33.9 ± 2.8 weeks and 2107.8 ± 679.8 g (465 to 4230g), respectively. The median age at the time of evaluation was 2.9 days (4 h to 27 days). The frequency of dermatological diagnoses was 100% and 98.5% of the sample had two or more, with an average of 4.67 ± 1.53 dermatoses for each newborn. The 10 most frequent diagnoses were lanugo (85.9%), salmon patch (72.4%), sebaceous hyperplasia (68.6%), physiological desquamation (54.8%), dermal melanocytosis (38.7%), Epstein pearls (37.2%), milia (32.2%), traumatic skin lesions (24%), toxic erythema (16.7%), and contact dermatitis (5%). Those with GA < 28 weeks showed more traumatic injuries and abrasions, whereas those with ≥ 28 weeks had physiological changes more frequently, and those with GA between 34-36^{6/7} weeks, had transient changes.

Conclusion: Dermatological diagnoses were frequent in our sample and those with higher GA showed a higher frequency of physiological (lanugo and salmon patch) and transient changes (toxic erythema and miliaria). Traumatic lesions and contact dermatitis were

among the 10 most frequent injuries, reinforcing the need to effectively implement neonatal skin care protocols, especially in preterm.

Keywords: Neonatal intensive care; Premature infant; Skin manifestations.

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Conflict of interest statement

Conflicts of interest The authors declare no conflicts of interest.

- [19 references](#)
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Observational Study

Arch Dis Child Fetal Neonatal Ed

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. 2023 Nov;108(6):612-616.

doi: 10.1136/archdischild-2022-325248. Epub 2023 May 11.

Hyper high haemoglobin content in red blood cells and erythropoietic transitions postnatally in infants of 22 to 26 weeks' gestation: a prospective cohort study

[Sara Marie Larsson](#)^{1,2}, [Tommy Ulinder](#)^{3,4}, [Alexander Rakow](#)⁵, [Mireille Vanpee](#)⁵, [Dirk Wackernagel](#)^{6,7}, [Karin Sävman](#)⁸, [Ingrid Hansen-Pupp](#)^{3,4}, [Ann Hellström](#)⁹, [David Ley](#)^{3,4}, [Ola Andersson](#)^{3,4}

Affiliations expand

- PMID: 37169579
- DOI: [10.1136/archdischild-2022-325248](https://doi.org/10.1136/archdischild-2022-325248)

Abstract

Objective: Blood cell populations, including red blood cells (RBC) unique to the extremely preterm (EPT) infant, are potentially lost due to frequent clinical blood sampling during neonatal intensive care. Currently, neonatal RBC population heterogeneity is not described by measurement of total haemoglobin or haematocrit. We therefore aimed to describe a subpopulation of large RBCs with hyper high haemoglobin content, >49 pg (Hyper-He) following EPT birth.

Design: Prospective observational cohort study.

Setting: Two Swedish study centres.

Participants: Infants (n=62) born between gestational weeks 22⁺⁰ to 26⁺⁶.

Methods: Prospective data (n=280) were collected from March 2020 to September 2022 as part of an ongoing randomised controlled trial. Blood was sampled from the umbilical cord, at postnatal day 1-14, 1 month, 40 weeks' postmenstrual age and at 3 months' corrected age.

Results: At birth, there was a considerable inter-individual variation; Hyper-He ranging from 1.5% to 24.9% (median 7.0%). An inverse association with birth weight and gestational age was observed; Spearman's rho (CI) -0.38 (-0.63 to -0.07) and -0.39 (-0.65 to -0.05), respectively. Overall, Hyper-He rapidly decreased, only 0.6%-5.0% (median 2.2%)

remaining 2 weeks postnatally. Adult levels (<1%) were reached at corresponding term age.

Conclusion: Our results point to gestational age and birth weight-dependent properties of the RBC population. Future work needs to verify results by different measurement techniques and elucidate the potential role of differing properties between endogenous and transfused RBCs in relation to neonatal morbidities during this important time frame of child development.

Trial registration number: [NCT04239690](#).

Keywords: growth; haematology; intensive care units, neonatal; neonatology.

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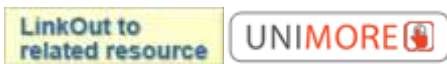
Conflict of interest statement

Competing interests: None declared.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated dataexpand

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J Perinatol

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. 2023 Nov;43(11):1374-1378.

doi: 10.1038/s41372-023-01685-6. Epub 2023 May 3.

The validity of hospital diagnostic and procedure codes reflecting morbidity in preterm neonates born <32 weeks gestation

[Kelli K Ryckman](#)^{1,2}, [Paul J Holdefer](#)^{3,4}, [Eva Sileo](#)³, [Claire Carlson](#)³, [Nancy Weathers](#)³, [Elizabeth A Jasper](#)^{5,6}, [Hyunkeun Cho](#)⁷, [Scott P Oltman](#)^{8,9}, [John M Dagle](#)¹⁰, [Laura L Jelliffe-Pawlowski](#)^{8,9}, [Elizabeth E Rogers](#)^{9,11}

Affiliations expand

- PMID: 37138163
- DOI: [10.1038/s41372-023-01685-6](https://doi.org/10.1038/s41372-023-01685-6)

Abstract

Objective: To determine the validity of diagnostic hospital billing codes for complications of prematurity in neonates <32 weeks gestation.

Study design: Retrospective cohort data from discharge summaries and clinical notes (n = 160) were reviewed by trained, blinded abstractors for the presence of intraventricular hemorrhage (IVH) grades 3 or 4, periventricular leukomalacia (PVL), necrotizing enterocolitis (NEC), stage 3 or higher, retinopathy of prematurity (ROP), and surgery for NEC or ROP. Data were compared to diagnostic billing codes from the neonatal electronic health record.

Results: IVH, PVL, ROP and ROP surgery had strong positive predictive values (PPV > 75%) and excellent negative predictive values (NPV > 95%). The PPVs for NEC (66.7%) and NEC surgery (37.1%) were low.

Conclusion: Diagnostic hospital billing codes were observed to be a valid metric to evaluate preterm neonatal morbidities and surgeries except in the instance of more ambiguous diagnoses such as NEC and NEC surgery.

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- [38 references](#)

SUPPLEMENTARY INFO

MeSH terms, Grants and fundingexpand

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nature portfolio UNIMORE 

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Eur J Sport Sci



. 2023 Nov;23(11):2129-2138.

doi: 10.1080/17461391.2023.2207082. Epub 2023 May 9.

[Influence of preterm birth on physical fitness in early childhood](#)

[Marcos D Martinez-Zamora](#)¹, [Pedro L Valenzuela](#)^{2,3}, [Inés Esteban Díez](#)⁴, [Óscar Martínez-de-Que](#)^{1,5}

Affiliations expand

- PMID: 37093663
- DOI: [10.1080/17461391.2023.2207082](https://doi.org/10.1080/17461391.2023.2207082)

Abstract

Evidence suggests that preterm birth is associated with an impaired physical fitness later in life, but whether these effects are already visible since early childhood remains unknown. We aimed to compare the physical fitness of preterm preschoolers with that of children born at term. Children aged three to six years and born preterm (<35 weeks) were recruited from a Neonatal Intensive Care Unit, and children born at term (>37 weeks) were included as controls. A variety of physical fitness indicators (strength, cardiorespiratory fitness, agility, flexibility and balance) were assessed with the PREFIT battery and the

adapted sit and reach test. Physical activity levels were measured through the PrePAQ questionnaire. A total of 98 preterm children (gestational age 32.4 ± 2.3 weeks, age 5.1 ± 0.8 years) and 74 controls (gestational age 39.9 ± 1.0 weeks, age 4.8 ± 0.9 years) were analysed. Despite no significant differences in physical activity levels ($p > 0.05$), preterm children showed an overall poorer physical fitness compared to controls. Specifically, preterm children had an impaired handgrip strength (-13.95% , $p < 0.001$), lower-limb muscle strength (-12.67% , $p = 0.003$), agility (-14.9% , $p = 0.001$), cardiorespiratory fitness (-12.73% , $p = 0.005$) and flexibility (-17.04% , $p = 0.001$) compared to controls. An inverse dose-response association was observed between the level of prematurity and physical fitness, with very preterm children (gestational age ≤ 32 weeks) presenting the poorest fitness levels. In summary, prematurity seems to impair physical fitness since early childhood, which might support the need for promoting preventive strategies (e.g. fitness monitoring and applying exercise interventions). **Highlights** Preterm children present an impaired physical fitness compared with peers born at term since early childhood (3-6 years), as reflected by lower muscle strength, agility, flexibility and cardiorespiratory fitness. A greater impairment of physical fitness is observed in children born very preterm (≤ 32 weeks of gestation). These findings might support the implementation of preventive strategies (e.g. fitness monitoring and exercise training) in preterm children since early childhood.

Keywords: Premature birth; cardiorespiratory fitness; children; exercise capacity; muscle strength; physical activity.

SUPPLEMENTARY INFO

MeSH termsexpand

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96

Arch Dis Child Fetal Neonatal Ed

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. 2023 Nov;108(6):594-598.

Effect of initial and subsequent mask applications on breathing and heart rate in preterm infants at birth

[Kristel L A M Kuypers](#)¹, [Anouk Hopman](#)², [Sophie J E Cramer](#)², [Janneke Dekker](#)², [Remco Visser](#)², [Stuart B Hooper](#)^{3,4}, [Arjan B Te Pas](#)²

Affiliations expand

- PMID: 37080734
- DOI: [10.1136/archdischild-2022-324835](https://doi.org/10.1136/archdischild-2022-324835)

Abstract

Objective: Application of a face mask may provoke the trigeminocardiac reflex, leading to apnoea and bradycardia. This study investigates whether re-application of a face mask in preterm infants at birth alters the risk of apnoea compared with the initial application, and identify factors that influence this risk.

Methods: Resuscitation videos and respiratory function monitor data collected from preterm infants <30 weeks gestation between 2018 and 2020 were reviewed. Breathing and heart rate before and after the initial and subsequent mask applications were analysed.

Results: In total, 111 infants were included with 404 mask applications (102 initial and 302 subsequent mask applications). In 254/404 (63%) applications, infants were breathing prior to mask application, followed by apnoea after 67/254 (26%) mask applications. Apnoea and bradycardia occurred significantly more often after the initial mask application compared with subsequent applications (apnoea initial: 32/67 (48%) and subsequent: 44/187 (24%), $p < 0.001$; bradycardia initial: 61% and subsequent 21%, $p < 0.001$). Apnoea was followed by bradycardia in 73% and 71% of the initial and subsequent mask applications, respectively ($p = 0.607$). In a logistic regression model, a lower breathing rate (OR 0.908 (95% CI 0.847 to 0.974), $p = 0.007$) and heart rate (OR 0.935 (95% CI 0.901 to 0.970), $p < 0.001$) prior to mask application were associated with an increased likelihood of becoming apnoeic following subsequent mask applications.

Conclusion: In preterm infants at birth, apnoea and bradycardia occurs more often after an initial mask application than subsequent applications, with lower heart and breathing rates increasing the risk of apnoea in subsequent applications.

Keywords: neonatology; resuscitation.

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Conflict of interest statement

Competing interests: KLAMK is the recipient of an unrestricted research grant from Fisher & Paykel Healthcare.

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97

Arch Dis Child Fetal Neonatal Ed

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. 2023 Nov;108(6):562-568.

doi: 10.1136/archdischild-2022-324987. Epub 2023 Apr 20.

[Estimated neonatal survival of very preterm births across the care pathway: a UK cohort 2016–2020](#)

[Sarah E Seaton](#)¹, [Ridhi Agarwal](#)², [Elizabeth S Draper](#)¹, [Alan C Fenton](#)³, [Jennifer J Kurinczuk](#)⁴, [Bradley N Manktelow](#)¹, [Lucy K Smith](#)⁵

Affiliations expand

- PMID: 37080732
- DOI: [10.1136/archdischild-2022-324987](https://doi.org/10.1136/archdischild-2022-324987)

Abstract

Objective: Currently used estimates of survival are nearly 10 years old and relate to only those babies admitted for neonatal care. Due to ongoing improvements in neonatal care, here we update estimates of survival for singleton and multiple births at 22⁺⁰ to 31⁺⁶ weeks gestational age across the perinatal care pathway by gestational age and birth weight.

Design: Retrospective analysis of routinely collected data.

Setting: A national cohort from the UK and British Crown Dependencies.

Patients: Babies born at 22⁺⁰ to 31⁺⁶ weeks gestational age from 1 January 2016 to 31 December 2020.

Interventions: None.

Main outcome measures: Survival to 28 days.

Results: Estimates of neonatal survival are provided for babies: (1) alive at the onset of care during the birthing process (n=43 763); (2) babies where survival-focused care was initiated (n=42 004); and (3) babies admitted for neonatal care (n=41 158). We have produced easy-to-use survival charts for singleton and multiple births. Generally, survival increased with increasing gestational age at birth and with increasing birth weight. For all births with a birthweight over 1000 g, survival was 90% or higher at all three stages of care.

Conclusions: Survival estimates are a vital tool to support and supplement clinical judgement within perinatal care. These up-to-date, national estimates of survival to 28 days are provided based on three stages of the perinatal care pathway to support ongoing clinical care. These novel results are a key resource for policy and practice including counselling parents and informing care provision.

Keywords: Mortality; Neonatology.

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Conflict of interest statement

Competing interests: None declared.

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Eur J Prev Cardiol

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. 2023 Oct 26;30(15):1608-1611.

doi: 10.1093/eurjpc/zwad119.

[Air pollution, cardiovascular disease, and urban greening: an ecological blueprint](#)

[Pier Mannuccio Mannucci](#)¹

Affiliations expand

- PMID: 37070466
- DOI: [10.1093/eurjpc/zwad119](https://doi.org/10.1093/eurjpc/zwad119)

Abstract

A number of studies and systematic reviews indicate that exposure to greenness reduces of all-cause, non accidental mortality, particularly from cardiopulmonary and cancer causes. There is also some evidence that green space residence may be associated with

improved pregnancy and birth outcomes, and with better school performances in children. Furthermore, because at least one third of the premature deaths are globally attributable to exposure to air pollution due household agents, particularly in fragile populations living in low-income countries (i.e., children, older and deprived people, pregnant women), that houseplants are an effective and economic mean for cleaning indoor air and thus reducing volatile organic compounds such as formaldehyde, benzene, toluene and others. On the whole more prospective studies are needed to further elucidate the mechanisms linking air pollution, greenness and health outcomes, although the multiple and interacting mechanisms depicted in this article are all biologically plausible.

Keywords: Air quality guidelines; Green space; Greenness; Outdoor pollutants; PM2.5; Particulate matter.

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Conflict of interest statement

Conflict of interest: None declared.

- [Cited by 1 article](#)

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Dev Med Child Neurol

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. 2023 Nov;65(11):1501-1510.

doi: 10.1111/dmcn.15620. Epub 2023 Apr 15.

Motor performance and attention outcomes in children born very preterm

[Rebecca N Brown](#)^{1,2}, [Alice C Burnett](#)^{2,3,4}, [Deanne K Thompson](#)^{2,3,5}, [Alicia J Spittle](#)^{2,6,7}, [Rachel Ellis](#)², [Jeanie L Y Cheong](#)^{2,6,8}, [Lex W Doyle](#)^{2,3,6,8}, [Leona Pascoe](#)^{1,2}, [Peter J Anderson](#)^{1,2}

Affiliations expand

- PMID: 37060580
- DOI: [10.1111/dmcn.15620](https://doi.org/10.1111/dmcn.15620)

Abstract

Aim: To examine the relationship between motor performance and attention in children born very preterm and at term, and investigate the presence of individual profiles of motor and attention performance.

Method: Attention and motor performance at 7 and 13 years were assessed in 197 children born very preterm (52.5% male) and 69 children born at term (47.8% male) between 2001 and 2003. Linear regression models were fitted including an interaction term for birth group. Subgroups of children with similar attention and motor performance profiles were identified using latent profile analysis.

Results: Balance was positively associated with all attention outcomes at both ages ($p < 0.006$). There were specific birth group interactions for aiming and catching and manual dexterity with attention at 13 years, with positive associations observed only for children born very preterm ($p < 0.001$). At 7 years, three profiles were observed: average attention and motor functioning; average motor functioning and low attention functioning; and low attention and motor functioning. At 13 years, two profiles of average attention and motor functioning emerged, as well as one profile of below-average attention and motor functioning. Children born very preterm were overrepresented in the lower functioning profiles (born very preterm 56%; born at term 29%).

Interpretation: Motor functioning at age 7 years may be a useful marker of later attention skills, particularly for children born very preterm who are at greater risk of poorer long-term cognitive outcomes.

What this paper adds: Balance was positively associated with attention in children born very preterm and at term. Relationships between motor performance and attention at age 13 years differed between children born very preterm and at term. Heterogeneous motor functioning and attention outcomes were noted for children born very preterm and at

term. Children born very preterm were more likely to have lower attention and motor functioning profiles than children born at term. There was greater movement in motor functioning and attention profiles between the ages of 7 and 13 years in children born very preterm.

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- [34 references](#)

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Publication types, MeSH termsexpand

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Pediatr Res

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. 2023 Nov;94(5):1707-1713.

doi: 10.1038/s41390-023-02597-z. Epub 2023 Apr 12.

[Functional morphometry: non-invasive estimation of the alveolar surface area in extremely preterm infants](#)

[Emma E Williams](#)¹, [J Gareth Jones](#)², [Donald McCurnin](#)³, [Mario Rüdiger](#)^{4,5}, [Mahesh Nanjundappa](#)⁶, [Anne Greenough](#)^{1,7}, [Theodore Dassios](#)^{8,9}

Affiliations expand

- PMID: 37045946
- PMCID: [PMC10624622](#)
- DOI: [10.1038/s41390-023-02597-z](#)

Free PMC article

Abstract

Background: The main pathophysiologic characteristic of chronic respiratory disease following extremely premature birth is arrested alveolar growth, which translates to a smaller alveolar surface area (S_A). We aimed to use non-invasive measurements to estimate the S_A in extremely preterm infants.

Methods: Paired measurements of the fraction of inspired oxygen and transcutaneous oxygen saturation were used to calculate the ventilation/perfusion ratio, which was translated to S_A using Fick's law of diffusion. The S_A was then adjusted using volumetric capnography.

Results: Thirty infants with a median (range) gestational age of 26.3 (22.9-27.9) weeks were studied. The median (range) adjusted S_A was 647.9 (316.4-902.7) cm^2 . The adjusted S_A was lower in the infants who required home oxygen [637.7 (323.5-837.5) cm^2] compared to those who did not [799.1 (444.2-902.7) cm^2 , $p = 0.016$]. In predicting the need for supplemental home oxygen, the adjusted S_A had an area under the receiver operator characteristic curve of 0.815 ($p = 0.017$). An adjusted $S_A \geq 688.6 \text{ cm}^2$ had 86% sensitivity and 77% specificity in predicting the need for supplemental home oxygen.

Conclusions: The alveolar surface area can be estimated non-invasively in extremely preterm infants. The adjusted alveolar surface area has the potential to predict the subsequent need for discharge home on supplemental oxygen.

Impact: We describe a novel biomarker of respiratory disease following extremely preterm birth. The adjusted alveolar surface area index was derived by non-invasive measurements of the ventilation/perfusion ratio and adjusted by concurrent measurements of volumetric capnography. The adjusted alveolar surface area was markedly reduced in extremely preterm infants studied at 7 days of life and could predict the need for discharge home on supplemental oxygen. This method could be used at the bedside to estimate the alveolar surface area and provide an index of the severity of lung disease, and assist in monitoring, clinical management and prognosis.

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Conflict of interest statement

The authors declare no competing interests.

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

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Arch Dis Child Fetal Neonatal Ed

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. 2023 Nov;108(6):581-587.

doi: 10.1136/archdischild-2022-325230. Epub 2023 Mar 30.

[Health-related quality of life in adults born extremely preterm or with extremely low birth weight in the postsurfactant era: a longitudinal cohort study](#)

[Christopher Selman](#)¹, [Rheanna Mainzer](#)², [Katherine Lee](#)^{2,3}, [Peter Anderson](#)^{4,5}, [Alice Burnett](#)^{3,4,6}, [Suzanne M Garland](#)^{7,8,9}, [George C Patton](#)^{3,10}, [Lauren Pigdon](#)^{4,11}, [Gehan Roberts](#)^{3,12,13}, [John Wark](#)^{14,15}, [Lex W Doyle](#)^{3,4,6,7}, [Jeanie Ling Yoong Cheong](#)^{4,7,11}; [Victorian Infant Collaborative Study Group](#)

Collaborators, Affiliations expand

- PMID: 36997308
- DOI: [10.1136/archdischild-2022-325230](https://doi.org/10.1136/archdischild-2022-325230)

Abstract

Objectives: To compare health-related quality of life (HRQoL) at 25 and 18 years in individuals born extremely preterm (EP, <28 weeks' gestation) or with extremely low birth weight (ELBW, birth weight <1000 g) with term-born (≥ 37 weeks) controls. Within the EP/ELBW cohort, to determine whether HRQoL differed between those with lower and higher IQs.

Methods: HRQoL was self-reported using the Health Utilities Index Mark 3 (HUI3) at 18 and 25 years by 297 EP/ELBW and 251 controls born in 1991-1992 in Victoria, Australia. Median differences (MDs) between groups were estimated using multiple imputation to handle missing data.

Results: Adults born EP/ELBW had lower HRQoL (median utility 0.89) at 25 years than controls (median utility 0.93, MD -0.040), but with substantial uncertainty in the estimate (95% CI -0.088 to 0.008) and a smaller reduction at 18 years (MD -0.016, 95% CI -0.061 to 0.029). On individual HUI3 items, there was suboptimal performance on speech (OR 9.28, 95% CI 3.09 to 27.93) and dexterity (OR 5.44, 95% CI 1.04 to 28.45) in the EP/ELBW cohort. Within the EP/ELBW cohort, individuals with lower IQ had lower HRQoL compared with those with higher IQ at 25 (MD -0.031, 95% CI -0.126 to 0.064) and 18 years (MD -0.034, 95% CI -0.107 to 0.040), but again with substantial uncertainty in the estimates.

Conclusions: Compared with term-born controls, young adults born EP/ELBW reported poorer HRQoL, as did those with lower IQ compared with those with higher IQ in the EP/ELBW cohort. Given the uncertainties, our findings need corroboration.

Keywords: Child Health; Neonatology; Statistics.

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Conflict of interest statement

Competing interests: None declared.

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Arch Dis Child Fetal Neonatal Ed

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. 2023 Nov;108(6):575-580.

doi: 10.1136/archdischild-2022-325011. Epub 2023 Mar 30.

[Fragility and resilience: parental and family perspectives on the impacts of extreme prematurity](#)

[Annie Janvier](#)^{1,2}, [Claude Julie Bourque](#)^{3,4}, [Rebecca Pearce](#)⁵, [Emilie Thivierge](#)⁶, [Laurie-Anne Duquette](#)⁷, [Magdalena Jaworski](#)^{6,8}, [Keith J Barrington](#)^{9,10}, [Anne R Synnes](#)¹¹, [Paige Church](#)¹², [Thuy Mai Luu](#)^{10,13}

Affiliations expand

- PMID: 36997307
- DOI: [10.1136/archdischild-2022-325011](https://doi.org/10.1136/archdischild-2022-325011)

Abstract

Objectives: Extremely preterm babies have a significant risk of neurodevelopmental impairment (NDI). There has been little investigation regarding the impact of prematurity on families. The objective of this study was to explore parental perspectives regarding the impact of prematurity on themselves/their family.

Methods: Over 1 year, parents of children born <29 weeks' gestational age (GA) who were between 18 months old and 7 years old and came for their follow-up visit were invited to participate. They were asked to categorise the impacts of prematurity on their life and their family as positive, negative or both and to describe those impacts in their own words. Thematic analysis was performed by a multidisciplinary group, including parents. Logistic regression was performed to compare parental responses.

Results: Among parents (n=248, 98% participation rate), most (74%) reported that their child's prematurity had both positive and negative impacts on their life or their family's life, while 18% reported only positive impacts and 8% only negative impacts. These proportions were not correlated with GA, brain injury, nor level of NDI. The positive impacts reported included: an improved outlook on life, such as gratitude and perspective (48%), stronger family relationships (31%) and the gift of the child (28%). The negative themes were stress and fear (42%), loss of equilibrium due to medical fragility (35%) and concerns about developmental outcomes including the child's future (18%).

Conclusion: Parents report both positive and negative impacts after an extremely preterm birth, independent of disability. These balanced perspectives should be included in neonatal research, clinical care and provider education.

Keywords: child development; ethics; infant development; intensive care units, neonatal; neonatology.

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Conflict of interest statement

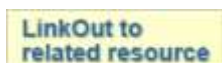
Competing interests: None declared.

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Randomized Controlled Trial

Indian J Pediatr

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. 2023 Nov;90(11):1103-1109.

doi: 10.1007/s12098-023-04489-w. Epub 2023 Mar 23.

Cardiopulmonary Ultrasound-Guided Treatment of Premature Infants with Respiratory Failure and Patent Ductus Arteriosus: A Randomized, Controlled Trial

[Zhiqun Zhang](#)^{1,2}, [Xinrui Lou](#)³, [Luyi Hua](#)³, [Xinhui Jia](#)³, [Lili Xu](#)⁴, [Min Zhao](#)⁵

Affiliations expand

- PMID: 36952111
- DOI: [10.1007/s12098-023-04489-w](https://doi.org/10.1007/s12098-023-04489-w)

Abstract

Objectives: To evaluate the role of cardiopulmonary ultrasonography in the treatment of preterm infants with respiratory failure combined with patent ductus arteriosus (PDA).

Methods: A single-center, prospective, randomized, controlled trial of premature infants born in the authors' hospital with a birth weight ≤ 1500 g and respiratory failure combined with PDA was conducted from January 2020 to December 2021. The included infants were randomly assigned to the cardiopulmonary ultrasound-guided therapy group or the traditional therapy group. The primary outcome of this study was data on respiratory support and PDA.

Results: A total of 76 premature infants were included in the study. There were 39 patients in the cardiopulmonary ultrasound-guided therapy group and 37 patients in the traditional therapy group. There was no difference in the baseline data, and the cardiopulmonary ultrasound-guided therapy group had a higher initial positive end-expiratory pressure [difference in median = -1.5 cm H₂O, 95% confidence interval (CI): -2.0 to -1.0, p < 0.0001], earlier use of ibuprofen to close the PDA (difference in median = 2.5 d, 95% CI: 1.0-4.0, p = 0.004), fewer patients requiring invasive respiratory support [risk ratio (RR) = 0.63, 95% CI: 0.41-0.99, p = 0.04], and a lower incidence of moderate to severe bronchopulmonary dysplasia (RR = 0.44, 95% CI: 0.44-0.96, p = 0.04). There was no difference in the incidence of adverse events.

Conclusions: For premature infants with respiratory failure combined with PDA, cardiopulmonary ultrasonography can better guide respiratory support. The timely administration of drugs helps treat PDA, thereby decreasing the risk of intubation and BPD.

Trial registration: <https://www.trials.com/index/> , TRN: 20220420024607012, date of registration: 2022/03/28, retrospectively registered.

Keywords: Cardiopulmonary ultrasound; Patent ductus arteriosus; Preterm infants; Respiratory failure.

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Clin Pediatr (Phila)

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. 2023 Nov;62(11):1375-1379.

doi: 10.1177/00099228231158367. Epub 2023 Mar 15.

Improving Birth Outcomes Among Low-Income Families: The Effect of a Home Visiting Intervention

[Sunny H Shin](#)^{1,2}, [Changyong Choi](#)³

Affiliations expand

- PMID: 36919818
- DOI: [10.1177/00099228231158367](https://doi.org/10.1177/00099228231158367)

Abstract

The American Academy of Pediatrics (AAP) recognizes the benefit of home visiting programs in promoting positive birth outcomes. Despite this recommendation, previous studies have found mixed results with respect to the impact of home visits on birth outcomes. We evaluated the impact of the Comprehensive Health Investment Project (CHIP) home visiting services on improving birth outcomes among low-income families. The present study used a sample of 1,110 children and families to examine how a team-based home visiting program influenced 2 significant birth outcomes, namely, birth weight and preterm birth. Using propensity score matching, the current study found that the home visited group had significantly lower rates of low birth weight compared with a propensity-matched comparison group ($P < .01$). Home visiting programs may play an important role in promoting positive birth outcomes, particularly when they are provided during pregnancy.

Keywords: PRAMS; birth outcomes; birth weight; home visiting.

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

Publication types, MeSH termsexpand

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Am J Pathol

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. 2023 Nov;193(11):1776-1788.

doi: 10.1016/j.ajpath.2023.02.003. Epub 2023 Feb 21.

[Placental Inflammation Significantly Correlates with Reduced Risk for Retinopathy of Prematurity](#)

[Leah A Owen](#)¹, [Charles Zhang](#)², [Kinsey Shirer](#)³, [Lara Carroll](#)⁴, [Blair Wood](#)⁵, [Kathryn Szczotka](#)⁶, [Colette Cornia](#)⁷, [Christopher Stubben](#)⁸, [Camille Fung](#)⁹, [Christian C Yost](#)⁹, [Lakshmi D Katikaneni](#)¹⁰, [Margaret M DeAngelis](#)¹¹, [Jessica Comstock](#)¹²

Affiliations expand

- PMID: 36822266
- PMID: PMC10616712 (available on 2024-11-01)
- DOI: [10.1016/j.ajpath.2023.02.003](https://doi.org/10.1016/j.ajpath.2023.02.003)

Abstract

Retinopathy of prematurity (ROP), a blinding condition affecting preterm infants, is an interruption of retinal vascular maturation that is incomplete when born preterm. Although

ROP demonstrates delayed onset following preterm birth, representing a window for therapeutic intervention, there are no curative or preventative measures available for this condition. The in utero environment, including placental function, is increasingly recognized for contributions to preterm infant disease risk. The current study identified a protective association between acute placental inflammation and preterm infant ROP development using logistic regression, with the most significant association found for infants without gestational exposure to maternal preeclampsia and those with earlier preterm birth. Expression analysis of proteins with described ROP risk associations demonstrated significantly decreased placental high temperature requirement A serine peptidase-1 (HTRA-1) and fatty acid binding protein 4 protein expression in infants with acute placental inflammation compared with those without. Within the postnatal peripheral circulation, HTRA-1 and vascular endothelial growth factor-A demonstrated inverse longitudinal trends for infants born in the presence of, compared with absence of, acute placental inflammation. An agnostic approach, including whole transcriptome and differential methylation placental analysis, further identify novel mediators and pathways that may underly protection. Taken together, these data build on emerging literature showing a protective association between acute placental inflammation and ROP development and identify novel mechanisms that may inform postnatal risk associations in preterm infants.

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- [Cited by 1 article](#)
- [48 references](#)

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[Review](#)

Am J Pathol



. 2023 Nov;193(11):1683-1690.

doi: 10.1016/j.ajpath.2023.01.013. Epub 2023 Feb 11.

Gut Microbiome and Retinopathy of Prematurity

[Jason Y Zhang](#)¹, [Mark J Greenwald](#)², [Sarah H Rodriguez](#)³

Affiliations expand

- PMID: 36780985
- DOI: [10.1016/j.ajpath.2023.01.013](https://doi.org/10.1016/j.ajpath.2023.01.013)

Abstract

Retinopathy of prematurity (ROP), a leading cause of childhood blindness worldwide, is strongly associated with gestational age and weight at birth. Yet, many extremely preterm infants never develop ROP or develop only mild ROP with spontaneous regression. In addition, a myriad of other factors play a role in the retinal pathology, one of which may include the early gut microbiome. The complications associated with early gestational age include dysbiosis of the dynamic neonatal gut microbiome, as evidenced by the development of often concomitant conditions, such as necrotizing enterocolitis. Given this, alongside growing evidence for a gut-retina axis, there is an increasing interest in how the early intestinal environment may play a role in the pathophysiology of ROP. Potential mechanisms include dysregulation of vascular endothelial growth factor and insulin-like growth factor 1. Furthermore, the gut microbiome may be impacted by other known risk factors for ROP, such as intermittent hypoxia and sepsis treated with antibiotics. This mini-review summarizes the literature supporting these proposed avenues, establishing a foundation to guide future studies.

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Review

Br J Nutr

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. 2023 Oct 28;130(8):1338-1342.

doi: 10.1017/S0007114523000338. Epub 2023 Feb 9.

[Are the current feeding volumes adequate for the growth of very preterm neonates?](#)

[Chrysoula Kosmeri](#)¹, [Vasileios Giapros](#)², [Antonios Gounaris](#)³, [Rozeta Sokou](#)⁴, [Ekaterini Siomou](#)¹, [Dimitrios Rallis](#)², [Alexandros Makis](#)¹, [Maria Baltogianni](#)²

Affiliations expand

- PMID: 36756759
- PMCID: [PMC10511681](#)
- DOI: [10.1017/S0007114523000338](#)

Free PMC article

Abstract

Postnatal growth failure, a common problem in very preterm neonates associated with adverse neurodevelopmental outcome, has recently been shown not to be inevitable. There is a wide discussion regarding feeding practices of very preterm neonates, specifically regarding feeding volumes and nutrients supply to avoid postnatal growth failure. Current guidelines recommend an energy intake of 115–140 kcal/kg per d with a considerably higher upper limit of 160 kcal/kg per d. The feeding volume corresponding to this energy supply is not higher than 200 ml/kg in most cases. From the other side, randomised and observational studies used higher feeding volumes, and these were associated with better weight gain and growth, while no complications were noted. Taking into account the above, nutritional practices should be individualised in each very and extremely preterm infant trying to reduce postnatal growth failure, pointing out that available data are inconclusive regarding the effect of high-volume feeds on growth. Large clinical trials are necessary to conclude in the best feeding practices of very preterm neonates.

Keywords: Feeding volume; Nutrition; Postnatal growth failure; Very preterm neonate.

- [Cited by 2 articles](#)
- [40 references](#)
- [1 figure](#)

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Publication types, MeSH termsexpand

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Perspect Psychol Sci

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. 2023 Nov;18(6):1271-1281.

doi: 10.1177/17456916231151584. Epub 2023 Feb 8.

Does Electrophysiological Maturation Shape Language Acquisition?

[Katharina H Menn](#)^{1,2,3}, [Claudia Männel](#)^{2,4}, [Lars Meyer](#)^{1,5}

Affiliations expand

- PMID: 36753616
- PMCID: [PMC10623610](#)
- DOI: [10.1177/17456916231151584](#)

Free PMC article

Abstract

Infants master temporal patterns of their native language at a developmental trajectory from slow to fast: Shortly after birth, they recognize the slow acoustic modulations specific to their native language before tuning into faster language-specific patterns between 6 and 12 months of age. We propose here that this trajectory is constrained by neuronal maturation—in particular, the gradual emergence of high-frequency neural oscillations in the infant electroencephalogram. Infants' initial focus on slow prosodic modulations is consistent with the prenatal availability of slow electrophysiological activity (i.e., theta- and delta-band oscillations). Our proposal is consistent with the temporal patterns of infant-directed speech, which initially amplifies slow modulations, approaching the faster modulation range of adult-directed speech only as infants' language has advanced sufficiently. Moreover, our proposal agrees with evidence from premature infants showing maturational age is a stronger predictor of language development than ex utero exposure to speech, indicating that premature infants cannot exploit their earlier availability of speech because of electrophysiological constraints. In sum, we provide a new perspective on language acquisition emphasizing neuronal development as a critical driving force of infants' language development.

Keywords: infant-directed speech; neural development; oscillations; temporal speech patterns.

Conflict of interest statement

The author(s) declared that there were no conflicts of interest with respect to the authorship or the publication of this article.

Update of

- doi: [10.31234/osf.io/y8xj5](https://doi.org/10.31234/osf.io/y8xj5)
- [112 references](#)
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Arch Gynecol Obstet

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. 2023 Nov;308(5):1447-1456.

doi: 10.1007/s00404-022-06753-4. Epub 2022 Sep 13.

[Wearable sensors for prediction of intraamniotic infection in women with preterm premature rupture of](#)

membranes: a prospective proof of principle study

[Romana Brun](#)¹, [Julia Girsberger](#)^{2,3}, [Martina Rothenbühler](#)⁴, [Catrin Argyle](#)⁴, [Juliane Hutmacher](#)⁵, [Christian Haslinger](#)⁶, [Brigitte Leeners](#)^{2,3}

Affiliations expand

- PMID: 36098832
- PMCID: [PMC9469066](#)
- DOI: [10.1007/s00404-022-06753-4](#)

Free PMC article

Abstract

Purpose: To evaluate the use of wearable sensors for prediction of intraamniotic infection in pregnant women with PPRM.

Materials and methods: In a prospective proof of principle study, we included 50 patients diagnosed with PPRM at the University Hospital Zurich between November 2017 and May 2020. Patients were instructed to wear a bracelet during the night, which measures physiological parameters including wrist skin temperature, heart rate, heart rate variability, and breathing rate. A two-way repeated measures ANOVA was performed to evaluate the difference over time of both the wearable device measured parameters and standard clinical monitoring values, such as body temperature, pulse, leucocytes, and C-reactive protein, between women with and without intraamniotic infection.

Results: Altogether, 23 patients (46%) were diagnosed with intraamniotic infection. Regarding the physiological parameters measured with the bracelet, we observed a significant difference in breathing rate (19 vs 16 per min, $P < .01$) and heart rate (72 vs 67 beats per min, $P = .03$) in women with intraamniotic infection compared to those without during the 3 days prior to birth. In parallel to these changes standard clinical monitoring values were significantly different in the intraamniotic infection group compared to women without infection in the 3 days preceding birth.

Conclusion: Our results suggest that wearable sensors are a promising, noninvasive, patient friendly approach to support the early detection of intraamniotic infection in

women with PPRM. However, confirmation of our findings in larger studies is required before implementing this technique in standard clinical management.

Keywords: Intraamniotic infection; Photoplethysmography; Preterm premature rupture of membranes; Wearable sensor.

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Conflict of interest statement

MR and CA were employees at Ava AG during the study time. BL serves on the Ava AG medical advisory board. All the other authors do not state any conflict of interest.

- [Cited by 2 articles](#)
- [46 references](#)
- [2 figures](#)

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Publication types, MeSH terms, Supplementary conceptsexpand

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Eur Child Adolesc Psychiatry

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. 2023 Nov;32(11):2291-2301.

doi: 10.1007/s00787-022-02073-9. Epub 2022 Sep 3.

Temperamental and psychomotor predictors of ADHD symptoms in

children born after a threatened preterm labour: a 6-year follow-up study

[Pablo Navalón](#)^{#1,2}, [Farah Ghosn](#)^{#1,3}, [Maite Ferrín](#)^{4,5}, [Belén Almansa](#)^{1,3}, [Alba Moreno-Giménez](#)^{1,3}, [Laura Campos-Berga](#)^{1,2}, [Rosa Sahuquillo-Leal](#)³, [Vicente Diago](#)⁶, [Máximo Vento](#)^{1,7}, [Ana García-Blanco](#)^{8,9,10}

Affiliations expand

- PMID: 36056973
- PMCID: [PMC10576661](#)
- DOI: [10.1007/s00787-022-02073-9](#)

Free PMC article

Abstract

Children born after threatened preterm labour (TPL), regardless of whether it ends in preterm birth, may represent an undescribed "ADHD cluster". The aim of this cohort study is to identify early temperament and psychomotor manifestations and risk factors of TPL children who present ADHD symptoms. One hundred and seventeen mother-child pairs were followed from TPL diagnosis until the child's 6 years of life. TPL children were divided according to the prematurity status into three groups: full-term TPL (n = 26), late-preterm TPL (n = 53), and very-preterm TPL (n = 38). A non-TPL group (n = 50) served as control. Temperament and psychomotor development at age 6 months and ADHD symptoms at age 6 years were assessed. Perinatal and psychosocial factors were also recorded. All TPL groups showed higher severity of ADHD symptoms compared with non-TPL children (difference in means + 4.19 for the full-term group, + 3.64 for the late-preterm group, and + 4.99 for the very-preterm group, all p s < 0.021). Concretely, very-preterm and late-preterm TPL children showed higher restless/impulsive behaviours, whereas full-term TPL children showed higher emotional lability behaviours. Higher surgency/extraversion and delayed fine motor skills at age 6 months predicted ADHD symptoms at 6 years in TPL children. Male sex, maternal state anxiety symptoms at TPL diagnosis, low parental education, and past maternal experience of traumatic events predicted higher ADHD symptoms in TPL children. Therefore, TPL children may have a higher risk for developing ADHD symptoms, presenting a phenotype that depends on the prematurity status.

Moreover, the specific combination of early manifestations and risk factors suggests that TPL children may conform an undescribed group at-risk of ADHD symptoms.

Keywords: ADHD; Neurodevelopmental disorders; Pregnancy; Psychomotor development; Trauma.

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Conflict of interest statement

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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

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

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Popul Stud (Camb)

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. 2023 Nov;77(3):459-474.

doi: 10.1080/00324728.2022.2080247. Epub 2022 Jun 7.

Preterm birth and educational disadvantage: Heterogeneous effects

[Anna Baranowska-Rataj](#)¹, [Kieron Barclay](#)^{2,3,4}, [Joan Costa-Font](#)³, [Mikko Myrskylä](#)^{2,3,5}, [Berkay Özcan](#)³

Affiliations expand

- PMID: 35670431
- DOI: [10.1080/00324728.2022.2080247](https://doi.org/10.1080/00324728.2022.2080247)

Abstract

Although preterm birth is the leading cause of perinatal morbidity and mortality in advanced economies, evidence about the consequences of prematurity in later life is limited. Using Swedish registers for cohorts born 1982-94 ($N = 1,087,750$), we examine the effects of preterm birth on school grades at age 16 using sibling fixed effects models. We further examine how school grades are affected by degree of prematurity and the compensating roles of family socio-economic resources and characteristics of school districts. Our results show that the negative effects of preterm birth are observed mostly among children born extremely preterm (<28 weeks); children born moderately preterm (32-<37 weeks) suffer no ill effects. We do not find any evidence for a moderating effect of parental socio-economic resources. Children born extremely preterm and in the top decile of school districts achieve as good grades as children born at full term in an average school district. Supplementary material for this article is available at: <http://dx.doi.org/10.1080/00324728.2022.2080247>.

Keywords: educational disadvantage; gestational age; parental effects; premature births; register-based research; school districts; sibling models.

SUPPLEMENTARY INFO

MeSH termsexpand

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Am J Perinatol

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. 2023 Nov;40(15):1695-1703.

doi: 10.1055/s-0041-1740010. Epub 2021 Dec 14.

[A Comparison of Vaginal and Intramuscular Progesterone for the Prevention of Recurrent Preterm Birth](#)

[Heather A Frey](#)¹, [Matthew M Finneran](#)², [Erinn M Hade](#)^{1,3}, [Colleen Waickman](#)¹, [Courtney D Lynch](#)¹, [Jay D Iams](#)¹, [Mark B Landon](#)¹

Affiliations expand

- PMID: 34905780
- DOI: [10.1055/s-0041-1740010](https://doi.org/10.1055/s-0041-1740010)

Abstract

Objective: This study aimed to examine whether vaginal progesterone is noninferior to 17- α hydroxyprogesterone caproate (17OHP-C) in the prevention of recurrent preterm birth (PTB).

Study design: This retrospective cohort study included singleton pregnancies among women with a history of spontaneous PTB who received prenatal care at a single tertiary center from 2011 to 2016. Pregnancies were excluded if progesterone was not initiated prior to 24 weeks or the fetus had a major congenital anomaly. The primary outcome was PTB <37 weeks. A priori, noninferiority was to be established if the upper bound of the adjusted two-sided 90% confidence interval (CI) for the difference in PTB fell below 9%. Inverse probability of treatment weighting (IPTW) was used to carefully control for confounding associated with choice of treatment and PTB. Adjusted differences in PTB proportions were estimated via IPTW regression, with standard errors adjustment for multiple pregnancies per woman. Secondary outcomes included PTB <34 and <28 weeks, spontaneous PTB, neonatal intensive care unit admission, and gestational age at delivery.

Results: Among 858 pregnancies, 41% ($n = 353$) received vaginal progesterone and 59% ($n = 505$) were given 17OHP-C. Vaginal progesterone use was more common later in the study period, and among women who established prenatal care later, had prior PTBs at later gestational ages, and whose race/ethnicity was neither non-Hispanic white nor non-Hispanic Black. Vaginal progesterone did not meet noninferiority criteria compared with

17-OHPC in examining PTB <37 weeks, with an IPTW adjusted difference of 3.4% (90% CI: -3.5, 10.3). For secondary outcomes, IPTW adjusted differences between treatment groups were generally small and CIs were wide.

Conclusion: We could not conclude noninferiority of vaginal progesterone to 17OHP-C; however, women and providers may be willing to accept a larger difference (>9%) when considering the cost and availability of vaginal progesterone versus 17OHP-C. A well-designed randomized trial is needed.

Key points: · Vaginal progesterone is not noninferior to 17OHP-C.. · PTB risk may be 10% higher with vaginal progesterone.. · Associations did not differ based on obesity status..

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Conflict of interest statement

None declared.

- [Cited by 1 article](#)

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Am J Perinatol

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. 2023 Nov;40(15):1659-1664.

doi: 10.1055/s-0041-1739413. Epub 2021 Dec 10.

The Impact of Group Prenatal Care on Interpregnancy Interval

[Justine M Keller¹](#), [Jessica A Norton²](#), [Fan Zhang¹](#), [Rachel Paul¹](#), [Tessa Madden¹](#), [Nandini Raghuraman¹](#), [Molly J Stout³](#), [Ebony B Carter¹](#)

Affiliations expand

- PMID: 34891199
- DOI: [10.1055/s-0041-1739413](https://doi.org/10.1055/s-0041-1739413)

Abstract

Objective: To evaluate whether participation in CenteringPregnancy group prenatal care is associated with decreased risk of an interpregnancy interval (IPI) ≤ 6 months.

Study design: We conducted a retrospective cohort study of women enrolled in Missouri Medicaid from 2007 to 2014 using maternal Medicaid data linked to infant birth certificate records. Inclusion criteria were women ≥ 11 years old, ≥ 1 viable singleton delivery during the study period, residency in St. Louis city or county, and ≥ 2 prenatal visits. The primary outcome was an IPI ≤ 6 months. Secondary outcomes included IPI ≤ 12 months, IPI ≤ 18 months, postpartum long-acting reversible contraception (LARC) uptake, and postpartum LARC or depot medroxyprogesterone acetate (DMPA) uptake. Data were analyzed using descriptive statistics and logistic regression. Backward stepwise logistic regression was used to adjust for potential confounders including maternal age, race, obesity, nulliparity, marital status, diabetes, hypertension, prior preterm birth, and maternal education.

Results: Of the 54,968 pregnancies meeting inclusion criteria, 1,550 (3%) participated in CenteringPregnancy. CenteringPregnancy participants were less likely to have an IPI ≤ 6 months (adjusted odds ratio [aOR]: 0.61; 95% confidence interval [CI]: 0.47-0.79) and an IPI ≤ 12 months (aOR: 0.74; 95% CI: 0.62-0.87). However, there was no difference for an IPI ≤ 18 months (aOR: 0.89; 95% CI: 0.77-1.13). Women in CenteringPregnancy were more likely to use LARC for postpartum contraception (aOR: 1.37; 95% CI: 1.20-1.57).

Conclusion: Participation in CenteringPregnancy is associated with a significant decrease in an IPI ≤ 6 and ≤ 12 months and a significant increase in postpartum LARC uptake among women enrolled in Missouri Medicaid compared with women in traditional prenatal care.

Key points: · CenteringPregnancy is associated with a significant decrease in interpregnancy intervals ≤ 6 and ≤ 12 months.. · LARC uptake is significantly higher among

patients participating in CenteringPregnancy.. · CenteringPregnancy participation enhances self-efficacy in making contraception decisions and promotes healthy pregnancy spacing..

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Conflict of interest statement

None declared.

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. 2023 Nov;40(15):1715-1724.

doi: 10.1055/s-0041-1740177. Epub 2021 Nov 28.

Neonatal Outcomes of Premature Infants Born to Women with the Novel Coronavirus (SARS-CoV-2) Infection: A Case Control Study

[Beril Yasa](#)¹, [Seyma Memur](#)¹, [Dilek Y Ozturk](#)¹, [Onur Bagci](#)¹, [Sait I Uslu](#)¹, [Merih Cetinkaya](#)¹

Affiliations expand

- PMID: 34839474
- DOI: [10.1055/s-0041-1740177](https://doi.org/10.1055/s-0041-1740177)

Abstract

Objective: Novel coronavirus disease 2019 (COVID-19) is a disease associated with atypical pneumonia caused by the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2). The first cases of COVID-19 were reported in Wuhan at the end of 2019. Transmission usually occurs via infected droplets and close personal contact; the possibility of vertical transmission is still under debate. This retrospective study aimed to analyze clinical characteristics of premature infants born to mothers with symptomatic COVID-19 disease.

Study design: This case control study compared the clinical and laboratory data of 20 premature infants born to mothers infected with SARS-CoV-2 with sex and gestational age-matched historical controls.

Results: The median gestational age and birth weight in both groups were similar. Respiratory distress developed in 11 (55.5%) infants in study group and 19 (47.5%) infants in control group. Mechanical ventilation and endotracheal surfactant administration rates were similar. Median duration of hospitalization was 8.5 (2-76) days in study group and 12 days in historical controls. Real-time reverse-transcription polymerase chain reaction tests (RT-PCR) of nasopharyngeal swab samples for SARS-CoV-2 were found to be negative twice, in the first 24 hours and later at 24 to 48 hours of life. No neutropenia or thrombocytopenia was detected in the study group. Patent ductus arteriosus, bronchopulmonary dysplasia, and necrotizing enterocolitis rates were similar between groups. No mortality was observed in both groups.

Conclusion: To the best of our knowledge, this is one of the few studies evaluating the clinical outcomes of premature infants born to SARS-CoV-2 infected mothers. There was no evidence of vertical transmission of SARS-CoV-2 from symptomatic SARS-CoV-2-infected women to the neonate in our cohort. The neonatal outcomes also seem to be favorable with no mortality in preterm infants.

Key points: · SARS-CoV-2 pandemic is a challenge for pregnant women.. · Neonatal outcomes of premature infants born to mothers infected with SARS-CoV-2 not well defined.. · SARS-CoV-2 infection seems to have no adverse effect on mortality and morbidity in premature infants..

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Conflict of interest statement

None declared.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS



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

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Review

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. 2023 Nov 2:S0761-8425(23)00261-9.

doi: 10.1016/j.rmr.2023.09.006. Online ahead of print.

[\[Bronchial diseases and heroin use. A systematic review\]](#)

[Article in French]

[M Underner](#)¹, [J Perriot](#)², [G Peiffer](#)³, [G Brousse](#)⁴, [N Jaafari](#)⁵

Affiliations expand

- PMID: 37925326
- DOI: [10.1016/j.rmr.2023.09.006](https://doi.org/10.1016/j.rmr.2023.09.006)

Abstract

Introduction: Heroin use can cause respiratory complications including asthma, chronic obstructive pulmonary disease (COPD) and bronchiectasis (BD).

Objectives: A general review of the literature presenting the data on the relationships between heroin consumption and bronchial complications, while underlining the difficulties of diagnosis and management.

Documentary sources: Medline, 1980-2022, keywords "asthma" or "bronchospasm" or "COPD" or "bronchiectasis" and "heroin" or "opiate" or "opiates", with limits pertaining to "Title/Abstract". Concerning asthma, 26 studies were included, as were 16 for COPD and 5 for BD.

Results: Asthma and COPD are more prevalent among heroin addicts, who are less compliant than other patients with their treatment. The authors found a positive association between frequency of asthma exacerbations, admission to intensive care and heroin inhalation. Late diagnosis of COPD worsens the course of the disease; emphysema and BD are poor prognostic factors.

Conclusion: Bronchial diseases in heroin users can be identified by means of respiratory function exploration and chest CT scans. These tests should be performed frequently in view of optimizing their care, which includes their weaning themselves from addictive substances.

Keywords: Asthma; Asthme; BPCO; Bronchectasies; Bronchiectasis; COPD; Emphysema; Emphysème; Heroin; Héroïne; Opiacés; Opiates.

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Chest

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. 2023 Nov 2:S0012-3692(23)05695-7.

doi: 10.1016/j.chest.2023.10.046. Online ahead of print.

Clinical response and remission in severe asthma patients treated with biologic therapies

[Susanne Hansen](#)¹, [Marianne Søndergaard](#)², [Anna von Bülow](#)², [Anne-Sofie Bjerrum](#)³, [Johannes Schmid](#)³, [Linda M Rasmussen](#)⁴, [Claus R Johnsen](#)⁴, [Truls Ingebrigtsen](#)⁵, [Kjell Erik Julius Håkansson](#)⁶, [Sofie Lock Johansson](#)⁷, [Maria Bisgaard](#)⁷, [Karin Dahl Assing](#)⁸, [Ole Hilberg](#)⁹, [Charlotte Ulrik](#)⁶, [Celeste Porsbjerg](#)¹⁰

Affiliations expand

- PMID: 37925144
- DOI: [10.1016/j.chest.2023.10.046](https://doi.org/10.1016/j.chest.2023.10.046)

Abstract

Background: The development of novel targeted biologic therapies for severe asthma has provided an opportunity to consider remission as a new treatment goal.

Research question: How many severe asthma patients treated with biologic therapy achieve clinical remission, and what predicts response to treatment?

Study design and methods: The Danish Severe Asthma Registry is a nationwide register including all adult patients receiving biologic therapy for severe asthma in Denmark. We conducted an observational cohort study and defined "clinical response" to treatment after 12 months as $\geq 50\%$ reduction in exacerbations, and/or a $\geq 50\%$ reduction in maintenance oral corticosteroid dose, if required. "Clinical remission" was defined by cessation of exacerbations and maintenance OCS, as well as a normalization of lung function ($FEV_1\% > 80\%$) and an Asthma Control Questionnaire-6 score ≤ 1.50 after 12 months of treatment.

Results: After 12 months of treatment of 501 biologically naïve patients, there were 104 (21%) patients with no response to treatment, whereas 397 (79%) had a clinical response. Among the latter, 97 (24%) fulfilled our criteria of clinical remission, corresponding to 19%

in the entire population. Remission was predicted by shorter duration of disease and lower BMI in our entire population of all patients treated with biologic therapy.

Interpretation: Clinical response was achieved in most adult patients initiating biologic therapy and clinical remission was observed in 19% of the patients after 12 months of treatment. Further studies are required to assess the long-term outcome of achieving clinical remission on biologic therapy.

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BMC Pulm Med



. 2023 Nov 3;23(1):424.

doi: 10.1186/s12890-023-02728-6.

[Screening and early diagnosis of chronic obstructive pulmonary disease: a population study](#)

[Wenhui Tang](#)¹, [Yan Rong](#)², [Hongmei Zhang](#)², [Wenji Lin](#)², [Wenmei Zeng](#)², [Wenhong Wu](#)²

Affiliations expand

- PMID: 37924038
- DOI: [10.1186/s12890-023-02728-6](https://doi.org/10.1186/s12890-023-02728-6)

Abstract

Background and objective: Although chronic obstructive pulmonary disease (COPD) is a common disease leading to further morbidity and significant mortality, there is still limited data on screening for COPD. The purpose of this study was to establish an early chronic obstructive pulmonary disease (COPD) screening system for the community and hospitals in Nanshan District in Shenzhen City, to improve the rate of early diagnosis and treatment of patients with COPD.

Methods: We identified individuals at high risk of COPD using a questionnaire survey and analyzed the relevant influencing factors in the early stages of COPD in high-risk groups.

Results: We collected a total of 5,000 COPD screening questionnaires, and a total of 449 patients were diagnosed with COPD by pulmonary function examination. The prevalence of COPD in people aged 20 and above in Nanshan District of Shenzhen City was estimated to be 8.98%, with a base of 5000. The severity classification as per the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria was as follows: GOLD I accounted for 34.74%; GOLD II accounted for 37.64%; GOLD III accounted for 16.04%; and GOLD IV accounted for 11.58%. Common features of early COPD that we identified were: (1) patients were mainly males, accounting for 68.0%; (2) COPD was common among people aged 50-59 years, comprising 31%; (3) 96.0% of patients often had severe respiratory symptoms and had frequent coughs when they did not have a cold; (4) 57.2% of patients experienced shortness of breath when walking quickly on level ground or climbing gentle slopes; (5) 72.6% of patients had a family history of bronchial asthma and COPD. Multivariate ordinal multi-classification logistic regression showed that gender, age, shortness of breath, and the use of firewood, grass, and coal stoves were all influencing factors in pulmonary function grading.

Conclusion: A screening questionnaire combined with a pulmonary function test should be adopted as a COPD screening strategy to be implemented at the primary level as a public health priority in China to reduce the incidence, disability, and mortality from COPD.

Keywords: Chronic obstructive pulmonary disease; Early diagnosis; Screening.

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- [18 references](#)

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Pediatr Pulmonol



. 2023 Nov 3.

doi: 10.1002/ppul.26745. Online ahead of print.

[Spirometry in the diagnosis of cough variant asthma in children](#)

[Chunyu Tian](#)¹, [Shiqiu Xiong](#)¹, [Shuo Li](#)¹, [Xin Song](#)¹, [Yantao Zhang](#)¹, [Xinmei Jiang](#)¹, [Xinyue Hou](#)¹, [Yifan Zhang](#)¹, [Chuanhe Liu](#)¹

Affiliations expand

- PMID: 37921541
- DOI: [10.1002/ppul.26745](https://doi.org/10.1002/ppul.26745)

Abstract

Objective: This study aimed to assess the diagnostic utility of spirometry, particularly focusing on small airway parameters, in children with cough variant asthma (CVA).

Methods: This study included children aged 5-12 years with a diagnosis of CVA. Pre- and postbronchodilation spirometry parameters, including FEV₁ %pred, FVC%pred, FEV₁/FVC%pred, PEF%pred, FEF₂₅ %pred, FEF₅₀ %pred, FEF₇₅ %pred, MMEF%pred, were recorded. Receiver operating characteristic curves were plotted, and the area under the curve (AUC) was calculated to assess the discriminatory potential of these spirometry parameters for CVA. A prediction model based on logistic regression (LR) was performed.

Results: A total of 200 patients with CVA and 73 control subjects were included. Baseline spirometry parameters in the CVA group, except for FVC%pred, were significantly lower

compared to the control group. After inhalation of salbutamol sulfate, all parameters showed significant improvement in the CVA group. However, these parameters, except for FEV₁ %pred and FVC%pred, remained lower in the CVA group compared to the control group. The improvement rate of each parameter in the CVA group, except for Δ FVC%, was significantly higher than that in the control group. Δ MMEF% achieved the highest AUC of 0.797 with a threshold value of 16.09%, followed by Δ FEF₇₅ % (0.792), Δ FEV₁ % (0.756), and Δ FEF₅₀ % (0.747) with threshold values of 19.01%, 4.48%, and 19.4%, respectively. The clinical prediction model included four variables (age, Δ FEF₂₅ %, Δ FEF₇₅ %, and Δ MMEF%) and demonstrated excellent performance distinguishing patients with and without CVA (AUC = 0.850). In the CVA group, the Δ FEV₁ % showed a positive correlation with small airway parameters.

Conclusions: This study highlights that children with CVA exhibit lower pulmonary function parameters compared to healthy children. Changes in small airway parameters during bronchodilator tests can be valuable in diagnosing CVA, and the LR prediction model incorporating age and several pulmonary parameters can assist physicians in accurately identifying CVA in clinical practice.

Keywords: children; cough variant asthma; diagnosis; spirometry.

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J Allergy Clin Immunol Pract

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. 2023 Oct 31:S2213-2198(23)01199-6.

Work-related asthma and its impact on quality of life and work productivity

[Eva Suarhana](#)¹, [Nicole Le Moual](#)², [Catherine Lemièrè](#)³, [Jean Bousquet](#)⁴, [Stephie Pierre](#)⁵, [Bernardo Sousa Pinto](#)⁶, [Alfi Afadiyanti Parfi](#)⁵, [Philippe Van Brussel](#)⁷, [Hormoz Nassiri Kigloo](#)⁸, [Olivier Vandenas](#)⁹, [Paul K Henneberger](#)¹⁰

Affiliations expand

- PMID: 37918649
- DOI: [10.1016/j.jaip.2023.10.044](https://doi.org/10.1016/j.jaip.2023.10.044)

Abstract

Background: The impact of Work-related asthma (WRA) on quality of life (QoL) and work productivity remains largely neglected/uncertain despite its high prevalence.

Objective: We aimed to investigate the association of WRA with QoL and work productivity as compared to subjects with asthma unrelated to work and those without asthma and rhinitis.

Methods: A cross-sectional survey was carried out among workers during their periodic occupational health visit in Belgium. The mini Asthma QoL Questionnaire (mAQLQ), Medical Outcome Study Short Form-8 (SF-8), and Work Productivity and Activity Impairment-General Health questionnaires were administered. Survey participants were divided into three groups: 1) WRA (current asthma with ≥ 2 respiratory symptoms at work, $n=89$); 2) non-WRA (current asthma without work-related respiratory symptoms, $n=119$); and 3) the reference group (no asthma and no lower respiratory, nasal, or eye symptoms; $n=815$). Associations of QoL and work productivity with WRA were evaluated by multivariable regression analyses.

Results: WRA and having poor asthma control were significantly associated with lower global mAQLQ scores compared to non-WRA. Asthmatic subjects had significantly lower physical and mental health components of the SF-8 instrument and overall work productivity compared to the reference group, with greater impairment in WRA than non-WRA. Moreover, workers with WRA had higher percentages of doctor visits and income reduction due to respiratory symptoms than non-WRA. Work-related rhinitis and depression were associated with reduced QoL, independent of the effect of WRA.

Conclusions: Comprehensive management of WRA should be done to reduce the worsening of QoL and work productivity of those affected.

Keywords: Quality of life; Socioeconomic burden; Work productivity; Work-related asthma.

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Respirology



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doi: 10.1111/resp.14620. Online ahead of print.

[Letter from Argentina](#)

[Hugo E Neffen](#)¹, [Martín Maillo](#)²

Affiliations expand

- PMID: 37915222
- DOI: [10.1111/resp.14620](https://doi.org/10.1111/resp.14620)

No abstract available

Keywords: Argentina; guidelines; mild asthma; severe asthma.

- [8 references](#)

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BMC Pulm Med



. 2023 Nov 1;23(1):419.

doi: 10.1186/s12890-023-02734-8.

[Evaluation of the prevalence of asthma and chronic obstructive pulmonary disease among opium users, and cigarette smokers and comparison with normal population in Kharameh: a cross-sectional study](#)

[Laleh Raeisy](#)¹, [Seyed Masoom Masoompour](#)², [Abbas Rezaianzadeh](#)³

Affiliations expand

- PMID: 37914995
- PMCID: [PMC10619218](#)

- DOI: [10.1186/s12890-023-02734-8](https://doi.org/10.1186/s12890-023-02734-8)

Free PMC article

Abstract

Background: Recent studies have suggested that opium use may increase mortality from pulmonary diseases. However, there are limited comprehensive studies regarding the prevalence of Asthma and Chronic Obstructive Pulmonary Disease (COPD) among tobacco and opium users has been published. We aimed to determine the prevalence of respiratory disease among tobacco and opium users.

Methods: This cross-sectional study of tobacco and opium users and matched controls was conducted in the Kharameh Cohort, Fars, Iran. The prevalence of COPD and asthma, along with the participants demographical and spirometry data were examined.

Results: The average age of participants was 57 ± 8 years. Never smokers had a significant higher BMI (26.6 vs. 24.8), FEV1 (91% vs. 82%) and FVC (96% vs. 88%) values compared to participants with a positive smoking status. There was a statistical difference in the prevalence of COPD, asthma, and asthma COPD overlap (ACO) based on the participants smoking status, with the highest prevalence among opium and cigarette smokers, followed by opium users alone. Based on multivariate analysis, higher age, lower BMI, lower education than under diploma, cigarette smoking and opium use were significantly correlated with higher COPD prevalence; while lower age, cigarette smoking and opium use were significantly correlated with higher asthma prevalence. Illiterate participants had a significantly higher prevalence of COPD (23.6%), asthma (22%), and ACO (7.9%) among the educational groups. Regarding the prevalence of asthma, the higher socio-economic group had the lowest prevalence.

Conclusions: Opium and tobacco users had a significantly higher prevalence of respiratory diseases, along with lower lung function tests based on spirometry evaluation.

Keywords: Asthma; COPD; Cohort; Iran; Prevalence.

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Conflict of interest statement

The authors declare no competing interests.

- [43 references](#)

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J Asthma

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. 2023 Nov 1:1-9.

doi: 10.1080/02770903.2023.2272798. Online ahead of print.

Pharmacological treatment of asthma in Sweden from 2005 to 2015

[Caroline Ahlroth Pind](#)^{1,2}, [Björn Ställberg](#)³, [Karin Lisspers](#)³, [Josefin Sundh](#)⁴, [Marta A Kisiel](#)⁵, [Hanna Sandelowsky](#)^{6,7,8}, [Anna Nager](#)⁶, [Mikael Hasselgren](#)^{9,10}, [Scott Montgomery](#)^{8,11,12}, [Christer Janson](#)²

Affiliations expand

- PMID: 37910450
- DOI: [10.1080/02770903.2023.2272798](https://doi.org/10.1080/02770903.2023.2272798)

Abstract

Objective: Despite access to effective therapies many asthma patients still do not have well-controlled disease. This is possibly related to underuse of inhaled corticosteroids (ICS) and overuse of short-acting β 2-agonists (SABA). Our aim was to investigate longitudinal trends and associated factors in asthma treatment.

Methods: Two separate cohorts of adults with physician-diagnosed asthma were randomly selected from 14 hospitals and 56 primary health centers in Sweden in 2005 ($n = 1182$) and 2015 ($n = 1225$). Information about symptoms, maintenance treatment, and use of rescue

medication was collected by questionnaires. Associations between treatment and sex, age, smoking, education, body mass index (BMI), physical activity, allergic asthma, and symptom control were analyzed using Pearson's chi²-test. Odds ratios (ORs) were calculated using logistic regression.

Results: Maintenance treatment with ICS together with long-acting β 2-agonists (LABA) and/or montelukast increased from 39.2% to 44.2% ($p = 0.012$). The use of ICS + LABA as-needed increased (11.1-18.9%, $p < 0.001$), while SABA use decreased (46.4- 41.8%, $p = 0.023$). Regular treatment with ICS did not change notably (54.2-57.2%, $p = 0.14$). Older age, former smoking, and poor symptom control were related to treatment with ICS + LABA/montelukast. In 2015, 22.7% reported daily use of SABA. A higher step of maintenance treatment, older age, obesity, shorter education, current smoking, allergic asthma, low or very high physical activity, and a history of exacerbations were associated with daily SABA use.

Conclusions: The use of ICS + LABA both for maintenance treatment and symptom relief has increased over time. Despite this, the problem of low use of ICS and high use of SABA remains.

Keywords: LABA; Longitudinal study; SABA; inhaled corticosteroids; long-acting β 2-agonists; short-acting β 2-agonists.

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J Bras Pneumol

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. 2023 Oct 30;49(5):e20230201.

doi: 10.36416/1806-3756/e20230201. eCollection 2023.

Mobile health applications designed for self-management of chronic pulmonary diseases in children and adolescents: a systematic mapping review

[Article in English, Portuguese]

[Vaia Sapouna](#)^{1,2}, [Pavlos Kitixis](#)¹, [Elpiniki Petrou](#)¹, [Theano Michailidou](#)¹, [Panagiotis Dalamarinis](#)¹, [Eleni Kortianou](#)¹

Affiliations expand

- PMID: 37909552
- DOI: [10.36416/1806-3756/e20230201](https://doi.org/10.36416/1806-3756/e20230201)

Free article

Abstract

Objective: Mobile health (mHealth) applications are scarce for children and adolescents with chronic pulmonary diseases (CPDs). This study aimed to map and describe the contents of the mHealth apps available for use in children and adolescents with CPDs.

Methods: We performed a systematic mapping review of published scientific literature in PubMed, Scopus, and Cochrane Library by February of 2023, using relevant keywords. Inclusion criteria were as follows: children aged < 18 years with CPDs; and studies published in English on mHealth apps.

Results: A total number of 353 studies were found, 9 of which met the inclusion criteria. These studies described seven mHealth apps for Android and iOS, designed either for asthma (n = 5) or for cystic fibrosis (n = 2). Five content areas were identified: education/information; pharmacological treatment; emergency; support; and non-pharmacological treatment. The studies (4, 2, and 3, respectively) showed consistent findings using qualitative, quantitative, and mixed methodologies.

Conclusions: This mapping review provided a guided selection of the most appropriate mHealth apps for use in children and adolescents with CPDs based on the needs of each

target population. However, these mHealth apps have limited capabilities to reinforce disease self-management and provide information related to treatment compliance.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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ERJ Open Res

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. 2023 Oct 30;9(5):00419-2023.

doi: 10.1183/23120541.00419-2023. eCollection 2023 Sep.

[Real-world characteristics of "super-responders" to mepolizumab and benralizumab in severe eosinophilic asthma and eosinophilic granulomatosis with polyangiitis](#)

[Andrea Portacci](#)^{1,2}, [Raffaele Campisi](#)^{3,2}, [Enrico Buonamico](#)¹, [Santi Nolasco](#)^{3,4}, [Corrado Pelaia](#)⁵, [Nunzio Crimi](#)⁴, [Alida Benfante](#)⁶, [Massimo Triggiani](#)⁷, [Giuseppe Spadaro](#)⁸, [Maria Filomena Caiaffa](#)⁹, [Giulia Scioscia](#)¹⁰, [Aikaterini Detoraki](#)¹¹, [Giuseppe Valenti](#)¹², [Francesco Papia](#)¹², [Alessandra Tomasello](#)⁶, [Nicola Scichilone](#)⁶, [Girolamo Pelaia](#)⁵, [Claudia Crimi](#)^{3,4}, [Giovanna Elisiana Carpagnano](#)¹

Affiliations expand

- PMID: 37908397

- PMID: [PMC10613971](#)
- DOI: [10.1183/23120541.00419-2023](#)

Free PMC article

Abstract

Background: The current definition of severe eosinophilic asthma (SEA) super-responders to biologic treatment does not include patients with other eosinophil-based comorbidities. Although eosinophilic granulomatosis with polyangiitis (EGPA) is frequently associated with SEA, we lack data on a possible super-response to biologic treatments in patients suffering from these two diseases. We aim to assess super-responder features in real-life patients with SEA and EGPA treated with mepolizumab and benralizumab.

Methods: We enrolled 39 patients with SEA and EGPA eligible for treatment with mepolizumab or benralizumab. Super-responder assessment was performed considering oral corticosteroid (OCS) cessation, lack of exacerbations, forced expiratory volume in 1 s and Asthma Control Test (ACT) improvement.

Results: Super-responders showed worse clinical baseline characteristics than non-super-responder patients, with a greater improvement in severe asthma exacerbations, OCS dose reduction and ACT score increase. Definition of super-responders was consistent only considering a 12-month course of monoclonal antibody, lacking sensitivity in earlier evaluations.

Conclusion: Mepolizumab and benralizumab are safe and effective in patients with EGPA and SEA, since a consistent proportion of patients show a super-response after 12 months of treatment. Further studies will address specific criteria for super-responder assessment in these patients.

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Conflict of interest statement

Conflict of interest: A. Portacci reports payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from AstraZeneca, GlaxoSmithKline, Chiesi and Sanofi. Conflict of interest: N. Crimi reports payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from AstraZeneca, GlaxoSmithKline and Sanofi. Conflict of interest: A. Benfante reports payment or honoraria for lectures, presentations, speakers' bureaus, manuscript

writing or educational events from AstraZeneca, GlaxoSmithKline and Sanofi. Conflict of interest: M. Triggiani reports consulting fees from AstraZeneca, GlaxoSmithKline and Novartis. Conflict of interest: G. Scioscia reports payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from AstraZeneca, GlaxoSmithKline and Sanofi. Conflict of interest: A. Detoraki reports payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from AstraZeneca, GlaxoSmithKline, Sanofi, Novartis and Lofarma. Conflict of interest: G. Valenti reports payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from GlaxoSmithKline and Sanofi. Conflict of interest: N. Scichilone reports payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from AstraZeneca, GlaxoSmithKline, Chiesi and Sanofi. Conflict of interest: G. Pelaia reports payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Chiesi, Sanofi, Guidotti, Menarini and Novartis. Conflict of interest: C. Crimi reports payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from Astrazeneca, GlaxoSmithKline, Sanofi, Menarini, ResMed and Fisher&Paykel. Conflict of interest: G.E. Carlagnano reports grants or contracts from AstraZeneca, Chiesi, GlaxoSmithKline, Sanofi and Grifols; payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from AstraZeneca, GlaxoSmithKline and Sanofi; and support for attending meetings and/or travel from Astrazeneca, Menarini and Chiesi.

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[Review](#)

Pharmacol Ther

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. 2023 Oct 29:108551.

doi: 10.1016/j.pharmthera.2023.108551. Online ahead of print.

Biologics for severe asthma and beyond

[Carlo Mümmler](#)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. KM reports speaker and/or advisory fees from AstraZeneca, Chiesi, GSK, Novartis, Sanofi.

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Int Arch Allergy Immunol

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. 2023 Oct 31:1-8.

doi: 10.1159/000533535. Online ahead of print.

[Factors Affecting the Ability to Discontinue Oral Corticosteroid Use in Patients with EGPA Treated with Anti-Interleukin-5 Therapy](#)

[Osamu Matsuno](#)¹

Affiliations expand

- PMID: 37906985
- DOI: [10.1159/000533535](https://doi.org/10.1159/000533535)

Abstract

Introduction: Patients with eosinophilic granulomatosis with polyangiitis (EGPA) and some with severe eosinophilic asthma require continuous long-term oral corticosteroid (OCS) treatment for disease control. The anti-interleukin-5 agent, mepolizumab, has recently become available for the treatment of severe eosinophilic asthma and EGPA, with promising results and safety profiles. The proportion of patients with EGPA who

discontinued oral steroids was 18% in the MIRRA trial. To compare patients with EGPA who were able to discontinue steroids with mepolizumab with those who could not.

Methods: Twenty patients with EGPA treated with mepolizumab were evaluated at Osaka Habikino Medical Center. The OCS dose, asthma control test score, fractional exhaled nitric oxide levels, peripheral eosinophil count, and spirometric parameters were evaluated before and after treatment.

Results: There was a significant reduction in the mean OCS dose from a prednisolone equivalent of 8.88 ± 4.99 mg/day to 3.18 ± 3.47 mg/day ($p < 0.001$). In this study, 40% of patients discontinued oral steroids. The most common reason for the failure to discontinue steroids in patients was poor asthma control. The percentage of predicted forced expiratory volume in 1 s significantly improved in patients with EGPA who could discontinue steroids after receiving mepolizumab.

Conclusion: In this real-world study, treatment with mepolizumab for EGPA was associated with a significant reduction in OCS use; however, poor asthma control was identified as an inhibiting factor for steroid reduction.

Keywords: Asthma; Eosinophilic granulomatosis with polyangiitis; Forced expiratory volume in 1 s; Mepolizumab; Oral corticosteroid.

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J R Soc Med

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. 2023 Oct 31:1410768231206033.

doi: 10.1177/01410768231206033. Online ahead of print.

Prevalence of multiple long-term conditions (multimorbidity) in England: a whole population study of over 60 million people

[Jonathan Valabhji](#)^{1,2,3}, [Emma Barron](#)¹, [Adrian Pratt](#)⁴, [Nasrin Hafezparast](#)⁵, [Rupert Dunbar-Rees](#)⁵, [Ellie Bragan Turner](#)⁵, [Kate Roberts](#)⁶, [Jacqueline Mathews](#)⁶, [Robbie Deegan](#)⁴, [Victoria Cornelius](#)¹, [Jason Pickles](#)¹, [Gary Wainman](#)¹, [Chirag Bakhai](#)^{1,7}, [Desmond G Johnston](#)^{2,3}, [Edward W Gregg](#)⁸, [Kamlesh Khunti](#)⁹

Affiliations expand

- PMID: 37905525
- DOI: [10.1177/01410768231206033](https://doi.org/10.1177/01410768231206033)

Abstract

Objectives: To determine the prevalence of multiple long-term conditions (MLTC) at whole English population level, stratifying by age, sex, socioeconomic status and ethnicity.

Design: A whole population study.

Setting: Individuals registered with a general practice in England and alive on 31 March 2020.

Participants: 60,004,883 individuals.

Main outcome measures: MLTC prevalence, defined as two or more of 35 conditions derived from a number of national patient-level datasets. Multivariable logistic regression was used to assess the independent associations of age, sex, ethnicity and deprivation decile with odds of MLTC.

Results: The overall prevalence of MLTC was 14.8% (8,878,231), varying from 0.9% (125,159) in those aged 0-19 years to 68.2% (1,905,979) in those aged 80 years and over. In multivariable regression analyses, compared with the 50-59 reference group, the odds ratio was 0.04 (95% confidence interval (CI): 0.04-0.04; $p < 0.001$) for those aged 0-19 years and 10.21 (10.18-10.24; $p < 0.001$) for those aged 80 years and over. Odds were higher for men compared with women, 1.02 (1.02-1.02; $p < 0.001$), for the most deprived decile compared with the least deprived, 2.26 (2.25-2.27; $p < 0.001$), and for Asian ethnicity compared with those of white ethnicity, 1.05 (1.04-1.05; $p < 0.001$). Odds were lower for black, mixed and

other ethnicities (0.94 (0.94-0.95) $p < 0.001$, 0.87 (0.87-0.88) $p < 0.001$ and 0.57 (0.56-0.57) $p < 0.001$, respectively). MLTC for persons aged 0-19 years were dominated by asthma, autism and epilepsy, for persons aged 20-49 years by depression and asthma, for persons aged 50-59 years by hypertension and depression and for those aged 60 years and older, by cardiometabolic factors and osteoarthritis. There were large numbers of combinations of conditions in each age group ranging from 5936 in those aged 0-19 years to 205,534 in those aged 80 years and over.

Conclusions: While this study provides useful insight into the burden across the English population to assist health service delivery planning, the heterogeneity of MLTC presents challenges for delivery optimisation.

Keywords: Epidemiologic studies; epidemiology; health policy; health service research; medical management; quality improvement.

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BMJ Open

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. 2023 Oct 30;13(10):e075209.

doi: 10.1136/bmjopen-2023-075209.

[Associations between spirometric impairments and microvascular complications in type 2 diabetes: a cross-sectional study](#)

[Charles F Hayfron-Benjamin](#)^{1,2}, [Charles Agyemang](#)^{3,4}, [Bert-Jan H van den Born](#)^{5,6}, [Albert G B Amoah](#)⁷, [Kwesi Nyan Amissah-Arthur](#)⁸, [Latif Musah](#)², [Benjamin Abaidoo](#)⁸, [Pelagia Awula](#)², [Henry](#)

[Wedoi Awuviri](#)², [Joseph Agyapong Abbey](#)², [Deladem A Fummey](#)², [Joana N Ackam](#)⁹, [Gloria Odom Asante](#)¹⁰, [Simone Hashimoto](#)^{11 12}, [Anke H Maitland-van der Zee](#)^{11 12}

Affiliations expand

- PMID: 37903605
- PMCID: [PMC10619106](#)
- DOI: [10.1136/bmjopen-2023-075209](https://doi.org/10.1136/bmjopen-2023-075209)

Free PMC article

Abstract

Objective: Evidence shows that the conventional cardiometabolic risk factors do not fully explain the burden of microvascular complications in type 2 diabetes (T2D). One potential factor is the impact of pulmonary dysfunction on systemic microvascular injury. We assessed the associations between spirometric impairments and systemic microvascular complications in T2D.

Design: Cross-sectional study.

Setting: National Diabetes Management and Research Centre in Ghana.

Participants: The study included 464 Ghanaians aged ≥ 35 years with established diagnosis of T2D without primary myocardial disease or previous/current heart failure. Participants were excluded if they had primary lung disease including asthma or chronic obstructive pulmonary disease.

Primary and secondary outcome measures: The associations of spirometric measures (forced expiratory volume in 1 s (FEV₁), forced vital capacity (FVC) and FEV₁/FVC ratio) with microvascular complications (nephropathy (albumin-creatinine ratio ≥ 3 mg/g), neuropathy (vibration perception threshold ≥ 25 V and/or Diabetic Neuropathy Symptom score > 1) and retinopathy (based on retinal photography)) were assessed using multivariable logistic regression models with adjustments for age, sex, diabetes duration, glycated haemoglobin concentration, suboptimal blood pressure control, smoking pack years and body mass index.

Results: In age and sex-adjusted models, lower Z-score FEV₁ was associated with higher odds of nephropathy (OR 1.55, 95% CI 1.19-2.02, $p=0.001$) and neuropathy (1.27 (1.01-1.65), 0.038) but not retinopathy (1.22 (0.87-1.70), 0.246). Similar observations were made for the associations of lower Z-score FVC with nephropathy (1.54 (1.19-2.01), 0.001),

neuropathy (1.25 (1.01-1.54), 0.037) and retinopathy (1.19 (0.85-1.68), 0.318). In the fully adjusted model, the associations remained significant for only lower Z-score FEV₁ with nephropathy (1.43 (1.09-1.87), 0.011) and neuropathy (1.34 (1.04-1.73), 0.024) and for lower Z-score FVC with nephropathy (1.45 (1.11-1.91), 0.007) and neuropathy (1.32 (1.03-1.69), 0.029). Lower Z-score FEV₁/FVC ratio was not significantly associated with microvascular complications in age and sex and fully adjusted models.

Conclusion: Our study shows positive but varying strengths of associations between pulmonary dysfunction and microvascular complications in different circulations. Future studies could explore the mechanisms linking pulmonary dysfunction to microvascular complications in T2D.

Keywords: diabetic nephropathy & vascular disease; diabetic neuropathy; diabetic retinopathy; pulmonary disease, chronic obstructive.

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Conflict of interest statement

Competing interests: None declared.

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

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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J Med Econ

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. 2023 Oct 30:1-9.

doi: 10.1080/13696998.2023.2277072. Online ahead of print.

How AI is advancing asthma management? insights into economic and clinical aspects

[Ahmad Z Al Meslamani](#)^{1,2}

Affiliations expand

- PMID: 37902681
- DOI: [10.1080/13696998.2023.2277072](https://doi.org/10.1080/13696998.2023.2277072)

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No abstract available

Keywords: A; A1; A19; A2; A20; AI; Asthma; Machine Learning; Prediction accuracy.

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JAMIA Open

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. 2023 Oct 26;6(4):ooad091.

doi: 10.1093/jamiaopen/ooad091. eCollection 2023 Dec.

Prediction of short-acting beta-agonist usage in patients with asthma using temporal-convolutional neural networks

[Nicholas Hiron](#)¹, [Angier Allen](#)², [Noah Matsuyoshi](#)¹, [Jason Su](#)³, [Leanne Kaye](#)², [Meredith A Barrett](#)²

Affiliations expand

- PMID: 37900973
- PMCID: [PMC10602590](#)
- DOI: [10.1093/jamiaopen/ooad091](#)

Free PMC article

Abstract

Objective: Changes in short-acting beta-agonist (SABA) use are an important signal of asthma control and risk of asthma exacerbations. Inhaler sensors passively capture SABA use and may provide longitudinal data to identify at-risk patients. We evaluate the performance of several ML models in predicting daily SABA use for participants with asthma and determine relevant features for predictive accuracy.

Methods: Participants with self-reported asthma enrolled in a digital health platform (Propeller Health, WI), which included a smartphone application and inhaler sensors that collected the date and time of SABA use. Linear regression, random forests, and temporal convolutional networks (TCN) were applied to predict expected SABA puffs/person/day from SABA usage and environmental triggers. The models were compared with a simple baseline model using explained variance (R^2), as well as using average precision (AP) and area under the receiving operator characteristic curve (ROC AUC) for predicting days with ≥ 1 -10 puffs.

Results: Data included 1.2 million days of data from 13 202 participants. A TCN outperformed other models in predicting puff count ($R^2 = 0.562$) and day-over-day change in puff count ($R^2 = 0.344$). The TCN predicted days with ≥ 10 puffs with an ROC AUC score of 0.952 and an AP of 0.762 for predicting a day with ≥ 1 puffs. SABA use over the

preceding 7 days had the highest feature importance, with a smaller but meaningful contribution from air pollutant features.

Conclusion: Predicted SABA use may serve as a valuable forward-looking signal to inform early clinical intervention and self-management. Further validation with known exacerbation events is needed.

Keywords: asthma; computer; neural networks; supervised machine learning; telemetry.

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Conflict of interest statement

N.H., A.A., N.M., L.K., and M.B. were employed by ResMed, Inc. at the time of writing. N.H. and N.M. were also employed by Propeller Health at the time of writing. J.S. has no interests to declare.

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

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Ann Allergy Asthma Immunol

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. 2023 Oct 26:S1081-1206(23)01380-7.

doi: 10.1016/j.anai.2023.10.028. Online ahead of print.

[Implementation of a Pediatric Synchronous Multidisciplinary Severe](#)

Asthma Clinic and Real-World Outcomes

[Divya Patel](#)¹, [Michelle Dilley Revier](#)², [Anoushka Tambay](#)³, [Bob Geng](#)³

Affiliations expand

- PMID: 37898325
- DOI: [10.1016/j.anai.2023.10.028](https://doi.org/10.1016/j.anai.2023.10.028)

No abstract available

Keywords: asthma education; children; clinical outcomes; coordinated care; difficult-to-control asthma; multidisciplinary; pediatric; severe asthma; therapy-resistant asthma; uncontrolled asthma.

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J Allergy Clin Immunol Pract

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. 2023 Oct 26:S2213-2198(23)01193-5.

doi: [10.1016/j.jaip.2023.10.039](https://doi.org/10.1016/j.jaip.2023.10.039). Online ahead of print.

The Art of Immunotherapy

[Harold S Nelson](#)¹

Affiliations expand

- PMID: 37898175
- DOI: [10.1016/j.jaip.2023.10.039](https://doi.org/10.1016/j.jaip.2023.10.039)

Abstract

Selection of a patient with rhinitis/conjunctivitis or asthma for allergy immunotherapy (AIT) requires several decisions. First, does the patient's sensitization, pattern of exposure to an allergen and degree of exposure to that allergen reasonably suggest a causal relationship? Does the level and duration of symptoms warrant the cost and inconvenience of immunotherapy, or is the patient motivated by the disease modifying potential of AIT? If AIT is selected, is the choice to be greater safety and convenience with SLIT-tablets, but with treatment probably limited to two or three allergens, or for SCIT where multiple allergen therapy is the rule and efficacy may be somewhat greater, at least initially, or does the physician go off-label into the unknowns of liquid SLIT? Are there extracts of sufficient potency to achieve likely effective doses? How does the physician deal with large local or systemic reactions, with gaps in treatment, with pollen seasons and the use of premedication or cautionary prescription of epinephrine autoinjectors? How can adherence to AIT be improved? These and other questions are addressed in this paper.

Keywords: AIT; Allergic asthma; SCIT; SLIT; allergic rhinitis/conjunctivitis; allergy immunotherapy; dosing; multi-allergic; patient selection; subcutaneous; sublingual.

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Editorial

Expert Rev Clin Immunol

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. 2023 Oct 28:1-4.

doi: 10.1080/1744666X.2023.2277864. Online ahead of print.

Insights into the immunological links between dietary habits and asthma

[Ahmad Z Al Meslamani](#)^{1,2}

Affiliations expand

- PMID: 37897370
- DOI: [10.1080/1744666X.2023.2277864](https://doi.org/10.1080/1744666X.2023.2277864)

No abstract available

Keywords: Asthma; diet; immunity; immunometabolism; trained immunity.

SUPPLEMENTARY INFO

Publication types expand

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Review

Respir Med

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. 2023 Oct 27:219:107430.

doi: 10.1016/j.rmed.2023.107430. Online ahead of print.

[A systematic review of methods of scoring inhaler technique](#)

[Ruth De Vos](#)¹, [Alexander Hicks](#)², [Mitch Lomax](#)³, [Heather Mackenzie](#)⁴, [Lauren Fox](#)⁵, [Thomas P Brown](#)⁶, [A J Chauhan](#)⁷

Affiliations expand

- PMID: 37890639
- DOI: [10.1016/j.rmed.2023.107430](https://doi.org/10.1016/j.rmed.2023.107430)

Free article

Abstract

Many inhaler devices are currently used in clinical practice to deliver medication, with each inhaler device offering different benefits to overcome technique issues. Inhaler technique remains poor, contributing to reduced airway drug deposition and consequently poor disease control. Scoring inhaler technique has been used within research as an outcome measure of inhaler technique assessment, and this systematic review collates and evaluates these scoring methods. The review protocol was prospectively registered in PROSPERO (CRD42020218869). A total of 172 articles were screened with 77 included, and the results presented using narrative synthesis due to the heterogeneity of the study design and data. The most frequently used scoring method awarded one point per step in the inhaler technique checklist and was included in 59/77 (77%) of articles; however limited and varied guidance was provided for score interpretation. Other inhaler technique scoring methods included grading the final inhaler technique score, expressing the total score as a percentage/ratio, deducting points from the final score when errors were made, and weighting steps within the checklist depending on how crucial the step was. Vast heterogeneity in the number of steps and content in the inhaler technique checklists was observed across all device types (range 5-19 steps). Only 4/77 (5%) of the inhaler technique measures had undertaken fundamental steps required in the scale development process for use in real world practice. This review demonstrates the demand for a tool that measures inhaler technique and highlights the current unmet need for one that has undergone validation.

Keywords: Asthma; COPD; Inhaler technique; Inhaler technique checklist; Inhaler technique score.

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Conflict of interest statement

Declaration of competing interest There is no conflict of interest.

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Can J Anaesth

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. 2023 Oct 26.

doi: 10.1007/s12630-023-02608-x. Online ahead of print.

[Ketamine sedation in the intensive care unit: a survey of Canadian intensivists](#)

[Sameer Sharif](#)^{1,2,3,4}, [Laveena Munshi](#)⁵, [Lisa Burry](#)^{5,6}, [Sangeeta Mehta](#)⁵, [Sara Gray](#)⁷, [Dipayan Chaudhuri](#)^{8,9}, [Mark Duffett](#)⁹, [Reed A Siemieniuk](#)⁹, [Bram Rochweg](#)^{8,9}

Affiliations [expand](#)

- PMID: 37884773
- DOI: [10.1007/s12630-023-02608-x](https://doi.org/10.1007/s12630-023-02608-x)

Abstract

in [English](#), [French](#)

Purpose: We sought to understand the beliefs and practices of Canadian intensivists regarding their use of ketamine as a sedative in critically ill patients and to gauge their interest in a randomized controlled trial (RCT) examining its use in the intensive care unit (ICU).

Methods: We designed and validated an electronic self-administered survey examining the use of ketamine as a sedative infusion for ICU patients. We surveyed 400 physician members of the Canadian Critical Care Society (CCCS) via email between February and April 2022 and sent three reminders at two-week intervals. The survey was redistributed in January 2023 to improve the response rate.

Results: We received 87/400 (22%) completed questionnaires. Most respondents reported they rarely use ketamine as a continuous infusion for sedation or analgesia in the ICU (52/87, 58%). Physicians reported the following conditions would make them more likely to use ketamine: asthma exacerbation (73/87, 82%), tolerance to opioids (68/87, 77%), status epilepticus (44/87, 50%), and severe acute respiratory distress syndrome (33/87, 38%). Concern for side-effects that limited respondents' use of ketamine include adverse psychotropic effects (61/87, 69%) and delirium (47/87, 53%). The majority of respondents agreed there is need for an RCT to evaluate ketamine as a sedative infusion in the ICU (62/87, 71%).

Conclusion: This survey of Canadian intensivists illustrates that use of ketamine as a continuous infusion for sedation is limited, and is at least partly driven by concerns of adverse psychotropic effects. Canadian physicians endorse the need for a trial investigating the safety and efficacy of ketamine as a sedative for critically ill patients.

Keywords: critical care; ketamine; sedation; survey.

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Pediatr Pulmonol



. 2023 Oct 26.

doi: 10.1002/ppul.26733. Online ahead of print.

Trajectories of psychosocial environmental factors and their associations with asthma symptom trajectories among children in Australia

[K M Shahunja](#)^{1,2,3}, [Peter D Sly](#)⁴, [Abdullah Mamun](#)^{1,2,3}

Affiliations expand

- PMID: 37882548
- DOI: [10.1002/ppul.26733](https://doi.org/10.1002/ppul.26733)

Abstract

Introduction: Several psychosocial factors, such as maternal mental health and parents' financial hardship, are associated with asthma symptoms among children. So, we aim to investigate the changing patterns of important psychosocial environmental factors and their associations with asthma symptom trajectories among children in Australia.

Methods: We considered asthma symptoms as wheezing (outcome) and psychosocial environmental factors (exposures) from 0/1 year to 14/15 years of the participants from the "Longitudinal Study of Australian Children (LSAC)" for this study. We used group-based trajectory modeling to identify the trajectory groups for both exposure and outcome variables. Associations between psychosocial factors and three distinct asthma symptom trajectories were assessed by multivariable logistic regression.

Results: We included 3917 children from the LSAC birth cohort in our study. We identified distinct trajectories for maternal depression, parents' financial hardship, parents' stressful

life events and parents' availability to their children from birth to 14/15 years of age. Compared to the "low/no" asthma symptom trajectory group, children exposed to a "moderate & increasing" maternal depression, "moderate & declining" parents' financial hardship, and "moderate & increasing" parents' stressful life events were significantly associated (relative risk ratio [RRR]: 1.55, 95% confidence interval [CI]: 1.27, 1.91; RRR: 1.40, 95%; CI: 1.15, 1.70; RRR: 1.77, 95%; CI: 1.45, 2.16) with "persistent high" asthma symptom trajectory.

Conclusion: Several psychosocial factors that are potential stressors for mental health increase the risk of having an adverse asthma symptom trajectory during childhood. Further attention should be given to reducing exposure to maternal depression, parents' financial hardship, and parents' stressful live events for long-term asthma control in children.

Keywords: Australia; asthma; children; psychosocial environment; trajectory.

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Chin Med J (Engl)

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. 2023 Oct 26.

doi: 10.1097/CM9.0000000000002855. Online ahead of print.

[Secular trends of asthma mortality in China and the United States from 1990 to 2019](#)

[Xiaochen Li](#)^{1,2}, [Mingzhou Guo](#)^{1,2}, [Yang Niu](#)^{1,2}, [Min Xie](#)^{1,2}, [Xiansheng Liu](#)^{1,2}

Affiliations expand

- PMID: 37882090
- DOI: [10.1097/CM9.0000000000002855](https://doi.org/10.1097/CM9.0000000000002855)

Abstract

Background: Asthma imposes a large healthcare burden in China and the United States (US). However, the trends of asthma mortality and the relative risk factors have not been comparatively analyzed between the countries. The aim of this study was to compare the mortality and risk factors between China and the US.

Methods: The deaths, and mortality rates of asthma in China and the US during 1990-2019 were obtained from the Global Burden of Disease Study 2019. The age-period-cohort model was used to estimate these mortality rates based on a log-linear scale with additive age, period, and cohort effects. The population attributable fractions of risk factors for asthma were estimated.

Results: In 1990-2019, the asthma mortality rate was higher in China than in the US. The crude and age-standardized asthma mortality rates trended downward in both China and the US from 1990 to 2019. The decline in mortality was more obvious in China. Mortality gap between the two countries was narrowing. A sex difference in asthma mortality was observed with higher mortality in males in China and females in the US. The age effects showed that mortality increased with age in adults older than 20 years, particularly in the elderly. Downward trends were generally observed in the period and cohort rate ratios in both countries, with China experiencing a more obvious decrease. Smoking and high body mass index (BMI) were the leading risk factors for asthma mortality in China and the US, respectively. Mortality attributable to occupational asthmagens and smoking decreased the most in China and the US, respectively.

Conclusions: In 1990-2019, the asthma mortality rate was higher in China than in the US; however, the mortality gap has narrowed. Mortality increased with age in adults. The improvements in asthma death risk with period and birth cohort were more obvious in China than in the US. Smoking, high BMI, and aging are major health problems associated with asthma control. The role of occupational asthmagens in asthma mortality underscores the importance of management and prevention of occupational asthma.

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J Manag Care Spec Pharm

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. 2023 Nov;29(11):1193-1204.

doi: 10.18553/jmcp.2023.23034. Epub 2023 Oct 5.

[A cost comparison of benralizumab, mepolizumab, and dupilumab in patients with severe asthma: A US third-party payer perspective](#)

[Xiao Xu](#)^{1,2}, [Caroline Schaefer](#)³, [Agota Szende](#)⁴, [Eduardo Genofre](#)⁵, [Rohit Katial](#)², [Yen Chung](#)⁵

Affiliations expand

- PMID: 37796731
- DOI: [10.18553/jmcp.2023.23034](https://doi.org/10.18553/jmcp.2023.23034)

Abstract

BACKGROUND: Clinical trials and real-world evidence (RWE) studies of biologics have demonstrated reduced exacerbations, decreased use of oral corticosteroids (OCS), and improvements in daily symptoms and health-related quality of life in patients with severe eosinophilic asthma (SEA). **OBJECTIVE:** To compare direct health care costs associated with biologic use for the treatment of SEA from a US third-party payer

perspective. **METHODS:** We developed a cost-minimization model to compare costs and cost offsets associated with 3 biologics-benralizumab, mepolizumab, and dupilumab-for 2- and 4-year periods. The model relied on longitudinal data from clinical trials to inform the primary (base case) analysis cost comparison and RWE study data, in a separate scenario, to compare costs in nonclinical trial settings. Primary model outcomes included exacerbations (including hospitalizations), OCS-dependent years (including associated complications), and total direct health care biologic costs. Results were calculated at the per patient and population level (per 1,000 patients). Sensitivity analyses with key model parameters were performed. **RESULTS:** Benralizumab had the lowest total biologic costs per patient for both the 2- and 4-year periods. Over 4 years, the marginal cost difference in total biologic costs per patient was \$23,061 lower for benralizumab vs mepolizumab and \$17,242 lower for benralizumab vs dupilumab. The 4-year population level analysis of benralizumab vs mepolizumab revealed \$4.8 million in marginal cost offsets due to 582 fewer exacerbations and 153 fewer OCS-dependent years and a marginal total cost savings of \$27.9 million per 1,000 patients for benralizumab. The 4-year population level analysis of benralizumab vs dupilumab revealed \$2.3 million in marginal cost offsets due to 291 fewer exacerbations and 64 fewer OCS-dependent years and marginal total cost savings of \$19.5 million per 1,000 patients for benralizumab. RWE data were available for a 2-year cost comparison scenario of benralizumab vs mepolizumab, which showed similar results to the base case analysis. Sensitivity analyses varying assumptions on key model parameter estimates confirmed results, with benralizumab having lower total direct health care costs in all scenarios tested, and showed that model results were most sensitive to changes in biologic costs and exacerbation reduction rates. **CONCLUSIONS:** Patients receiving benralizumab had higher nonbiologic cost offsets because of reductions in exacerbations and OCS-dependent years, leading to greater cost savings for third-party payers compared with patients receiving mepolizumab or dupilumab. Taken together with biologic costs, benralizumab presents greater savings in health care costs for payers than patients with SEA who use mepolizumab or dupilumab. **DISCLOSURES:** This study was funded by AstraZeneca (Cambridge, UK). Drs Xu, Chung, Genofre, and Katial are or were AstraZeneca employees at the time this research was conducted and may be shareholders of AstraZeneca. Ms Schaefer and Dr Szende are employees of Labcorp Drug Development, which received funding from AstraZeneca to perform this research.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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J Allergy Clin Immunol Glob



. 2023 Jul 3;2(4):100134.

doi: 10.1016/j.jacig.2023.100134. eCollection 2023 Nov.

Chronic rhinosinusitis with nasal polyps and allergic rhinitis as different multimorbid treatable traits in asthma

[José Antonio Castillo](#)^{1,2,3}, [Vicente Plaza](#)⁴, [Gustavo Rodrigo](#)⁵, [Berta Juliá](#)⁶, [César Picado](#)^{2,7}, [Cristina Fernández](#)⁸, [Joaquim Mullol](#)^{2,3,9}

Affiliations expand

- PMID: 37781668
- PMCID: [PMC10510007](#)
- DOI: [10.1016/j.jacig.2023.100134](#)

Free PMC article

Abstract

Background: Respiratory multimorbidities are linked to asthma, such as allergic rhinitis (AR) with early allergic asthma and chronic rhinosinusitis (CRS) with nasal polyps (CRSwNP) with late nonallergic asthma.

Objective: Our aim was to investigate the association of asthma severity and control with specific upper airway phenotypes.

Method: Patients with asthma were prospectively recruited from 23 pulmonology and ear, nose, and throat clinics. Asthma severity and control, as well as upper airway comorbidities (AR and non-AR [NAR], CRSwNP, and CRS without nasal polyps [CRSsNP]) were assessed according to international consensus guidelines definitions.

Results: A total of 492 asthmatic patients were included. Half of the asthmatic patients (49.6%) had associated rhinitis (37.0% had AR and 12.6% had NAR) and 36.2% had CRS (16.7% had CRSsNP and 19.5% had CRSwNP), whereas 14.2% had no sinonasal symptoms. Most cases of AR (78%) and NAR (84%) were present in patients with mild-to-moderate asthma, whereas CRSwNP was more frequent in patients with severe asthma (35% [$P < .001$]), mainly nonatopic asthma (44% [$P < .001$]). Patients with severe asthma with CRSwNP had worse asthma control, which was correlated ($r = 0.249$ [$P = .034$]) with sinus occupancy. Multiple logistic regression analysis showed that late-onset asthma, intolerance of aspirin and/or nonsteroidal anti-inflammatory drugs, and CRSwNP were independently associated with severe asthma.

Conclusion: Severe asthma is associated with CRSwNP, with sinus occupancy affecting asthma control. This study has identified 2 main different upper airway treatable traits, AR and CRSwNP, which need further evaluation to improve management and control of patients with asthma.

Keywords: Asthma; allergic rhinitis; asthma control; asthma severity; chronic rhinosinusitis with nasal polyps; united airway disease.

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

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J Allergy Clin Immunol Glob

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. 2023 Aug 3;2(4):100161.

doi: 10.1016/j.jacig.2023.100161. eCollection 2023 Nov.

Respiratory-syncytial virus immunoprophylaxis on asthma symptoms development in prematurity with bronchopulmonary dysplasia

[Li-Ching Fang](#)¹, [Jen-Yu Wang](#)², [Hsin-Hui Yu](#)³, [Li-Chieh Wang](#)³, [Bor-Luen Chiang](#)^{3 4 5}

Affiliations [expand](#)

- PMID: 37781666
- PMCID: [PMC10510012](#)
- DOI: [10.1016/j.jacig.2023.100161](#)

Free PMC article

Abstract

Background: Infants with respiratory-syncytial virus bronchiolitis hospitalization are more likely to develop wheezing and subsequent asthma. Reportedly, palivizumab prophylaxis effectively prevents respiratory-syncytial virus hospitalization in high-risk children-such as premature infants or infants with bronchopulmonary dysplasia (BPD).

Objective: We sought to explore the effect of respiratory-syncytial virus immunoprophylaxis on the risk of asthma development in premature infants with BPD in subtropical areas.

Methods: This case-control study included preterm children with BPD born at Mackay Memorial Hospital, Taipei, Taiwan, from 1999 to 2015. Overall, medical records of 616 eligible participants were retrospectively collected from their birth to the time they attained an age of 5 to 20 years. The primary outcome was onset of active asthma.

Results: Overall, 576 consecutive cases met the inclusion criteria. Of these, 306 (53.2%) patients had palivizumab exposure and 191 (33.2%) were diagnosed with asthma. Patients

with history of respiratory-syncytial virus bronchiolitis hospitalization had a higher risk of developing asthma in the future (adjusted odds ratio, 3.77; 95% CI, 2.30-6.20, $P < .001$; hazard ratio, 2.56; 95% CI, 1.81-3.62, $P < .001$). Palivizumab prophylaxis reduced future asthma development through the inhibition of respiratory-syncytial virus bronchiolitis hospitalization (coefficient, -0.021; 95% CI, -0.031 to -0.011, $P = .027$). Asthmatic children who received palivizumab immunoprophylaxis had a lesser active asthma duration than those who did not ($P = .005$).

Conclusions: Children with BPD with hospitalization for respiratory-syncytial virus bronchiolitis had higher risk of developing asthma compared with those without respiratory-syncytial virus infection. Prophylactic palivizumab might reduce later asthma development through inhibition of respiratory-syncytial virus bronchiolitis hospitalization. For those already developing asthma, palivizumab could reduce active asthma duration.

Keywords: Asthma; RSV bronchiolitis; bronchopulmonary dysplasia; palivizumab; prematurity.

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

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[Review](#)

J Allergy Clin Immunol Glob

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. 2023 Jul 5;2(4):100135.

doi: 10.1016/j.jacig.2023.100135. eCollection 2023 Nov.

Endogenous inhibitory mechanisms in asthma

[Sergio E Chiarella](#)¹, [Peter J Barnes](#)²

Affiliations expand

- PMID: 37781649
- PMCID: [PMC10509980](#)
- DOI: [10.1016/j.jacig.2023.100135](#)

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Abstract

Endogenous inhibitory mechanisms promote resolution of inflammation, enhance tissue repair and integrity, and promote homeostasis in the lung. These mechanisms include steroid hormones, regulatory T cells, IL-10, prostaglandin E₂, prostaglandin I₂, lipoxins, resolvins, protectins, maresins, glucagon-like peptide-1 receptor, adrenomedullin, nitric oxide, and carbon monoxide. Here we review the most recent literature regarding these endogenous inhibitory mechanisms in asthma, which remain a promising target for the prevention and treatment of asthma.

Keywords: Asthma; IL-10; Treg cell; adrenomedullin; airway inflammation; carbon monoxide; endogenous; glucagon-like peptide-1 receptor; inhibition; inhibitory; lipoxin; maresin; mechanism; nitric oxide; pathway; prostaglandin; protectin; resolving.

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

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Biomed Pharmacother



. 2023 Nov;167:115556.

doi: 10.1016/j.biopha.2023.115556. Epub 2023 Sep 29.

[Discovery of zolinium TSG1180 as a novel agonist of transgelin-2 for treating asthma](#)

[Hong-Kai Yuan](#)¹, [Bo Li](#)², [Leyun Wu](#)², [Xue-Ling Wang](#)¹, [Zhi-Ying Lv](#)¹, [Zhikai Liu](#)³, [Zhijian Xu](#)², [Jin Lu](#)¹, [Cai-Tao Chen](#)¹, [Yong-Qing Yang](#)⁴, [Weiliang Zhu](#)⁵, [Lei-Miao Yin](#)⁶

Affiliations expand

- PMID: 37778269
- DOI: [10.1016/j.biopha.2023.115556](https://doi.org/10.1016/j.biopha.2023.115556)

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Abstract

Asthma is a complex and heterogeneous respiratory disease that causes serious social and economic burdens. Current drugs such as β_2 -agonists cannot fully control asthma. Our previous study found that Transgelin-2 is a potential target for treating asthmatic pulmonary resistance. Herein, we discovered a zolinium compound, TSG1180, that showed a strong interaction with Transgelin-2. The equilibrium dissociation constants (KD) of TSG1180 to Transgelin-2 were determined to be 5.363×10^{-6} and 9.81×10^{-6} M by surface plasmon resonance (SPR) and isothermal titration calorimetry (ITC). Cellular thermal shift

assay (CETSA) results showed that the thermal stability of Transgelin-2 increased after coincubation of TSG1180 with lysates of airway smooth muscle cells (ASMCs). Molecular docking showed that Arg39 may be the key residue for the binding. Then, the SPR result showed that the binding affinity of TSG1180 to Transgelin-2 mutant (R39E) was decreased by 1.69-fold. Real time cell analysis (RTCA) showed that TSG1180 treatment could relax ASMCs by 19 % ($P < 0.05$). Once Transgelin-2 was inhibited, TSG1180 cannot induce a relaxation effect, suggesting that the relaxation effect was specifically mediated by Transgelin-2. In vivo study showed TSG1180 effectively reduced pulmonary resistance by 64 % in methacholine-induced mice model ($P < 0.05$). Furthermore, the phosphorylation of Ezrin at T567 was increased by 8.06-fold, the phosphorylation of ROCK at Y722 was reduced by 38 % and the phosphorylation of RhoA at S188 was increased by 52 % after TSG1180 treatment. These results suggested that TSG1180 could be a Transgelin-2 agonist for further optimization and development as an anti-asthma drug.

Keywords: Agonist; Asthma; Ezrin; Mechanism; Molecular docking; Transgelin-2.

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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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Respir Med



. 2023 Nov:218:107414.

doi: 10.1016/j.rmed.2023.107414. Epub 2023 Sep 29.

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

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

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- PMID: 37776915
- DOI: [10.1016/j.rmed.2023.107414](https://doi.org/10.1016/j.rmed.2023.107414)

Free article

Abstract

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

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

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Conflict of interest statement

Declaration of competing interest Dr. Linda Rogers receives research funding including salary support from Sanofi (Global) and Gene DX (formerly Sema 4). She has served on advisory boards and performed consulting work for Astra Zeneca, Sanofi (US) and Teva Pharmaceuticals. She has received travel funding and lecture honoraria from the American College of Chest Physicians. Dr. Sven Seys company receives grants/contracts from Sanofi, Novartis, GSK, and is an employee of Galenus Health and Hippo Dx, and received speakers fee from Teva Pharmaceuticals. Dr. Milos Jenesak has performed consulting for Novartis, Sanofi Genzyme, Astra Zeneca, and GSK, has received payment/honoraria for lectures, presentatinos, speakers bureaus, manuscript writing or educational events from Sanofi Genzyme and Novartis. Dr. Hanania's institution receives grants or contract from Astra Zeneca, GSK, Sanofi, Genentech, and Teva and consulting fees from Astra Zeneca, GSK, Sanofi, Genentech, Teva, and Amgen, andspeaking fees from Regeneron. Dr. Bjermer has no conflicts to declare in relation to this manuscript. Dr. Zuzana Diamant received speaker or consultant honoraria and/or served on advisory boards at: Antabio, Arcede, Foresee Pharmaceuticals, GlaxoSmithKline, Hippo-Dx, QPS-Netherlands, Sanofi-Genzyme-Regeneron, all outside the submitted work. During the last 3 years of her assignment as Research Director Respiratory and Allergy, QPS-Netherlands received European grant from ERA4TB and funding from Foresee Pharmaceuticals for early clinical studies. She serves as associate editor for Allergy and Respiratory Medicine and acts as Chair of the Asthma Expert Panel at EUFOREA. submitted work.

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Chem Biol Interact

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. 2023 Nov 1:385:110737.

doi: 10.1016/j.cbi.2023.110737. Epub 2023 Sep 27.

Emerging applications and prospects of NFκB decoy oligodeoxynucleotides in managing respiratory diseases

[Jessica Katrine Datsyuk](#)¹, [Keshav Raj Paudel](#)², [Rashi Rajput](#)¹, [Sofia Kokkinis](#)¹, [Tammam El Sherkawi](#)¹, [Sachin Kumar Singh](#)³, [Gaurav Gupta](#)⁴, [Dinesh Kumar Chellappan](#)⁵, [Stewart Yeung](#)¹, [Philip Michael Hansbro](#)⁶, [Brian Gregory George Oliver](#)⁷, [Hélder A Santos](#)⁸, [Kamal Dua](#)⁹, [Gabriele De Rubis](#)¹⁰

Affiliations expand

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- DOI: [10.1016/j.cbi.2023.110737](https://doi.org/10.1016/j.cbi.2023.110737)

Abstract

Chronic respiratory diseases like asthma and Chronic Obstructive Pulmonary Disease (COPD) have been a burden to society for an extended period. Currently, there are only preventative treatments in the form of mono- or multiple-drug therapy available to patients who need to utilize it daily. Hence, throughout the years there has been a substantial amount of research in understanding what causes inflammation in the context of these diseases. For example, the transcription factor NFκB has a pivotal role in causing chronic inflammation. Subsequent research has been exploring ways to block the activation of NFκB as a potential therapeutic strategy for many inflammatory diseases. One of the possible ways through which this is probable is the utilisation of decoy oligodeoxynucleotides, which are synthetic, short, single-stranded DNA fragments that mimic the consensus binding site of a targeted transcription factor, thereby functionally inactivating it. However, limitations to the implementation of decoy oligodeoxynucleotides include their rapid degradation by intracellular nucleases and the lack of targeted tissue specificity. An advantageous approach to overcome these limitations involves using nanoparticles as a vessel for drug delivery. In this review, all of those key elements will be explored as to how they come together as an application to treat chronic inflammation in respiratory diseases.

Keywords: Asthma; COPD; Decoy oligodeoxynucleotides; Inflammation; NFκB; Nanoparticles.

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Conflict of interest statement

Declaration of competing interest The authors of the literature review, 'Emerging Applications and Prospects of NFκB Decoy Oligodeoxynucleotides in Managing Respiratory Diseases' have no conflicts of interest to declare.

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. 2023 Nov;15(16):1327-1340.

doi: 10.2217/imt-2023-0109. Epub 2023 Sep 29.

[Tezepelumab for the treatment of severe asthma: a plain language](#)

summary of the PATHWAY and NAVIGATOR studies

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

Affiliations expand

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- DOI: [10.2217/imt-2023-0109](https://doi.org/10.2217/imt-2023-0109)

Free article

Abstract

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

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

What are the key takeaways?: The results showed that participants who had monthly doses of tezepelumab had fewer severe asthma attacks and better lung function than those who had placebo. In both studies, the health issues that the participants had were similar between the tezepelumab and placebo treatment groups. Overall, the studies showed that tezepelumab worked in a broad population of people with severe asthma and that the study participants had an acceptable level of health issues during the studies. These results led to the approval of tezepelumab for people with severe asthma aged 12 and above in the USA, EU and other countries. **Clinical Trial Registration:** PATHWAY study: [NCT02054130](https://clinicaltrials.gov/ct2/show/study/NCT02054130); NAVIGATOR study: [NCT03347279](https://clinicaltrials.gov/ct2/show/study/NCT03347279) (ClinicalTrials.gov).

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

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated dataexpand

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Eur Respir J

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. 2023 Nov 2;62(5):2300558.

doi: 10.1183/13993003.00558-2023. Print 2023 Nov.

[Dupilumab leads to better-controlled asthma and quality of life in children: the VOYAGE study](#)

[Alessandro G Fiocchi](#)¹, [Wanda Phipatanakul](#)², [Robert S Zeiger](#)³, [Sandy R Durrani](#)⁴, [Jeremy Cole](#)⁵, [Jérôme Msihid](#)⁶, [Rebecca Gall](#)⁴, [Juby A Jacob-Nara](#)⁷, [Yamo Deniz](#)⁴, [Paul J Rowe](#)⁷, [David J Lederer](#)⁴, [Meghan Hardin](#)⁸, [Yi Zhang](#)⁴, [Asif H Khan](#)⁶

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- PMID: 37734856
- PMCID: [PMC10620476](#)
- DOI: [10.1183/13993003.00558-2023](#)

Free PMC article

Abstract

Background: Dupilumab has shown long-term treatment benefits in children with uncontrolled asthma. We assessed in more detail the impact of dupilumab on asthma control and health-related quality of life (HRQoL) in children and their caregivers.

Methods: Children aged 6-11 years with uncontrolled moderate-to-severe type 2 asthma (baseline blood eosinophils ≥ 150 cells· μL^{-1} or fractional exhaled nitric oxide ≥ 20 ppb; $n=350$) were treated with dupilumab or placebo for 52 weeks in the VOYAGE study. Primary outcomes of these analyses were asthma control (change from baseline in Asthma Control Questionnaire 7 Interviewer-Administered (ACQ-7-IA) and achieving a clinically meaningful response of ≥ 0.5 points); proportion of patients achieving well-controlled asthma or better (ACQ-7-IA ≤ 0.75 points); effect on patients' (Standardised Paediatric Asthma Quality of Life Questionnaire Interviewer-Administered (PAQLQ(S)-IA)) and caregivers' (Paediatric Asthma Caregiver's Quality of Life Questionnaire (PACQLQ)) HRQoL; and allergic rhinitis-related QoL.

Results: Dupilumab *versus* placebo significantly improved children's ACQ-7-IA scores by week 4 with sustained improvements through week 52 (least squares mean difference at week 52: -0.44, 95% CI -0.59- -0.30; $p<0.0001$); a higher proportion achieved a clinically meaningful response (week 52: 86% *versus* 75%; $p=0.0051$). At weeks 24 and 52, more children who received dupilumab achieved well-controlled asthma (ACQ-7-IA ≤ 0.75 points: 61% *versus* 43%; $p=0.0001$ and 70% *versus* 46%; $p<0.0001$, respectively). Significant improvements in PAQLQ(S)-IA and PACQLQ scores were observed by week 52.

Conclusions: In children aged 6-11 years with moderate-to-severe type 2 asthma, dupilumab treatment was associated with rapid, sustained improvements in asthma control. HRQoL was significantly improved for children and their caregivers.

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Conflict of interest statement

Conflict of interest: A.G. Fiocchi has served as an advisory board member for Abbott, Danone, DBV Technologies, HiPP Organic, Novartis and Stallergenes Greer, and reports research sponsorship from Danone, Ferrero, HiPP Organic and Sanofi. W. Phipatanakul has served as a consultant and has received clinical trial support/medication support from Genentech, GSK for Asthma Therapeutics, Merck, Regeneron Pharmaceuticals Inc. and Sanofi. R.S. Zeiger has served as a deputy editor for the AAAAI and a consultant for the ACAAI, received research support from ALK and the NIH, received research support from and served as an advisory board member for AstraZeneca, Genentech/Novartis, GSK and Teva, served as an advisory board member for Sanofi-Regeneron Pharmaceuticals Inc., and reports royalties from UpToDate. J. Cole has no conflicts of interest to disclose. J. Msihid, J.A. Jacob-Nara, P.J. Rowe, M. Hardin and A.H. Khan are Sanofi employees and may hold stock and/or stock options in the company. S.R. Durrani, R. Gall, Y. Deniz and D.J. Lederer are employees and shareholders of Regeneron Pharmaceuticals Inc. Y. Zhang is a former employee of Regeneron Pharmaceuticals Inc. and may hold shares and/or share options in the company.

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Adv Ther

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. 2023 Nov;40(11):4957-4971.

doi: 10.1007/s12325-023-02659-y. Epub 2023 Sep 19.

[Effect of Tezepelumab on Lung Function in Patients With Severe,](#)

Uncontrolled Asthma in the Phase 3 NAVIGATOR Study

[Andrew Menzies-Gow](#)^{1,2}, [Christopher S Ambrose](#)³, [Gene Colice](#)⁴, [Gillian Hunter](#)⁵, [Bill Cook](#)³, [Nestor A Molfino](#)⁶, [Jean-Pierre Llanos](#)⁷, [Elliot Israel](#)⁸

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- PMID: 37723356
- PMCID: [PMC10567907](#)
- DOI: [10.1007/s12325-023-02659-y](#)

Free PMC article

Abstract

Introduction: Severe asthma is associated with airway inflammation and airway obstruction. In the phase 3 NAVIGATOR study, tezepelumab treatment significantly improved pre-bronchodilator forced expiratory volume in 1 s (FEV₁) compared with placebo in patients with severe, uncontrolled asthma. This analysis assessed the effect of tezepelumab versus placebo on additional lung function parameters in patients from NAVIGATOR.

Methods: NAVIGATOR was a multicenter, randomized, double-blind, placebo-controlled study. Patients (12-80 years old) receiving medium- or high-dose inhaled corticosteroids and at least one additional controller medication, with or without oral corticosteroids, were randomized 1:1 to tezepelumab 210 mg or placebo subcutaneously every 4 weeks for 52 weeks. Changes from baseline to week 52 in pre-bronchodilator FEV₁, post-bronchodilator FEV₁, forced vital capacity (FVC), pre-bronchodilator FEV₁/FVC ratio, pre-bronchodilator forced expiratory flow between 25 and 75% of vital capacity (FEF₂₅₋₇₅), and morning and evening peak expiratory flow (PEF) were assessed.

Results: Tezepelumab treatment improved all evaluated lung function parameters over 52 weeks compared with placebo [least-squares mean difference (95% confidence interval): pre-bronchodilator FEV₁, 0.13 (0.08, 0.18) L; post-bronchodilator FEV₁, 0.12 (0.07, 0.16) L; FVC, 0.13 (0.07, 0.19) L; FEV₁/FVC ratio, 2.06% (1.22%, 2.90%); FEF₂₅₋₇₅, 0.13 (0.07, 0.19) L/s; morning PEF, 16.6 (8.1, 25.1) L/min; and evening PEF, 14.9 (6.3, 23.4) L/min]. Improvements were observed as early as weeks 1-2 and were maintained over 52 weeks. Greater improvements in lung function compared with placebo were observed in patients with a

disease duration of less than 20 years, those with baseline post-bronchodilator FEV₁ reversibility of at least 20%, and in patients with a baseline post-bronchodilator FEV₁/FVC ratio of less than 0.7.

Conclusion: These findings further support the benefits of tezepelumab treatment in improving airflow limitation in patients with severe, uncontrolled asthma.

Clinical trial registration: NAVIGATOR ([NCT03347279](https://clinicaltrials.gov/ct2/show/study/NCT03347279)).

Keywords: Biologics; Forced expiratory volume in 1 s (FEV1); Pulmonary function; Tezepelumab; Thymic stromal lymphopoietin (TSLP).

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Conflict of interest statement

Andrew Menzies-Gow has a new and additional affiliation of Respiratory and Immunology, BioPharmaceuticals Medical, AstraZeneca, Cambridge, UK; is an employee of AstraZeneca and has attended advisory board meetings for AstraZeneca, GSK, Novartis, Regeneron, Sanofi, and Teva Pharmaceuticals; has received speaker fees from AstraZeneca, Novartis, Sanofi, and Teva Pharmaceuticals; has participated in research with AstraZeneca, for which his institution has been remunerated; has attended international conferences with Teva Pharmaceuticals; and has consultancy agreements with AstraZeneca and Sanofi. Christopher S. Ambrose, Gene Colice, Gillian Hunter, and Bill Cook are employees of AstraZeneca and may own stock or stock options in AstraZeneca. Nestor A. Molino and Jean-Pierre Llanos are employees of Amgen and own stock in Amgen. Elliot Israel has served as a consultant to and received personal fees from 4D Pharma, AB Science, Amgen, AstraZeneca, Avillion, Biometry, Cowen, Equillum, Genentech, GSK, Merck, Novartis, Pneuma Respiratory, PPS Health, Regeneron Pharmaceuticals, Sanofi, Sienna Biopharmaceuticals, and Teva Pharmaceuticals; has received nonfinancial support from Circassia, Teva Pharmaceuticals, and Vorso Corp; and has received clinical research grants from AstraZeneca, Avillion, Genentech, Gossamer Bio, Novartis, and Sanofi.

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Review

Respirology

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. 2023 Nov;28(11):1023-1035.

doi: 10.1111/resp.14593. Epub 2023 Sep 15.

[Asthma and landscape fire smoke: A Thoracic Society of Australia and New Zealand position statement](#)

[Vanessa M McDonald](#)^{1,2,3}, [Gregory Archbold](#)², [Tesfalidet Beyene](#)^{1,2}, [Bronwyn K Brew](#)⁴, [Peter Franklin](#)⁵, [Peter G Gibson](#)^{1,2,3}, [John Harrington](#)^{2,3}, [Philip M Hansbro](#)^{6,7}, [Fay H Johnston](#)⁸, [Paul D Robinson](#)^{9,10}, [Michael Sutherland](#)¹¹, [Deborah Yates](#)^{12,13}, [Graeme R Zosky](#)^{8,14}, [Michael J Abramson](#)¹⁵

Affiliations expand

- PMID: 37712340
- DOI: [10.1111/resp.14593](https://doi.org/10.1111/resp.14593)

Free article

Abstract

Landscape fires are increasing in frequency and severity globally. In Australia, extreme bushfires cause a large and increasing health and socioeconomic burden for communities and governments. People with asthma are particularly vulnerable to the effects of landscape fire smoke (LFS) exposure. Here, we present a position statement from the Thoracic Society of Australia and New Zealand. Within this statement we provide a review of the impact of LFS on adults and children with asthma, highlighting the greater impact of

LFS on vulnerable groups, particularly older people, pregnant women and Aboriginal and Torres Strait Islander peoples. We also highlight the development of asthma on the background of risk factors (smoking, occupation and atopy). Within this document we present advice for asthma management, smoke mitigation strategies and access to air quality information, that should be implemented during periods of LFS. We promote clinician awareness, and the implementation of public health messaging and preparation, especially for people with asthma.

Keywords: asthma; exacerbation; impacts risk; landscape fire smoke; management; mitigation; pathogenesis.

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Adv Ther

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. 2023 Nov;40(11):4721-4740.

doi: 10.1007/s12325-023-02647-2. Epub 2023 Sep 12.

[Efficacy of Biologics in Patients with Allergic Severe Asthma, Overall and by Blood Eosinophil Count: A Literature Review](#)

[Jonathan A Bernstein](#)^{1,2}, [Jean-Pierre Llanos](#)³, [Gillian Hunter](#)⁴, [Neil Martin](#)^{5,6}, [Christopher S Ambrose](#)⁷

Affiliations expand

- PMID: 37698716
- PMCID: [PMC10567947](#)
- DOI: [10.1007/s12325-023-02647-2](#)

Free PMC article

Abstract

Patients with uncontrolled, allergic severe asthma may be prescribed biologic therapies to reduce exacerbations and improve disease control. Randomized controlled trials (RCTs) of these therapies have differed in design, with varying results overall and by baseline blood eosinophil count (BEC). This study describes published annualized asthma exacerbation rate (AAER) reductions from RCTs in patients with allergic severe asthma, overall and by baseline BEC category. A literature search was performed to identify published phase 3 RCT data of US Food and Drug Administration–approved biologics for severe asthma in patients with severe, uncontrolled asthma and confirmed sensitization to perennial aeroallergens. Analyses focused on AAER reduction versus placebo in the overall population and/or in those with an elevated or low BEC at baseline or screening. Baseline serum total immunoglobulin E levels varied between RCT populations. In patients with allergic severe asthma across all BEC categories, data were available for tezepelumab, dupilumab, benralizumab and omalizumab only; the greatest AAER reduction was observed with tezepelumab. In patients with allergic severe asthma and BECs of ≥ 260 cells/ μL or ≥ 300 cells/ μL , AAER reductions were observed with all biologics (tezepelumab, dupilumab, mepolizumab, benralizumab and omalizumab); the greatest AAER reduction was observed with tezepelumab and the smallest AAER reduction was observed with omalizumab. In patients with allergic severe asthma and BECs of < 260 cells/ μL or < 300 cells/ μL (regardless of historical BEC), an AAER reduction was observed with tezepelumab

but not with benralizumab or omalizumab. Differential mechanisms of action may explain the differences in results observed between biologics. Among patients with allergic severe asthma, the efficacy of biologics in RCTs varied considerably overall and by BEC. Tezepelumab was the only biologic to demonstrate AAER reductions consistently across all subgroups. These differences can inform provider treatment decisions when selecting biologic treatments for patients with allergic severe asthma.

Keywords: Allergic asthma; Biologic; Blood eosinophil; Efficacy; Exacerbations; Literature review; Perennial allergy; Randomized placebo-controlled trial; Severe asthma.

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Conflict of interest statement

Jonathan A. Bernstein has served as a consultant for Amgen, AstraZeneca, Genentech, Merck, Novartis and Sanofi Regeneron; has participated in research with Amgen, AstraZeneca, Genentech, Merck, Novartis and Sanofi Regeneron; and has received speaker fees from AstraZeneca, Genentech, GSK, Novartis, Optinose and Sanofi Regeneron. Jean-Pierre Llanos is an employee of Amgen and owns stock in Amgen. Gillian Hunter, Neil Martin and Christopher S. Ambrose are employees of AstraZeneca and may own stock or stock options in AstraZeneca.

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- [3 figures](#)

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Immunotherapy

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. 2023 Nov;15(16):1389-1400.

doi: 10.2217/imt-2023-0072. Epub 2023 Sep 11.

Modification of allergen subcutaneous immunotherapy safety precautions and systemic allergic reaction rate reduction

[Keren Mahlab-Guri](#)¹, [David Mishayev](#)², [Marina Yakovlev](#)³, [Ilan Asher](#)¹, [Zev Sthoeger](#)¹, [Alex Guri](#)⁴, [Daniel Elbirt](#)¹, [Shay Nemet](#)¹, [Shira Rosenberg-Bezalel](#)¹

Affiliations expand

- PMID: 37694383
- DOI: [10.2217/imt-2023-0072](https://doi.org/10.2217/imt-2023-0072)

Abstract

Background: Despite their life-threatening potential, medical team mistakes during subcutaneous immunotherapy are rarely discussed. Real data are missing, and a survey study estimated that dosing errors are responsible for 25% of systemic reactions during immunotherapy. To minimize errors, we modified our safety precautions and compared the rates of systemic allergic reactions before and after the change. **Methods:** Our retrospective comparative cohort study compared systemic allergic reaction rates during 2012-2015 and 2016-2019, after a second check of the injected allergen/s by another nurse/physician was added to the treatment protocol. **Results:** The rate of systemic allergic reaction per injection was reduced from 0.93 to 0.71%; $p = 0.023$. **Conclusion:** A second check prior to injection is beneficial and can reduce the allergic reaction rate during immunotherapy.

Keywords: allergic rhinitis; asthma; safety precautions; subcutaneous immunotherapy; systemic allergic reaction.

Plain language summary

Many people suffer from allergies to dust or pollen, and they might suffer from a running nose when they come into contact with the allergens. This reaction is called hayfever or allergic rhinitis. Immunotherapy is a treatment which can help to treat patients with allergic

rhinitis. During treatment, the patients receive injections of small amounts of dust or pollen, and with time become less allergic. The injections themselves might cause allergic reactions such as rash, hives, swelling or trouble breathing. Sometimes these allergic reactions are related to mistakes made by the medical team. In our study we changed safety instruction to add a second check of the materials and amounts before the injections were given to the patient. This was checked by two different nurses. We compared the number of allergic reactions to the shots before and after the change. We found that the number of allergic reactions was 9.3 for 1000 injections before and 7.1 for 1000 injections after the change. We think that a second check of the materials and amounts before giving the injections is helpful and can prevent some of the allergic reactions.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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J Allergy Clin Immunol Glob

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. 2023 Nov;2(4):1-4.

doi: 10.1016/j.jacig.2023.100143.

[Reduced prevalence of childhood asthma after housing renovations in an underresourced community](#)

[Andrew F Beck](#)¹, [Larry Wymer](#)², [Eugene Pinzer](#)³, [Warren Friedman](#)³, [Peter J Ashley](#)³, [Stephen Vesper](#)²

Affiliations expand

- PMID: 37680344
- PMCID: [PMC10481638](#)
- DOI: [10.1016/j.jacig.2023.100143](#)

Free PMC article

Abstract

Background: Despite improvements in asthma symptom management and asthma morbidity, the prevalence of asthma in the United States remains high, especially in underresourced communities.

Objective: Our goal was to determine whether housing renovations affect the prevalence of asthma in an underresourced community.

Methods: The Fay Apartments (~800 units) in Cincinnati, Ohio, were renovated to "green building" standards between 2010 and 2012 and renamed the Villages at Roll Hill. The prevalence of asthma among 7-year-olds in the Villages at Roll Hill was determined by accessing Ohio Medicaid data for the years 2013 to 2021.

Results: In the first 6 years after the renovations (2013–2018), the prevalence of asthma among 7-year-olds in the community averaged 12.7%. In contrast, in postrenovation years 7 through 9 (2019–2021), the average prevalence of asthma was 5.9%. Logistic regression modeling for the log odds of asthma diagnosis in this age group was used to test the statistical significance of asthma prevalence for 2013–2018 versus for 2019–2021. The model resulted in demonstration of a significant ($P < .001$) reduction in asthma prevalence between 2013–2018 and 2019–2021.

Conclusions: The renovation of an underresourced community's housing resulted in a lower prevalence of asthma for 7-year-olds who were born after the renovations had been completed.

Keywords: African American; Black; asthma; green building; infants.

Conflict of interest statement

Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interest. The views expressed in this article are those of the authors and do not

necessarily represent the views or policies of the US Environmental Protection Agency (EPA). Any mention of trade names, products, or services does not imply an endorsement by the US government or the EPA. The EPA does not endorse any commercial products, services, or enterprises. The findings and conclusions in this article are those of the authors and do not necessarily represent the official positions of the EPA or US Department of Housing and Urban Development.

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

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Grants and funding [expand](#)

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Pediatr Pulmonol

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. 2023 Nov;58(11):3293-3302.

doi: 10.1002/ppul.26659. Epub 2023 Sep 6.

[Mechanisms of ventilatory limitation to maximum exercise in children and adolescents with chronic airway diseases](#)

[Márcio Vinícius Fagundes Donadio](#)^{1,2}, [Marta Amor Barbosa](#)¹, [Fernanda Maria Vendrusculo](#)², [Tamara Iturriaga Ramirez](#)³, [Elena Santana-Sosa](#)³, [Veronica Sanz-Santiago](#)⁴, [Margarita Perez-Ruiz](#)⁵

Affiliations expand

- PMID: 37671821
- DOI: [10.1002/ppul.26659](https://doi.org/10.1002/ppul.26659)

Abstract

Introduction: Exercise intolerance is common in chronic airway diseases (CAD), but its mechanisms are still poorly understood. The aim of this study was to evaluate exercise capacity and its association with lung function, ventilatory limitation, and ventilatory efficiency in children and adolescents with cystic fibrosis (CF) and asthma when compared to healthy controls.

Methods: Cross-sectional study including patients with mild-to-moderate asthma, CF and healthy children and adolescents. Anthropometric data, lung function (spirometry) and exercise capacity (cardiopulmonary exercise testing) were evaluated. Primary outcomes were peak oxygen consumption (VO_2 peak), forced expiratory volume in 1 s (FEV_1), breathing reserve (BR), ventilatory equivalent for oxygen consumption (V_E/VO_2) and for carbon dioxide production (V_E/VCO_2), both at the ventilatory threshold (VT_1) and peak exercise.

Results: Mean age of 147 patients included was 11.8 ± 3.0 years. There were differences between asthmatics and CF children when compared to their healthy peers for anthropometric and lung function measurements. Asthmatics showed lower VO_2 peak when compared to both healthy and CF subjects, although no differences were found between healthy and CF patients. A lower BR was found when CF patients were compared to both healthy and asthmatic. Both CF and asthmatic patients presented higher values for V_E/VO_2 and V_E/VCO_2 at VT_1 when compared to healthy individuals. For both V_E/VO_2 and V_E/VCO_2 at peak exercise CF patients presented higher values when compared to their healthy peers.

Conclusion: Patients with CF achieved good exercise capacity despite low ventilatory efficiency, low BR, and reduced lung function. However, asthmatics reported reduced cardiorespiratory capacity and normal ventilatory efficiency at peak exercise. These results demonstrate differences in the mechanisms of ventilatory limitation to maximum exercise testing in children and adolescents with CAD.

Keywords: asthma; breathing reserve; carbon dioxide production; cystic fibrosis; equivalent for oxygen consumption.

- [45 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Supplementary conceptsexpand

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Ann Am Thorac Soc

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. 2023 Nov;20(11):1614-1623.

doi: 10.1513/AnnalsATS.202305-481OC.

[Adverse Events during Adulthood, Child Maltreatment, and Asthma among British Adults in the UK Biobank](#)

[Yueh-Ying Han¹](#), [Wei Chen¹](#), [Erick Forno¹](#), [Juan C Celedón¹](#)

Affiliations expand

- PMID: 37668472
- DOI: [10.1513/AnnalsATS.202305-481OC](https://doi.org/10.1513/AnnalsATS.202305-481OC)

Abstract

Rationale: Intimate partner violence and child maltreatment have been separately associated with asthma in adults. No study has concurrently examined of adulthood adverse events (including, but not limited to, intimate partner violence) and child maltreatment on asthma in adults. **Objectives:** To concurrently examine of adulthood adverse events and child maltreatment on asthma in adults. **Methods:** This was a cross-sectional study of adulthood adverse events and child maltreatment on current asthma in 87,891 adults 40-69 years old who participated in the UK Biobank. Adulthood adverse events were assessed using questions adapted from a national crime survey. Child maltreatment was ascertained using the Childhood Trauma Screener questionnaire. Current asthma was defined as physician-diagnosed asthma and current wheeze and was further classified as noneosinophilic or eosinophilic according to eosinophil count (<300 vs. \geq 300 cells per microliter). **Results:** In a multivariable analysis, participants who reported two or more types of adulthood adverse events had 1.19-1.45 times significantly higher odds of asthma than those who did not, whereas participants who reported two or more types of child maltreatment had 1.25-1.59 significantly higher odds of asthma than those who reported no child maltreatment. After stratification by sex, similar results were obtained for child maltreatment in women and men, whereas adulthood adverse events were only significantly associated with asthma in women. Similar findings were observed in analyses that were restricted to never-smokers and former smokers with <10 pack-years of smoking and in analyses of noneosinophilic and eosinophilic asthma. **Conclusions:** In a cohort of British adults, child maltreatment was associated with current asthma in men and women, whereas adulthood adverse events were associated with current asthma in women only. This was independent of cigarette smoking or eosinophil count.

Keywords: UK Biobank; adults; adversity; asthma; child maltreatment.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grants and fundingexpand

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Am J Obstet Gynecol MFM

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. 2023 Nov;5(11):101147.

doi: 10.1016/j.ajogmf.2023.101147. Epub 2023 Sep 3.

Association between asthma and hypertensive disorders of pregnancy: a secondary analysis of the Nulliparous Pregnancy Outcomes Study: monitoring mothers-to-be (nuMoM2b) prospective cohort study

[Rachel Meislin](#)¹, [Sonali Bose](#)², [Xiaoning Huang](#)³, [Robert Wharton](#)⁴, [Jana Ponce](#)⁵, [Hyagriv Simhan](#)⁶, [David Haas](#)⁷, [George Saade](#)⁸, [Robert Silver](#)⁹, [Judith Chung](#)¹⁰, [Brian M Mercer](#)¹¹, [William A Grobman](#)¹², [Sadiya S Khan](#)¹³, [Angela Bianco](#)¹⁴

Affiliations expand

- PMID: 37660759
- DOI: [10.1016/j.ajogmf.2023.101147](https://doi.org/10.1016/j.ajogmf.2023.101147)

No abstract available

SUPPLEMENTARY INFO

Publication types expand

FULL TEXT LINKS



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. 2023 Nov;241:107746.

doi: 10.1016/j.cmpb.2023.107746. Epub 2023 Aug 10.

Automated detection of airflow obstructive diseases: A systematic review of the last decade (2013–2022)

[Shuting Xu](#)¹, [Ravinesh C Deo](#)², [Jeffrey Soar](#)³, [Prabal Datta Barua](#)⁴, [Oliver Faust](#)⁵, [Nusrat Homaira](#)⁶, [Adam Jaffe](#)⁷, [Arm Luthful Kabir](#)⁸, [U Rajendra Acharya](#)⁹

Affiliations expand

- PMID: 37660550
- DOI: [10.1016/j.cmpb.2023.107746](https://doi.org/10.1016/j.cmpb.2023.107746)

Abstract

Background and objective: Obstructive airway diseases, including asthma and Chronic Obstructive Pulmonary Disease (COPD), are two of the most common chronic respiratory health problems. Both of these conditions require health professional expertise in making a diagnosis. Hence, this process is time intensive for healthcare providers and the diagnostic quality is subject to intra- and inter- operator variability. In this study we investigate the role of automated detection of obstructive airway diseases to reduce cost and improve diagnostic quality.

Methods: We investigated the existing body of evidence and applied Preferred Reporting Items for Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to search records in IEEE, Google scholar, and PubMed databases. We identified 65 papers that were published from 2013 to 2022 and these papers cover 67 different studies. The review process was structured according to the medical data that was used for disease detection. We identified six main categories, namely air flow, genetic, imaging, signals, and miscellaneous. For each of these categories, we report both disease detection methods and their performance.

Results: We found that medical imaging was used in 14 of the reviewed studies as data for automated obstructive airway disease detection. Genetics and physiological signals were used in 13 studies. Medical records and air flow were used in 9 and 7 studies, respectively. Most papers were published in 2020 and we found three times more work on Machine Learning (ML) when compared to Deep Learning (DL). Statistical analysis shows that DL techniques achieve higher Accuracy (ACC) when compared to ML. Convolutional Neural Network (CNN) is the most common DL classifier and Support Vector Machine (SVM) is the most widely used ML classifier. During our review, we discovered only two publicly available asthma and COPD datasets. Most studies used private clinical datasets, so data size and data composition are inconsistent.

Conclusions: Our review results indicate that Artificial Intelligence (AI) can improve both decision quality and efficiency of health professionals during COPD and asthma diagnosis. However, we found several limitations in this review, such as a lack of dataset consistency, a limited dataset and remote monitoring was not sufficiently explored. We appeal to society to accept and trust computer aided airflow obstructive diseases diagnosis and we encourage health professionals to work closely with AI scientists to promote automated detection in clinical practice and hospital settings.

Keywords: Artificial Intelligence; Asthma; Chronic Obstructive Pulmonary Disease.

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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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Paediatr Drugs

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. 2023 Nov;25(6):677-693.

doi: 10.1007/s40272-023-00589-4. Epub 2023 Sep 2.

Developments in the Management of Severe Asthma in Children and Adolescents: Focus on Dupilumab and Tezepelumab

[Yoni E van Dijk](#)^{1,2}, [Niels W Rutjes](#)^{1,2}, [Korneliusz Golebski](#)¹, [Havva Şahin](#)², [Simone Hashimoto](#)^{1,2}, [Anke-Hilse Maitland-van der Zee](#)^{1,2}, [Susanne J H Vijverberg](#)^{3,4}

Affiliations [expand](#)

- PMID: 37658954
- PMCID: [PMC10600295](#)
- DOI: [10.1007/s40272-023-00589-4](#)

Free PMC article

Abstract

Severe asthma in children and adolescents exerts a substantial health, financial, and societal burden. Severe asthma is a heterogeneous condition with multiple clinical phenotypes and underlying inflammatory patterns that might be different in individual patients. Various add-on treatments have been developed to treat severe asthma, including monoclonal antibodies (biologics) targeting inflammatory mediators. Biologics that are currently approved to treat children (≥ 6 years of age) or adolescents (≥ 12 years of age) with severe asthma include: anti-immunoglobulin E (omalizumab), anti-interleukin (IL)-5 (mepolizumab), anti-IL5 receptor (benralizumab), anti-IL4/IL13 receptor (dupilumab),

and antithymic stromal lymphopoietin (TSLP) (tezepelumab). However, access to these targeted treatments varies across countries and relies on few and crude indicators. There is a need for better treatment stratification to guide which children might benefit from these treatments. In this narrative review we will assess the most recent developments in the treatment of severe pediatric asthma, as well as potential biomarkers to assess treatment efficacy for this patient population.

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Conflict of interest statement

N.R. has received a fee for participating in advisory boards for Sanofi (2021) and GSK (2018). A.H.M.v.d.Z. has been reimbursed for visiting the ATS by Chiesi, received a fee for participating in advisory boards for Boehringer Ingelheim and AstraZeneca, and received an unrestricted research grant from GSK. Y.E.v.D., G.K, S.H., S.H. and S.J.H.V. have nothing to disclose.

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

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

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Respir Med

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. 2023 Nov:218:107344.

doi: 10.1016/j.rmed.2023.107344. Epub 2023 Sep 1.

Dupilumab efficacy in high sleep disturbance management among patients with type 2 asthma

[Jorge F Maspero](#)¹, [Shirin Shafazand](#)², [Jeremy Cole](#)³, [Ian D Pavord](#)⁴, [William W Busse](#)⁵, [Jérôme Msihid](#)⁶, [Rebecca Gall](#)⁷, [Xavier Soler](#)⁷, [Amr Radwan](#)⁷, [Asif H Khan](#)⁶, [Lucia de Prado Gómez](#)⁸, [Juby A Jacob-Nara](#)⁹

Affiliations expand

- PMID: 37659435
- DOI: [10.1016/j.rmed.2023.107344](https://doi.org/10.1016/j.rmed.2023.107344)

Free article

Abstract

Background: Patients with asthma often experience sleep disturbances. We assessed the 5-item Asthma Control Questionnaire (ACQ-5) score ≥ 2.5 as a useful threshold to identify patients with moderate-to-severe type 2 asthma and high sleep disturbance (HSD) and investigated dupilumab efficacy on clinical and sleep-related outcomes among patients with HSD.

Methods: QUEST ([NCT02414854](#)) data were used in this post hoc analysis. A composite endpoint from validated patient-reported outcomes was developed to identify patients with HSD using sleep-related items from the ACQ-5, Asthma-Related Quality-of-Life Questionnaire, Rhino-Conjunctivitis Quality-of-Life Questionnaire, and Sino-Nasal Outcome Test-22. Impairment in at least 1 item was considered an indication of HSD. Change from baseline to Week 52 in nighttime symptoms, ACQ-5 score, lung function, annualized severe exacerbation rates (AER), and short-acting β -agonists use during treatment was used to assess dupilumab efficacy.

Results: In type 2 asthma patients, 64% had HSD at baseline; of those with ACQ-5 ≥ 2.5 at baseline, 82% had HSD. In this population, dupilumab reduced nighttime symptoms and ACQ-5 score by 0.31 and 0.56 points, respectively, by Week 52 versus placebo, and led to a 66% reduction in AER during QUEST and 0.34 L improvement in pre-bronchodilator (pre-BD) forced expiratory volume in 1 s (FEV₁) at Week 52.

Conclusion: A majority of patients with moderate-to-severe type 2 asthma with ACQ-5 ≥ 2.5 at baseline had HSD. Dupilumab reduced nighttime symptoms and exacerbations,

and improved lung function, overall asthma control, and quality of life. Further studies are needed to confirm the association between ACQ-5 score ≥ 2.5 and higher sleep disturbance rates.

Keywords: Antibodies; Asthma; Biological products; Monoclonal; Quality of life; Questionnaires; Sleep quality.

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Thorax

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. 2023 Nov;78(11):1138-1141.

doi: 10.1136/thorax-2022-219781. Epub 2023 Sep 1.

[Super-responders to anti-IL-5/anti-IL-5R are characterised by high sputum eosinophil counts at baseline](#)

[Sara Gerday](#)¹, [Sophie Graff](#)², [Catherine Moermans](#)², [Françoise Guissard](#)³, [Virginie Paulus](#)³, [Monique Henket](#)³, [Renaud Louis](#)^{2,3}, [Florence Schleich](#)^{2,3}

Affiliations expand

- PMID: 37657926

- DOI: [10.1136/thorax-2022-219781](https://doi.org/10.1136/thorax-2022-219781)

Free article

Abstract

Several clinical trials have demonstrated that anti-IL-5(R) biologics were able to improve lung function, asthma control and chronic oral corticosteroid exposure and reduce exacerbations among eosinophilic asthmatic patients. However, a certain variability in clinical responses to anti-IL-5(R) biologics was brought to light. Our study aimed at evaluating the role of baseline sputum eosinophils in identifying super-responders to mepolizumab and benralizumab. Our study reinforces the importance to examine sputum eosinophils in patients suffering from severe asthma before starting a biologic as it is associated with the intensity of response to mepolizumab and benralizumab.

Keywords: Asthma.

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Conflict of interest statement

Competing interests: GERDAY Sara, GRAFF Sophie, MOERMANS Catherine, GUISSARD Françoise, PAULUS Virginie and HENKET Monique declare no competing interests. LOUIS Renaud reports grants from GSK, Astrazeneca, Chiesi; royalties from patent AU2016328384, CA2997506, EP 3337393, US2020345266; consulting fees from Astrazeneca; lecture payments from GSK, Chiesi; participation on a data safety monitoring board or advisory board for Astrazeneca ANDHI in practice study and leadership or fiduciary role in other board, society, committee or advocacy group for ERS task force on guidelines on asthma diagnosis, outside the submitted work. SCHLEICH Florence reports grants from GSK, Astrazeneca, Chiesi; consulting fees from GSK, Astrazeneca, Sanofi; lecture payments from GSK, Astrazeneca, Teva, Chiesi and Amgen and support for attending meetings/travel from Chiesi, outside the submitted work.

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Pediatr Pulmonol



. 2023 Nov;58(11):3113-3121.

doi: 10.1002/ppul.26630. Epub 2023 Sep 1.

[Examining barriers and facilitators in asthma inhaler technique education and technology-enhanced educational tools in children: A mixed methods evaluation using the theoretical domains framework](#)

[Antonia O'Connor](#)^{1,2}, [Andrew Tai](#)^{1,2,3}, [Malcolm Brinn](#)^{4,5}, [Amy Hoang](#)⁶, [Daniele Cataldi](#)⁶, [Kristin Carson-Chahhoud](#)^{2,4,5}

Affiliations expand

- PMID: 37655538
- DOI: [10.1002/ppul.26630](https://doi.org/10.1002/ppul.26630)

Abstract

Introduction: Educational interventions for asthma inhaler technique have been identified as successful in improving technique in children, yet inhaler technique has not improved over time. New approaches should be considered, including the use of technology-based interventions such as smartphone and tablet applications. Adoption and implementation of such technology in healthcare has been historically slow. This mixed-methods study aimed

to identify the barriers and facilitators of delivering and receiving asthma inhaler education for children in a hospital setting, including technology-based interventions.

Methods: Children with asthma, their caregivers, and healthcare professionals who regularly provide asthma education, were invited to participate in a qualitative interview and brief questionnaire to describe their experiences, knowledge, beliefs, and recommendations about asthma education delivery. The Theoretical Domains Framework was used to develop questions for the semistructured moderator guide, questionnaire, and provide the rigorous evaluation framework for deductive thematic analysis.

Results: Sixteen interviews and questionnaires were conducted with participants. Overall, healthcare professionals perceived more barriers in asthma inhaler education delivery than asthmatic children and their caregivers to receiving the education. Healthcare professionals and caregivers identified time-pressures within a hospital setting as a barrier for providing sufficient education. However, all participants felt they had adequate knowledge in their asthma management skills and inhaler technique. Technology-based innovations were viewed positively by all participant groups to improve asthma education.

Conclusions: Several barriers and facilitators to current hospital-based asthma education delivery were reported by target end-users. Future programs should consider these findings when developing asthma inhaler educational interventions, particularly those using technology-enhanced information delivery.

Keywords: asthma; asthma education; behavior change; inhaler technique; technology-based interventions.

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. 2023 Nov 1;325(5):L552-L567.

doi: 10.1152/ajplung.00192.2023. Epub 2023 Aug 29.

Early-life exposure to cigarette smoke primes lung function and DNA methylation changes at *Cyp1a1* upon exposure later in life

[Chinonye Doris Onuzulu](#)¹, [Samantha Lee](#)¹, [Sujata Basu](#)², [Jeannette Comte](#)², [Yan Hai](#)¹, [Nikhon Hizon](#)¹, [Shivam Chadha](#)¹, [Maria Shenna Fauni](#)¹, [Shana Kahnemou](#)^{2,3}, [Bo Xiang](#)^{2,4}, [Andrew J Halayko](#)^{2,3}, [Vernon W Dolinsky](#)^{2,4}, [Christopher D Pascoe](#)^{2,3}, [Meaghan J Jones](#)^{1,2}

Affiliations expand

- PMID: 37642652
- DOI: [10.1152/ajplung.00192.2023](https://doi.org/10.1152/ajplung.00192.2023)

Free article

Abstract

Prenatal and early-life exposure to cigarette smoke (CS) has repeatedly been shown to induce stable, long-term changes in DNA methylation (DNAm) in offspring. It has been hypothesized that these changes might be functionally related to the known outcomes of prenatal and early-life CS exposure, which include impaired lung development, altered lung function, and increased risk of asthma and wheeze. However, to date, few studies have examined DNAm changes induced by prenatal CS in tissues of the lung, and even fewer have attempted to examine the specific influences of prenatal versus early postnatal exposures. Here, we have established a mouse model of CS exposure which isolates the effects of prenatal and early postnatal CS exposures in early life. We have used this model to measure the effects of prenatal and/or postnatal CS exposures on lung function and immune cell infiltration as well as DNAm and expression of *Cyp1a1*, a candidate gene previously observed to demonstrate DNAm differences on CS exposure in humans. Our study revealed that exposure to CS prenatally and in the early postnatal period causes long-lasting differences in offspring lung function, gene expression, and

lung *Cyp1a1* DNAm, which wane over time but are reestablished on reexposure to CS in adulthood. This study creates a testable mouse model that can be used to investigate the effects of prenatal and early postnatal CS exposures and will contribute to the design of intervention strategies to mediate these detrimental effects. **NEW & NOTEWORTHY** Here, we isolated effects of prenatal from early postnatal cigarette smoke and showed that exposure to cigarette smoke early in life causes changes in offspring DNA methylation at *Cyp1a1* that last through early adulthood but not into late adulthood. We also showed that smoking in adulthood reestablished these DNA methylation patterns at *Cyp1a1*, suggesting that a mechanism other than DNA methylation results in long-term memory associated with early-life cigarette smoke exposures at this gene.

Keywords: DNA methylation; cigarette smoke; early life; lung function; priming.

SUPPLEMENTARY INFO

MeSH terms, Substances, Grants and fundingexpand

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Review

Pediatr Pulmonol

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. 2023 Nov;58(11):3032-3037.

doi: 10.1002/ppul.26654. Epub 2023 Aug 29.

[Pediatric pulmonology 2022 year in review: Asthma](#)

[Nicole Stephenson](#)¹, [Andre Espaillet](#)¹, [Ceila E Loughlin](#)¹

Affiliations expand

- PMID: 37642280
- DOI: [10.1002/ppul.26654](https://doi.org/10.1002/ppul.26654)

Abstract

In 2022, new research studies influenced the field of pediatric asthma with improvements in diagnosis and evaluation; new treatment options including biologic therapies; changes in risk factors for asthma; and increased discussion about the impact of social determinants of health on asthma. Additionally, three years after the start of the COVID-19 pandemic, we continue to see the impact of SARS-CoV-2 virus on pediatric asthma care. In this review article, we summarize the significant findings from publications in Pediatric Pulmonology and other relevant journals from the last year. We hope this review will provide new insight within the field of pediatric asthma, as well as guidance for implementation into clinical practice.

Keywords: allergy; asthma; child; pediatric; wheezing.

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- [25 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Respirology

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. 2023 Nov;28(11):1078-1079.

doi: 10.1111/resp.14583. Epub 2023 Aug 23.

Can we predict asthma exacerbations?

[Fanny Wai San Ko](#)¹

Affiliations expand

- PMID: 37610215
- DOI: [10.1111/resp.14583](https://doi.org/10.1111/resp.14583)

Free article

No abstract available

Keywords: asthma; exacerbations; prediction.

SUPPLEMENTARY INFO

MeSH termsexpand

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49

Respirology

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. 2023 Nov;28(11):986-988.

doi: 10.1111/resp.14585. Epub 2023 Aug 23.

[Asthma registries: Tedious paperwork or a versatile tool for the generation of knowledge–Insights from the Australasian Severe Asthma Registry \(ASAR\)](#)

[Erin S Harvey](#)^{1,2,3}, [Matthew J Peters](#)^{4,5}

Affiliations [expand](#)

- PMID: 37609796
- DOI: [10.1111/resp.14585](https://doi.org/10.1111/resp.14585)

Free article

No abstract available

Keywords: clinical quality registry; real-world; registry; severe asthma.

- [15 references](#)

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Review



Eosinophilic plastic bronchitis: Case series and review of the literature

[Alexander I Gipsman¹](#), [Lance Feld¹](#), [Brandy Johnson¹](#), [Joshua P Needleman²](#), [Heather Boas¹](#), [Nancy Lin^{1,3}](#), [Brittany DePasquale⁴](#), [Jennifer Pogoriler^{3,5}](#), [Karen M McDowell⁶](#), [Joseph C Piccione^{1,3}](#)

Affiliations expand

- PMID: 37606213
- DOI: [10.1002/ppul.26650](https://doi.org/10.1002/ppul.26650)

Abstract

Plastic bronchitis is a term used to describe group of life-threatening disorders characterized by the presence of large obstructing casts in the airways. Eosinophilic plastic bronchitis is a subtype of plastic bronchitis that occurs mainly in children and has not been well-described in the literature. Patients may have a history of asthma or atopy, but many do not. They often present with cough and wheezing, and frequently have complete collapse of one lung seen on imaging. The severity of presentation varies depending on the location of the casts, ranging from mild symptoms to severe airway obstruction and death. Bronchoscopy is often required to both diagnose and treat this condition. A variety of medical therapies have been used, although no formal studies have evaluated their efficacy. Symptoms may resolve after initial cast removal, but in some patients, cast formation recurs. Here, we report a case series of nine patients with eosinophilic plastic bronchitis and review the existing literature of this condition.

Keywords: Charcot–Leyden crystals; asthma; asthma & early wheeze; bronchoscopy; cryoextraction; mucus disorders; plastic bronchitis; pulmonology (general).

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Randomized Controlled Trial

Am J Respir Crit Care Med

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. 2023 Nov 1;208(9):995-997.

doi: 10.1164/rccm.202306-1102LE.

[Effects of Dupilumab on Mucus Plugging and Ventilation Defects in Patients with Moderate-to-Severe Asthma: A Randomized, Double-Blind, Placebo-Controlled Trial](#)

[Sarah Svenningsen](#)^{1,2,3}, [Melanie Kjarsgaard](#)^{1,3}, [Ehsan Haider](#)^{2,4}, [Carmen Venegas](#)^{1,3}, [Norman Konyer](#)², [Yonni Friedlander](#)^{1,2}, [Neha Nasir](#)⁵, [Colm Boylan](#)^{2,4}, [Miranda Kirby](#)⁵, [Parameswaran Nair](#)^{1,3}

Affiliations expand

- PMID: 37603097

- DOI: [10.1164/rccm.202306-1102LE](https://doi.org/10.1164/rccm.202306-1102LE)

No abstract available

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doi: 10.1016/j.envpol.2023.122396. Epub 2023 Aug 16.

[Short-term exposure to ultrafine particles and mortality and hospital admissions due to respiratory and cardiovascular diseases in Copenhagen, Denmark](#)

[Marie L Bergmann](#)¹, [Zorana J Andersen](#)¹, [Andreas Massling](#)², [Paula A Kindler](#)³, [Steffen Loft](#)¹, [Heresh Amini](#)⁴, [Thomas Cole-Hunter](#)¹, [Yuming Guo](#)⁵, [Matija Maric](#)¹, [Claus Nordstrøm](#)², [Mahmood Taghavi](#)¹, [Stéphane Tuffier](#)¹, [Rina So](#)¹, [Jiawei Zhang](#)¹, [Youn-Hee Lim](#)⁶

Affiliations expand

- PMID: 37595732
- DOI: [10.1016/j.envpol.2023.122396](https://doi.org/10.1016/j.envpol.2023.122396)

Free article

Abstract

Ultrafine particles (UFP; particulate matter <0.1 μm in diameter) may be more harmful to human health than larger particles, but epidemiological evidence on their health effects is still limited. In this study, we examined the association between short-term exposure to UFP and mortality and hospital admissions in Copenhagen, Denmark. Daily concentrations of UFP (measured as particle number concentration in a size range 11-700 nm) and meteorological variables were monitored at an urban background station in central Copenhagen during 2002-2018. Daily counts of deaths from all non-accidental causes, as well as deaths and hospital admissions from cardiovascular and respiratory diseases were obtained from Danish registers. Mortality and hospital admissions associated with an interquartile range (IQR) increase in UFP exposure on a concurrent day and up to six preceding days prior to the death or admission were examined in a case-crossover study design. Odds ratios (OR) with 95% confidence intervals (CI) per one IQR increase in UFP were estimated after adjusting for temperature and relative humidity. We observed 140,079 deaths in total, 236,003 respiratory and 342,074 cardiovascular hospital admissions between 2002 and 2018. Hospital admissions due to respiratory and cardiovascular diseases were significantly positively associated with one IQR increase in UFP (OR: 1.04 [95% CI: 1.01, 1.07], lag 0-4, and 1.02 [1.00, 1.04], lag 0-1, respectively). Among the specific causes, the strongest associations were found for chronic obstructive pulmonary disease (COPD) mortality and asthma hospital admissions and two-day means (lag 0-1) of UFP (OR: 1.13 [1.01, 1.26] and 1.08 [1.00, 1.16], respectively, per one IQR increase in UFP). Based on 17 years of UFP monitoring data, we present novel findings showing that short-term exposure to UFP can trigger respiratory and cardiovascular diseases mortality and morbidity in Copenhagen, Denmark. The strongest associations with UFP were observed with COPD mortality and asthma hospital admissions.

Keywords: Air pollution; Cardiovascular diseases; Mortality; Particle number concentration; Respiratory tract diseases; Ultrafine particles.

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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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Respir Med



. 2023 Nov;218:107391.

doi: 10.1016/j.rmed.2023.107391. Epub 2023 Aug 16.

[Impulse oscillometry defined small airway dysfunction in asthmatic patients with normal spirometry: Prevalence, clinical associations, and impact on asthma control](#)

[Marcello Cottini](#)¹, [Benedetta Bondi](#)², [Diego Bagnasco](#)³, [Fulvio Braido](#)³, [Giovanni Passalacqua](#)³, [Anita Licini](#)¹, [Carlo Lombardi](#)⁴, [Alvise Berti](#)⁵, [Pasquale Comberiati](#)⁶, [Massimo Landi](#)⁷, [Enrico Heffler](#)⁸, [Giovanni Paoletti](#)⁸

Affiliations expand

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Abstract

Background: The small-airway dysfunction (SAD), detected with impulse oscillometry (IOS) methods, has been recently better characterized in patients with asthma. However, little is known about SAD in asthmatic patients with normal spirometry (NS).

Objective: In this study, we aimed to investigate, in an unselected sample of 321 patients with physician-diagnosed asthma and NS, prevalence, clinical characterization, and impact on asthma control of IOS-defined SAD. As a secondary objective of the study, we focused on comparing the difference between IOS- and spirometry-defined SAD.

Methods: Consecutive patients with a previous diagnosis of asthma but normal spirometry at the moment of the enrollment were stratified by the presence of IOS-defined SAD (difference in resistance at 5 Hz and at 20 Hz [R5-R20] greater than $0.07 \text{ kPa} \times \text{s} \times \text{L}^{-1}$). We have also assessed the presence of SAD defined by spirometry, according to $\text{FEF}_{25-75} < 65\%$ of the predicted. Clinical and laboratory features were collected, and univariable and multivariable analyses were used to analyze cross-sectional associations between clinical variables and outcomes (SAD).

Results: IOS-defined SAD was present in 54.1% of the cohort. In contrast, spirometry-defined SAD was present in only 10% of patients. Subjects with IOS-defined SAD showed less well-controlled asthma and a higher mean inhaled corticosteroid dosage use compared with subjects without SAD (both $P < .001$). Overweight (odds ratio [OR], 1.14; 95% CI, 1.05-1.23), exacerbation history (OR, 3.06; 95% CI, 1.34-6.97), asthma-related night awakenings (OR, 6.88; 95% CI, 2.13-22.23), exercise-induced asthma symptoms (OR, 33.5; 95% CI, 9.51-117.8), and controlled asthma (OR, 0.22; 95% CI, 0.06-0.84) were independently associated with SAD.

Conclusions: Asthmatic patients with IOS-defined SAD showed less well-controlled asthma, more severe exacerbations and higher mean inhaled corticosteroid dosage. We confirmed exercise-induced asthma, asthma-related night awakenings, exacerbation history, and overweight as independently associated with SAD, while showing well-controlled asthma as inversely associated. SAD may be overlooked by standard spirometry.

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Conflict of interest statement

Declaration of competing interest All authors have no conflicts of interest to disclose about this paper.

SUPPLEMENTARY INFO

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Pediatr Pulmonol

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. 2023 Nov;58(11):3349-3353.

doi: 10.1002/ppul.26638. Epub 2023 Aug 18.

[The relation of prenatal acid suppressant medication exposure to severe bronchiolitis and childhood asthma](#)

[Anna Chen Arroyo](#)¹, [Lacey B Robinson](#)², [Kaitlyn James](#)^{3,4}, [Sijia Li](#)⁵, [Mohammad Kamal Faridi](#)⁵, [Camille E Powe](#)^{3,4,6}, [Carlos A Camargo Jr](#)^{3,5,7}

Affiliations expand

- PMID: 37594143
- DOI: [10.1002/ppul.26638](https://doi.org/10.1002/ppul.26638)

No abstract available

- [7 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grants and funding expand

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Review

Am J Rhinol Allergy

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. 2023 Nov;37(6):766-776.

doi: 10.1177/19458924231193528. Epub 2023 Aug 9.

[Efficacy of Sublingual Immunotherapy in Allergic Rhinitis Patients with Asthma: A Systematic Review and Meta-Analysis](#)

[Dijiang Ma](#)¹, [Qiling Zheng](#)¹, [Jianing Sun](#)¹, [Shenjun Tang](#)¹, [Wudan He](#)¹

Affiliations expand

- PMID: 37559376
- DOI: [10.1177/19458924231193528](https://doi.org/10.1177/19458924231193528)

Abstract

Objective: Sublingual immunotherapy (SLIT) has been widely applied to treat patients with allergic rhinitis (AR). However, meta-analyses on the efficacy of SLIT in AR patients with asthma are still limited.

Methods: Literature without language limitation published before October 28, 2022, were retrieved from PubMed, EMBASE, and Cochrane Library. STATA 16.0 software was used for the meta-analysis of the extracted data. The results reported were symptom scores, drug scores, adverse effects rates, and cost of treatment.

Results: Ten studies involving 1722 patients met the inclusion criteria. The total rhinitis score (TRSS) (weighted mean difference [WMD] = -1.23, 95% CI: -1.39--1.06, $P < .001$) and total asthma symptom score (TASS) (WMD = -1.00, 95% CI: -1.12-0.89, $P < .001$) were significantly lower in the SLIT group than the placebo group. The SLIT group had higher rates of treatment-related adverse events (relative risk [RR] = 2.82, 95% CI: 1.77-4.48, $P < .001$) and total costs of treatment (standardized mean difference [SMD] = 0.71, 95% CI: 0.45-0.97, $P < .001$). There was no significant difference in inhaled corticosteroids (ICS) dose ($P = .195$), fractional exhaled nitric oxide (FeNO) ($P = .158$), forced expiratory volume in 1 s (FEV1) ($P = .237$), and direct costs of treatment ($P = .630$) between the SLIT and placebo groups.

Conclusion: SLIT may be a therapeutic method for improving rhinitis symptoms and asthma symptoms in AR patients with asthma. However, as there was significant heterogeneity in results, more high-quality and well-designed studies are needed in the future to elucidate the efficacy of SLIT.

Keywords: allergic rhinitis; asthma; efficacy; meta-analysis; sublingual immunotherapy.

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

Publication types, MeSH terms, Substancesexpand

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56

Respirology



. 2023 Nov;28(11):1053-1059.

doi: 10.1111/resp.14568. Epub 2023 Aug 7.

Safety and efficacy of bronchial thermoplasty in Australia 5 years post-procedure

[Monica Hatch](#)¹, [Paul Lilburn](#)^{2,3}, [Caroline Scott](#)⁴, [Alvin Ing](#)³, [David Langton](#)^{1,5}

Affiliations expand

- PMID: 37550800
- DOI: [10.1111/resp.14568](https://doi.org/10.1111/resp.14568)

Free article

Abstract

Background and objective: Outside clinical trials, there is limited long-term data following bronchial thermoplasty (BT). In a cohort of real-world severe asthmatics in an era of biological therapy, we sought to evaluate the safety and efficacy of BT 5 years post-treatment.

Methods: Every patient treated with BT at two Australian tertiary centres were recalled at 5 years, and evaluated by interview and record review, Asthma Control Questionnaire (ACQ), spirometry and high-resolution CT Chest. CT scans were interpreted using the modified Reiff and BRICS CT scoring systems for bronchiectasis.

Results: Fifty-one patients were evaluated. At baseline, this cohort had a mean age of 59.0 ± 11.8 years, mean ACQ of 3.0 ± 1.0, mean FEV1 of 55.5 ± 18.8% predicted, and 53% were receiving maintenance oral steroids in addition to triple inhaled therapy. At 5 years, there was a sustained improvement in ACQ scores to 1.8 ± 1.0 (p < 0.001). Steroid requiring

exacerbation frequency was reduced from 3.8 ± 3.6 to 1.0 ± 1.6 exacerbations per annum ($p < 0.001$). 44% of patients had been weaned off oral steroids. No change in spirometry was observed. CT scanning identified minor degrees of localized radiological bronchiectasis in 23/47 patients with the modified Reiff score increasing from 0.6 ± 2.6 at baseline to 1.3 ± 2.5 ($p < 0.001$). However, no patients exhibited clinical features of bronchiectasis, such as recurrent bacterial infection.

Conclusion: Sustained clinical benefit from BT at 5 years was demonstrated in this cohort of very severe asthmatics. Mild, localized radiological bronchiectasis was identified in a portion of patients without clinical features of bronchiectasis.

Keywords: BT; asthma; bronchial thermoplasty; bronchoscopy and interventional techniques; cohort study; radiological bronchiectasis.

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J Affect Disord

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. 2023 Nov 1:340:312-320.

doi: 10.1016/j.jad.2023.08.037. Epub 2023 Aug 6.

Maternal anxiety during pregnancy and children's asthma in preschool age: The Ma'anshan birth cohort study

[Ji-Xing Zhou](#)¹, [Yufan Guo](#)¹, [Yu-Zhu Teng](#)¹, [Lin-Lin Zhu](#)¹, [Jingru Lu](#)¹, [Xue-Mei Hao](#)¹, [Shuang-Qin Yan](#)², [Fang-Biao Tao](#)¹, [Kun Huang](#)³

Affiliations expand

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- DOI: [10.1016/j.jad.2023.08.037](https://doi.org/10.1016/j.jad.2023.08.037)

Abstract

Background: The fetal immune system and consequent elevated risk of asthma in childhood may be impacted by maternal anxiety during pregnancy. Limited studies have evaluated whether there was a sensitive period and cumulative effect of the relationship between prenatal anxiety and children's asthma.

Methods: 3131 mother-child pairs made up the study's sample from the Ma'anshan Birth Cohort Study in China. Maternal anxiety status was repeated three times using the pregnancy-related anxiety questionnaire in the 1st, 2nd and 3rd trimesters of pregnancy. Diagnostic information on asthma was collected three times at 24, 36, and 48 months of age.

Results: After adjusting for confounders, children born to mothers with anxiety in the 1st, 2nd and 3rd trimesters of pregnancy all had an elevated risk of total asthma from 12 to 48 months of age. After further adjusting prenatal anxiety in the other trimesters, no association was observed between prenatal anxiety in any trimester and preschoolers' asthma. Children of mothers with persistently high anxiety score trajectory during pregnancy had an elevated risk of total asthma and high prevalence trajectory of asthma. Cumulative effects analysis showed that the more frequent the mother's anxiety, the higher the risk of her offspring developing a high prevalence trajectory of asthma from 12 to 48 months of age. The results of the subgroup analysis by age showed similar associations overall.

Conclusions: Maternal antenatal anxiety was associated with an elevated risk of preschool children's asthma, and a possible cumulative effect was observed. Maternal mental health conditions during pregnancy should receive constant attention throughout pregnancy, not just during one period.

Keywords: Anxiety; Asthma; Cohort; Pregnancy; Preschool age; Trajectory.

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Conflict of interest statement

Declaration of competing interest We declare no competing interests in this study. Ethics approval and consent to participate: all participants have signed an informed consent form; the study was approved by the ethics committees of Anhui medical university (No. 20131195). We confirm that all methods in this study were performed in accordance with the relevant guidelines and regulations.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Respir Med

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. 2023 Nov;218:107375.

doi: 10.1016/j.rmed.2023.107375. Epub 2023 Aug 1.

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

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

Affiliations expand

- PMID: 37536444
- DOI: [10.1016/j.rmed.2023.107375](https://doi.org/10.1016/j.rmed.2023.107375)

Abstract

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

Procedures: We examined the baseline change in FEV1 and FVC in response to albuterol among 931 participants with poorly controlled asthma pooled from three clinical trials conducted by the American Lung Association - Airways Clinical Research Centers. We defined BDR based on four definitions and analyzed the association of each with asthma control as measured by the Asthma Control Test or Asthma Control Questionnaire, and asthma symptom burden as measured by the Asthma Symptom Utility Index.

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

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

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

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Conflict of interest statement

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

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Pediatr Pulmonol

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. 2023 Nov;58(11):3046-3053.

doi: 10.1002/ppul.26617. Epub 2023 Aug 2.

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

[Colin Rogerson](#)^{1,2}, [Arthur Owora](#)¹, [Tian He](#)³, [Aaron Carroll](#)¹, [Titus Schleyer](#)², [Samer AbuSultaneh](#)¹, [Wanzhu Tu](#)³, [Eneida Mendonca](#)^{1,4}

Affiliations expand

- PMID: 37530483
- DOI: [10.1002/ppul.26617](https://doi.org/10.1002/ppul.26617)

Abstract

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

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

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

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

Keywords: critical care; informatics; pediatrics; pulmonology.

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Editorial

Thorax

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. 2023 Nov;78(11):1061-1062.

doi: 10.1136/thorax-2023-220454. Epub 2023 Jul 31.

'Let Africa Breathe': air pollution, environmental exposures and lung health – an ongoing challenge

[Aneesa Vanker](#)¹

Affiliations expand

- PMID: 37524390
- DOI: [10.1136/thorax-2023-220454](https://doi.org/10.1136/thorax-2023-220454)

No abstract available

Keywords: Asthma; Clinical Epidemiology.

Conflict of interest statement

Competing interests: None declared.

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Publication types, MeSH terms, Substancesexpand

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Meta-Analysis

Respir Med



. 2023 Nov;218:107377.

doi: 10.1016/j.rmed.2023.107377. Epub 2023 Jul 29.

[A network meta-analysis of the association between patient traits and response to regular dosing with ICS/long-acting \$\beta_2\$ -agonist plus short-acting \$\beta_2\$ agonist reliever or maintenance and reliever therapy for asthma](#)

[Arzu Yorgancioğlu](#)¹, [Alvaro A Cruz](#)², [Gabriel Garcia](#)³, [Kim L Lavoie](#)⁴, [Nicolas Roche](#)⁵, [Abhijith P G](#)⁶, [Manish Verma](#)⁷, [Anurita Majumdar](#)⁸, [Swarnendu Chatterjee](#)⁹

Affiliations expand

- PMID: 37524150
- DOI: [10.1016/j.rmed.2023.107377](https://doi.org/10.1016/j.rmed.2023.107377)

Free article

Abstract

Introduction: Current treatment for moderate-severe asthma with inhaled corticosteroid (ICS)-based therapy can follow two strategies: a single inhaler maintenance and reliever therapy (MART) regimen, or regular dosing with ICS/long-acting β_2 -agonist used as maintenance therapy plus a separate short acting β_2 -agonist reliever inhaler. It would be clinically useful to understand the potential of patient traits to influence regular dosing or MART treatment outcomes.

Objectives: A systematic literature review (SLR) and meta-analysis was conducted to identify specific patient traits that may predict improved clinical outcomes with regular dosing or MART.

Results: The SLR identified 28 studies in patients with moderate-severe asthma assessing regular dosing or MART treatments and reporting the traits and outcomes of interest. Network meta-regressions found no significant difference in the relative efficacy of regular dosing as compared with MART on any of the clinical outcomes (exacerbation rate, time to first exacerbation, FEV₁, reliever use and adherence) for any of the patient traits (baseline lung function, baseline ACQ, age, BMI, and smoking history) evaluated. However, some trends towards traits influencing treatment efficacy were identified. Inconsistent reporting of traits and outcomes was observed between trials.

Conclusions: The analysed patient traits evaluated in this study were associated with similar efficacy for the analysed outcomes to either regular dosing or MART; however, trends from the data observed encourage future analyses for possible identification of additional traits, or a combination of traits, that may be of interest. More comparable reporting of clinically important traits and outcomes would improve future analyses.

Keywords: Asthma; Maintenance therapy; Patient characteristics; Reliever therapy.

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Conflict of interest statement

Declaration of competing interest The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Arzu Yorgancioğlu has received research grants from Novartis, MSD, AstraZeneca, and Sanofi, and has acted as a speaker/consultant for AstraZeneca, Abdi İbrahim, GSK, Novartis, Chiesi and Bilim. Alvaro Cruz has received personal fees from GSK, AstraZeneca, Sanofi, Boehringer Ingelheim, Chiesi, Crossjet, Eurofarma, Abdi Ibrahim and Glennmark. Gabriel Garcia has received research grants from Novartis, GSK, Boehringer Ingelheim, AstraZeneca, and Sanofi, and for acting as a consultant/advisor/speaker for GSK, AstraZeneca, Novartis, and Sanofi. Kim L. Lavoie has received consulting fees/speaker fees from GSK, Abbvie, Boehringer Ingelheim, Janssen, Bausch, Astellas, Novartis, AstraZeneca, X-Facto and Sojecci Inc. Nicolas Roche has received grants and personal fees from Boehringer Ingelheim, Novartis, Pfizer, GSK and personal fees from Austral, Biosency, MSD, AstraZeneca, Chiesi, Sanofi, Zambon. Abhijith PG was employed by GSK at the time of the study. Manish Verma, Anurita Majumdar and Swarnendu Chatterjee are full time employees of GSK and hold stocks/shares in GSK.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Respir Med

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. 2023 Nov:218:107361.

doi: 10.1016/j.rmed.2023.107361. Epub 2023 Jul 28.

[EUFOREA pocket guide on the diagnosis and management of asthma: An](#)

educational and practical tool for general practitioners, non-respiratory physicians, paramedics and patients

[Zuzana Diamant](#)¹, [Milos Jesenak](#)², [Nicola A Hanania](#)³, [Liam G Heaney](#)⁴, [Ratko Djukanovic](#)⁵, [Dermot Ryan](#)⁶, [Santiago Quirce](#)⁷, [Vibeke Backer](#)⁸, [Mina Gaga](#)⁹, [Ian Pavord](#)¹⁰, [Darío Antolín-Amérigo](#)¹¹, [Sara Assaf](#)¹², [Petros Bakakos](#)¹³, [Anna Bobcakova](#)¹⁴, [William Busse](#)¹⁵, [Jasper Kappen](#)¹⁶, [Stelios Loukides](#)¹⁷, [Maurits van Maaren](#)¹⁸, [Petr Panzner](#)¹⁹, [Helena Pite](#)²⁰, [Antonio Spanevello](#)²¹, [Henning Stenberg](#)²², [Ilja Striz](#)²³, [Boony Thio](#)²⁴, [Martina Koziar Vasakova](#)²⁵, [Diego Conti](#)²⁶, [Wytse Fokkens](#)²⁷, [Susanne Lau](#)²⁸, [Glenis K Scadding](#)²⁹, [Elizabeth Van Staeyen](#)³⁰, [Peter W Hellings](#)³¹, [Leif Bjermer](#)³²

Affiliations expand

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- DOI: [10.1016/j.rmed.2023.107361](https://doi.org/10.1016/j.rmed.2023.107361)

Free article

No abstract available

Keywords: Asthma comorbidities; Asthma diagnosis; Asthma management; Asthma treatment algorithm.

Conflict of interest statement

Declaration of competing interest ZD: received consultancy fees/lecture fees/fees for attending advisory boards from ALK, Antabio, Foresee Pharmaceuticals, GlaxoSmithKline, Hippo-Dx, QPS-Netherlands, Sanofi-Genzyme; she served as Director Respiratory & Allergy at QPS-NL and this CRO received research grants for clinical trials from HAL Allergy, Janssen Research & Development LLC, Patara pharma, Cerbios, Merck Sharp & Dohme, Novartis, Foresee Pharmaceuticals and ERA4TB (IMI-project). MJ: ALK, Stallergenes-Greer, Chiesi, GSK, Pfizer, Novartis, AstraZeneca and SANOFI. NH: Received honoraria for serving as advisor or consultant for GSK, AstraZeneca, Sanofi, Regeneron, Amgen, Genentech, Novartis and Teva. His institution received research grant support of his behalf from GSK, Genentech, Sanofi, Teva, Novartis, and AstraZeneca. LH: Has received grant funding, participated in advisory boards and given lectures at meetings supported by Amgen, AstraZeneca, Boehringer Ingelheim, Chiesi, Circassia, Hoffmann la Roche, GlaxoSmithKline, Novartis, Theravance, Evelo Biosciences, Sanofi, and Teva; he has received grants from MedImmune, Novartis UK, Roche/ Genentech Inc, and Glaxo Smith Kline, Amgen, Genentech/Hoffman la Roche, Astra Zeneca, MedImmune, Glaxo Smith Kline, Aerocrine and Vitalograph; he has received sponsorship for attending international scientific

meetings from AstraZeneca, Boehringer Ingelheim, Chiesi, GSK and Napp Pharmaceuticals; he has also taken part in asthma clinical trials sponsored by AstraZeneca, Boehringer Ingelheim, Hoffmann la Roche, and GlaxoSmithKline for which his institution received remuneration; he is the Academic Lead for the Medical Research Council Stratified Medicine UK Consortium in Severe Asthma which involves industrial partnerships with a number of pharmaceutical companies including Amgen, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Hoffmann la Roche, and Janssen. RD: Declares consulting fees from Synairgen, Sanofi and Galapagos, lecture fees from GSK, AZ and Airways Vista and he holds shares from Synairgen. DR: No COIs related to this work. SQ: ALK, Allergy Therapeutics, AstraZeneca, Chiesi, GSK, Leti, Mundipharma, Novartis, Sanofi-Genzyme, Teva. VB: Has worked as advisor, supervisor, investigator of pharmaceutical studies, unrestricted grants, and others with: AstraZeneca, GSK, MSD & Shering Plough, ALK-Abello; Chiesi, Novartis, Pharmaxis, Pfizer, Boehringer Ingelheim, Aerocrine, Teva, Sanofi, Birk NPC as. MG: No COIs related to this work. IP: In the last 5 years IDP has received speaker's honoraria for speaking at sponsored meetings from Astra Zeneca, Boehringer Ingelheim, Aerocrine, Almirall, Novartis, Teva, Chiesi, Sanofi/Regeneron, Menarini and GSK and payments for organising educational events from AZ, GSK, Sanofi/Regeneron and Teva. He has received honoraria for attending advisory panels with Genentech, Sanofi/Regeneron, Astra Zeneca, Boehringer Ingelheim, GSK, Novartis, Teva, Merck, Circassia, Chiesi and Knopp and payments to support FDA approval meetings from GSK. He has received sponsorship to attend international scientific meetings from Boehringer Ingelheim, GSK, AstraZeneca, Teva and Chiesi. He has received a grant from Chiesi to support a phase 2 clinical trial in Oxford. DAA: Has received honoraria as grants/contracts from Sociedad Española de Alergología e Inmunología Clínica (SEAIC), as consulting fees from ALK-Abelló, AstraZeneca, Chiesi and Gebro, as speaker from AstraZeneca, Chiesi, Gebro, GSK, Leti Pharma, Mundipharma, Novartis, Roxall, Sanofi. AS: GSK support for an asthma biologic clinical trial 2021-ongoing. PB: Has received honoraria for presentations and consultancy fees from AstraZeneca, Boehringer Ingelheim, Chiesi, ELPEN, GSK, Menarini, Novartis, Sanofi, and Gilead. AB: Takeda, Novartis, Viatrix, ALK, Zentiva, MERCK, Stallergenes Greer, Ewopharma, Astra Zeneca, Chiesi, S&D Pharma, Mundipharma, Berlin Chemie. WB: GlaxoSmithKline, Sanofi, Regeneron. JK: Grants and/or personal fees from ALK, Chiesi, GSK, Novartis, AstraZeneca, Sanofi, Boehringer, Teva, Viatrix, Stallergen, Abbot, all outside the submitted work. SL: Honorarium AstraZeneca, GSK, Chiesi Hellas, Sanofi, Elpen, Menarini, Guidoti. MVM: No COIs related to this work. PP: ALK, AstraZeneca, Stallergenes. HP: No COIs related to this work. AS: Reports lecture fees and/or consultancies from AstraZeneca, Chiesi, B.I., GSK, Merck, Novartis, Zambon, Sanofi. HS: No COIs related to this work. IS: No COIs related to this work. BT: No COIs related to this work. MKV: GlaxoSmithKline, AstraZeneca. Diego Conti: No COIs related to this work. WF: The department of Otorhinolaryngology of the Amsterdam University Medical centre, location AMC received grants for research in Rhinology from: ALK, AllergyTherapeutics, Novartis, EU, GSK, MYLAN, Sanofi-Aventis, and Zon-MW; personal COIs: for consultation and/or speaker fees from Dianosic, GSK, Novartis and Sanofi-Aventis/Regeneron. SL: Advisory Board Sanof-Aventis, GSK and Leo-Pharma. Honoraria by DBV Technologies, Allergopharma, Leti, Nutricia, Sanofi-Aventis. GKS: Honoraria for articles, speaker and

advisory boards: ALK, AstraZeneca, Capnia, Church & Dwight, Circassia, Noucor, GSK, Meda/Mylan/Viatrix, Merck, Sanofi- Regeneron, Stallergenes. Scientific Chief Editor, Rhinology Section, Frontiers in Allergy. Board Member, Lead for Allergic Rhinitis, EUFOREA. Chair of Data Monitoring Board for Paediatric AR trials of HDM SLIT. EVS: No COIs related to this work. PH: Recipient of research grants, honoraria and/or lecture fees of Sanofi, Regeneron, Viatrix, GSK, and Novartis. LB: No COIs related to this work.

SUPPLEMENTARY INFO

MeSH termsexpand

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Randomized Controlled Trial

J Pediatr (Rio J)

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. 2023 Nov-Dec;99(6):635-640.

doi: 10.1016/j.jpmed.2023.05.007. Epub 2023 Jun 20.

Factors associated with respiratory morbidity in the first year of life

[Samantha M Lessa](#)¹, [Daniela C Tietzmann](#)², [Sérgio L Amantéa](#)³

Affiliations expand

- PMID: 37353206

- PMID: [PMC10594016](#)
- DOI: [10.1016/j.jpmed.2023.05.007](#)

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Abstract

Objectives: To investigate the association between socioeconomic and nutritional factors with respiratory morbidity in the first year of life in different regions of Brazil.

Methodology: A nested case-control study within a randomized field trial was conducted in three capital cities (Porto Alegre, Manaus, and Salvador), representing different macro-regions of the country. Cases were defined as children with a reported previous diagnosis of asthma, bronchiolitis, or pneumonia. Corresponding controls were matched by age and sex in a 2:1 ratio, selected consecutively from the original cohort, resulting in a sample of 222 children. Bivariate analyses were performed to assess the association between sociodemographic and nutritional variables with respiratory morbidity outcomes, calculating odds ratios (OR) and their respective confidence intervals (95% CI). Values of $p < 0.05$ were considered significant. Potential confounding factors were adjusted through multivariate analysis (logistic regression).

Results: Maternal smoking and breastfeeding for less than six months showed a significant association and increased risk of respiratory disease (OR=2.12 and 2.05, respectively). Children born in the Southern region of Brazil also demonstrated a higher association and risk of respiratory morbidity. The consumption of ultra-processed foods did not show a significant association or increased risk of respiratory disease.

Conclusions: Maternal smoking, breastfeeding for less than six months, and being born in the Southern region of Brazil are risk factors for the development of respiratory morbidity in the first year of life. The consumption of ultra-processed foods does not appear to pose a risk, but it was prevalent in more than 80% of the population, limiting its discriminatory power of analysis.

Keywords: Acute respiratory infection; Child; Risk factors.

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Conflict of interest statement

Conflicts of interest The authors declare no conflicts of interest.

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

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Br J Clin Pharmacol

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. 2023 Nov;89(11):3273-3290.

doi: 10.1111/bcp.15801. Epub 2023 Jul 6.

[Modelling Asthma Treatment Responses \(MASTER\): Effect of individual patient characteristics on the risk of exacerbation in moderate or severe asthma: A time-to-event analysis of randomized clinical trials](#)

[Sean Oosterholt](#)¹, [Ian D Pavord](#)², [Guy Brusselle](#)³, [Arzu Yorgancıoğlu](#)⁴, [Paulo M Pitrez](#)⁵, [Abhijith Pg](#)⁶, [Chirag Teli](#)⁷, [Oscar Della Pasqua](#)^{1,8}

Affiliations expand

- PMID: 37221636

- DOI: [10.1111/bcp.15801](https://doi.org/10.1111/bcp.15801)

Abstract

Aims: There is limited understanding of how clinical and demographic characteristics are associated with exacerbation risk in patients with moderate-to-severe asthma, and how these factors correlate with symptom control and treatment response. Here we assess the relationship between baseline characteristics and exacerbation risk during regular dosing with inhaled corticosteroids (ICS) monotherapy or in combination with long-acting beta2-agonists (ICS/LABA) in clinical trial patients with varying levels of symptom control, as assessed by the asthma control questionnaire (ACQ-5).

Methods: A time-to-event model was developed using pooled patient data (N = 16 282) from nine clinical studies [Correction added on 26 July 2023, after first online publication: The N value in the preceding sentence has been corrected in this version.]. A parametric hazard function was used to describe the time-to-first exacerbation. Covariate analysis included the assessment of the effect of seasonal variation, clinical and demographic baseline characteristics on baseline hazard. Predictive performance was evaluated by standard graphical and statistical methods.

Results: An exponential hazard model best described the time-to-first exacerbation in moderate-to-severe asthma patients. Body mass index, smoking status, sex, ACQ-5, % predicted forced expiratory volume over 1 s (FEV₁ p) and season were identified as statistically significant covariates affecting baseline hazard irrespective of ICS or ICS/LABA use. Fluticasone propionate/salmeterol (FP/SAL) combination therapy resulted in a significant reduction in the baseline hazard (30.8%) relative to FP monotherapy.

Conclusions: Interindividual differences at baseline and seasonal variation affect the exacerbation risk independently from drug treatment. Moreover, it appears that even when a comparable level of symptom control is achieved in a group of patients, each individual may have a different exacerbation risk, depending on their baseline characteristics and time of the year. These findings highlight the importance of personalized interventions in moderate-to-severe asthma patients.

Keywords: asthma exacerbation; asthma symptom control; fluticasone propionate/salmeterol combination therapy; inhaled corticosteroids; patient characteristics; time-to-event modelling.

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- [58 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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J Asthma

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. 2023 Nov;60(11):2021-2029.

doi: 10.1080/02770903.2023.2213327. Epub 2023 May 31.

[Patterns of allergic sensitization in adults with severe asthma: the ATLAS non-interventional study](#)

[Eva Lücke](#)¹, [Burkhard Schraven](#)^{2,3,4}, [Katrin Borucki](#)⁵, [Anke Lux](#)⁶, [Dirk Reinhold](#)^{2,3,4}, [Qingyu Wu](#)¹, [Jens Schreiber](#)^{1,3,4}

Affiliations expand

- PMID: 37167019
- DOI: [10.1080/02770903.2023.2213327](https://doi.org/10.1080/02770903.2023.2213327)

Abstract

Objectives: Severe asthma is heterogeneous, with childhood-onset asthma believed more likely to be allergic, whereas adult-onset asthma is considered typically non-allergic. However, the allergic diagnosis is typically by exclusion: if patients do not react to an

allergen panel, which is not standardized and often limited to few allergens, they are considered non-allergic. The overall aim of the ATLAS study was to characterize the sensitization to allergens in severe asthma (independent of phenotype).

Methods: Single-visit, cross-sectional, non-interventional study in adults with severe asthma. Analyses were conducted for total and specific immunoglobulin E against 53 allergens, overall and in subgroups, including age at asthma onset (<20 [childhood-onset] and >40 years of age).

Results: Among 1010 recruited patients, 28.4% reported childhood-onset asthma and 33.6% onset >40 years of age. After excluding patients receiving omalizumab/anti-IL5 therapy, 27.6% were not sensitized to any tested allergens, whereas 19.1% were sensitized to >10 allergens. All allergens triggered sensitization in some patients. Baseline characteristics in the two onset subgroups were similar; 23.2% with childhood-onset asthma were not sensitized to any allergen, compared to 32.0% with onset >40 years of age.

Conclusion: When a broad panel of allergens is used for sensitization testing, as many as three quarters of patients with severe asthma display sensitivity to at least one allergen, with substantial overlaps in all characteristics between the two age-at-onset subgroups. All of the tested allergens triggered a response in at least some patients, emphasizing the importance of including a broad range of allergens in any testing panel.

Keywords: Asthma; allergens; eosinophils; immunoglobulin E; subgroups.

FULL TEXT LINKS



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J Asthma

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. 2023 Nov;60(11):1997-2001.

doi: 10.1080/02770903.2023.2209172. Epub 2023 May 31.

Bronchodilator responsiveness testing with inhaled budesonide/formoterol in asthma

Luis J Nannini^{1,2}, N Brandan¹, O M Fernández¹

Affiliations expand

- PMID: 37115806
- DOI: [10.1080/02770903.2023.2209172](https://doi.org/10.1080/02770903.2023.2209172)

Abstract

Background: The choice of bronchodilators for responsiveness testing (BRT) is a clinical decision according to ATS/ERS. Since January 2019 we use budesonide/formoterol for BRT in asthma at our center in Argentina. The aim was to compare budesonide/formoterol with salbutamol for BRT in stable asthmatic patients that were followed up in a short-acting beta₂ agonist (SABA)-free asthma center.

Methods: From the Hospital database, we found for the same patient at least one BRT using salbutamol 200 µg and another with budesonide/formoterol 320/9 µg.

Results: We found similar BRT between salbutamol and budesonide/formoterol in 101 asthmatic individuals (26 males) aged 38.14 ± 16.1 yrs (mean \pm Standard deviation). The absolute response was 0.18 ± 0.21 L in FEV₁ after salbutamol and 0.20 ± 0.22 L in FEV₁ after budesonide/formoterol. Afterwards, we showed 202 patients tested with budesonide/formoterol; the mean absolute response was 0.21 ± 0.22 L in FEV₁. There were no unexpected safety findings.

Conclusions: In asthmatic patients, we demonstrated similar efficacy between Budesonide/formoterol and salbutamol for BRT.

Keywords: Asthma; bronchodilator responsiveness; budesonide/formoterol; salbutamol; spirometry.

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J Asthma

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. 2023 Nov;60(11):1935-1941.

doi: 10.1080/02770903.2023.2203743. Epub 2023 Apr 27.

Does asthma-bronchiectasis overlap syndrome (ABOS) really exist?

[Angelica Tiotiu](#)^{1,2}, [Miguel-Angel Martinez-Garcia](#)^{3,4}, [Paula Mendez-Brea](#)⁵, [Iria Roibas-Veiga](#)⁵, [Francisco-Javier Gonzalez-Barcala](#)^{4,6,7,8}

Affiliations expand

- PMID: 37071539
- DOI: [10.1080/02770903.2023.2203743](https://doi.org/10.1080/02770903.2023.2203743)

Abstract

Objective: To analyze the relationship between asthma and bronchiectasis, as well as the necessary conditions that this connection must meet for this group of patients to be considered a special phenotype.

Data sources: We performed a PubMed search using the MeSH terms "asthma" and "bronchiectasis." The literature research was limited to clinical trials, meta-analyses, randomized controlled trials, cohort studies, and systematic reviews, involving adult patients, published until November 30th, 2022.

Study selections: Selected papers were initially evaluated by the Authors, to assess their eligibility in contributing to the statements.

Results: The prevalence of bronchiectasis is higher than expected in patients with asthma, particularly in those with more severe disease, and in some patients, between 1.4% and 7%

of them, asthma alone could be the cause of bronchiectasis. Both diseases share etiopathogenic mechanisms, such as neutrophilic and eosinophilic inflammation, altered airway microbiota, mucus hypersecretion, allergen sensitization, immune dysfunction, altered microRNA, dysfunctional neutrophilic activity, and variants of the HLA system. Besides that, they also share comorbidities, such as gastroesophageal reflux disease and psychiatric illnesses. The clinical presentation of asthma is very similar to patients with bronchiectasis, which could cause mistakes with diagnoses and delays in being prescribed the correct treatment. The coexistence of asthma and bronchiectasis also poses difficulties for the therapeutic focus.

Conclusions: The evidence available seems to support that the asthma-bronchiectasis phenotype really exists although longitudinal studies which consistently demonstrate that asthma is the cause of bronchiectasis are still lacking.

Keywords: Asthma; bronchiectasis; comorbidities; eosinophils; exacerbation; overlap; prognosis.

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J Asthma

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. 2023 Nov;60(11):1951-1959.

doi: 10.1080/02770903.2023.2200854. Epub 2023 Apr 23.

[One-day systemic corticosteroid administration for asthma and future "short bursts" risk in real clinical practice](#)

[Takeshi Matsumoto](#)¹, [Akiko Kaneko](#)¹, [Takahiro Fujiki](#)¹, [Yusuke Kusakabe](#)¹, [Emi Nakayama](#)¹, [Ayaka Tanaka](#)¹, [Naoki Yamamoto](#)¹, [Mayuko Tashima](#)¹, [Chikara Ito](#)¹, [Kensaku Aihara](#)¹, [Shinpachi Yamaoka](#)¹, [Michiaki Mishima](#)¹

Affiliations expand

- PMID: 37042221
- DOI: [10.1080/02770903.2023.2200854](https://doi.org/10.1080/02770903.2023.2200854)

Abstract

Objective: Systemic corticosteroid administration, also called short bursts (SB), is harmful for patients with asthma; however, the actual burden of one-day SB remains unsolved. This study aimed to elucidate the characteristics of patients requiring one-day SB against asthma in clinical practice.

Methods: Consecutive patients who regularly visited our hospital for asthma treatment between January 2019 and December 2020 were reviewed and followed for one year. SB was defined as ≥ 3 days of systemic corticosteroid treatment for an exacerbation. One-day SB was defined as one-day of systemic corticosteroid to treat an exacerbation. The one-day SB group included patients who received only one-day SB but no SB during the preceding year. Frequent SB was defined as that occurring ≥ 2 times/year.

Results: Data on 229 patients were analyzed. Among them, 2.6% (95% confidence interval 1.2-5.6%) were in the one-day SB group. The one-day SB group was female-dominant, obese, non-eosinophilic, and non-atopic. The median one-day SB was 1.5 times/year and almost half of one-day SB were performed by patients themselves. Independent of the low pulmonary function, high blood eosinophil count, and inhaled corticosteroid dose, one-day SB was associated with future frequent SB (adjusted odds ratio = 18.2, 95% confidence interval 1.1-288, $P = 0.040$, compared to the no SB group).

Conclusions: Although one-day SB was not frequently experienced, even one-day SB without conventional SB was associated with future frequent SB. It is important to grasp the actual condition of one-day SB and to reinforce the treatment used.

Keywords: Exacerbation; conventional short burst; inner-city hospital; one-day short burst; real world.

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Eur Ann Allergy Clin Immunol



. 2023 Nov;55(6):283-293.

doi: 10.23822/EurAnnACI.1764-1489.256. Epub 2022 Jun 7.

Overview of asthma patients followed up in a tertiary clinic

[Z Çelebi Sözen](#)¹, [B Özdel Öztürk](#)¹, [Ö Aydın](#)¹, [S Bavbek](#)¹, [D Mungan](#)¹

Affiliations expand

- PMID: 35670696
- DOI: [10.23822/EurAnnACI.1764-1489.256](https://doi.org/10.23822/EurAnnACI.1764-1489.256)

Free article

Abstract

Background. Asthma is a disease that combines different biological mechanisms, inflammatory pathways, and phenotypic features. Our aim was to investigate the demographic and disease characteristics of patients with asthma and to reveal the distribution with different phenotypes according to endotype groups. **Methods.** Patients were identified as eosinophilic if the absolute eosinophil count was measured at least once $\geq 300/\mu\text{L}$ during the oral corticosteroid free period or $\geq 150/\mu\text{L}$ under oral corticosteroids. Patients sensitive to at least one inhalant allergen with skin prick test and/ or sptgE measurement were defined as allergic. They were categorized into four main endotypes. **Results.** Data of 405 asthma patients with a median age of 50.9 years were analyzed. The prominent clinical and phenotypic characteristics of the study group were being obese (43.2%) or overweight (32%), severe asthma (49.6%), adult-onset (56.1%) or late-onset asthma (35.3%). The distribution of the four main endotypes according to eosinophilic and/or allergic status, is as follows: 22.7% allergic-eosinophilic (AE), 27.9%

nonallergic-eosinophilic (NAE), 22.9% allergic-noneosinophilic (ANE), 26.4% nonallergic-noneosinophilic (NANE). While most severe asthma patients were in the AE and NAE groups, those with early-onset asthma were in AE and ANE, and those with late-onset asthma were in the NAE and NANE groups. The proportion of uncontrolled patients was higher in the NAE group. Among the severe asthma patients, the rate of uncontrolled disease was higher in those with NANE asthma. **Conclusions.** Different phenotypes were more closely related to some endotypes. This may allow the clinicians to identify patients and predict appropriate treatment modalities and response for individualized care.

Keywords: Asthma endotypes; asthma onset; asthma phenotypes; asthma severity; obese asthma.

FULL TEXT LINKS



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

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Allergy Asthma Proc

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. 2023 Nov 1;44(6):402-412.

doi: 10.2500/aap.2023.44.230063.

[Prevalence and bidirectional association between rhinitis and urticaria: A systematic review and meta-analysis](#)

[Shu-Ying Xu](#), [He-Qun Lv](#), [Chun-Li Zeng](#), [Yong-Jun Peng](#)

- PMID: 37919842

- DOI: [10.2500/aap.2023.44.230063](https://doi.org/10.2500/aap.2023.44.230063)

Abstract

Background: Rhinitis, allergic rhinitis in particular, and urticaria are both common diseases globally. However, there is controversy with regard to the correlation between rhinitis and urticaria. **Objective:** To examine the accurate association between rhinitis and urticaria. **Methods:** Three medical literature data bases were searched from data base inception until January 11, 2022. The prevalence and association between rhinitis and urticaria were estimated by meta-analysis. Quality assessment was performed by using the Newcastle-Ottawa Scale. Pooled odds ratios (OR) with 95% confidence intervals (CI) and pooled prevalence were calculated by using random-effects models. **Results:** Urticaria prevalence in patients with rhinitis was 17.6% (95% CI, 13.2%-21.9%). The pooled prevalence of rhinitis was 31.3% (95% CI, 24.2%-38.4%) in patients with urticaria, and rhinitis prevalence in patients with acute urticaria and chronic urticaria was 31.6% (95% CI, 7.4%-55.8%) and 28.7% (95% CI, 20.4%-36.9%), respectively. Rhinitis occurrence was significantly associated with urticaria (OR 2.67 [95% CI, 2.625-2.715]). Urticaria and rhinitis were diagnosed based on different criteria, possibly resulting in a potential error of misclassification. **Conclusion:** Rhinitis and urticaria were significantly correlated. Physicians should be cognizant with regard to this relationship and address nasal or skin symptoms in patients.

FULL TEXT LINKS



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BMJ Open

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. 2023 Nov 2;13(11):e076614.

doi: 10.1136/bmjopen-2023-076614.

Intranasal antihistamines and corticosteroids in the treatment of allergic rhinitis: a systematic review and meta-analysis protocol

[Bernardo Sousa-Pinto](#)^{1,2}, [Rafael José Vieira](#)^{1,2}, [Jan Brozek](#)³, [António Cardoso-Fernandes](#)^{1,2}, [Nuno Lourenço-Silva](#)^{1,2}, [Renato Ferreira-da-Silva](#)^{1,2}, [André Ferreira](#)^{2,4,5}, [Sara Gil-Mata](#)^{1,2}, [Anna Bedbrook](#)⁶, [Ludger Klimek](#)^{7,8}, [Joao A Fonseca](#)^{1,2}, [Torsten Zuberbier](#)^{9,10}, [Holger J Schünemann](#)³, [Jean Bousquet](#)^{11,10,12}

Affiliations expand

- PMID: 37918935
- DOI: [10.1136/bmjopen-2023-076614](https://doi.org/10.1136/bmjopen-2023-076614)

Free article

Abstract

Introduction: Intranasal antihistamines and corticosteroids are some of the most frequently used drug classes in the treatment of allergic rhinitis. However, there is uncertainty as to whether effectiveness differences may exist among different intranasal specific medications. This systematic review aims to analyse and synthesise all evidence from randomised controlled trials (RCTs) on the effectiveness of intranasal antihistamines and corticosteroids in rhinitis nasal and ocular symptoms and in rhinoconjunctivitis-related quality-of-life.

Methods and analysis: We will search four electronic bibliographic databases and three clinical trials databases for RCTs (1) assessing patients ≥ 12 years old with seasonal or perennial allergic rhinitis and (2) comparing the use of intranasal antihistamines or corticosteroids versus placebo. Assessed outcomes will include the Total Nasal Symptom Score (TNSS), the Total Ocular Symptom Score (TOSS) and the Rhinoconjunctivitis Quality-of-Life Questionnaire (RQLQ). We will assess the methodological quality of included primary studies by using the Cochrane risk-of-bias tool. Certainty in the body of evidence for the analysed outcomes will be assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. We will perform a random-effects meta-analysis for each assessed medication and outcome, presenting results as pooled mean differences and standardised mean differences. Heterogeneity will be

explored by sensitivity and subgroup analyses, considering (1) the risk of bias, (2) the follow-up period and (3) the drug dose.

Ethics and dissemination: Ethical considerations will not be required. Results will be disseminated in a peer-review journal.

Prospero registration number: CRD42023416573.

Keywords: Allergy; Asthma; Chronic airways disease; Immunology.

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Conflict of interest statement

Competing interests: LK reports grants from Allergopharma, MEDA/Mylan, ALK Abelló, LETI Pharma, Stallergenes, Sanofi, ASIT biotech, Lofarma Quintiles, AstraZeneca, GSK and Immunotk, and personal fees from Allergopharma, MEDA/Mylan, HAL Allergie, LETI Pharma, Sanofi, Allergy Therapeut and Cassella Med, outside the submitted work. JAF reports grants from Astrazeneca and Mundipharma; and personal fees from AstraZeneca, Mundipharma, Sanofi, GSK and Teva, outside the submitted work. TZ reports grants from Novartis and Henkel; personal fees from Bayer Health Care, FAES, Novartis, Henkel, AstraZeneca, AbbVie, ALK, Almirall, Astellas, Bencard, Berlin Chemie, HAL, Leti, Meda, Menarini, Merck, MSD, Pfizer, Sanofi, Stallergenes, Takeda, Teva, UCB, Kryolan and L'Oréal, outside the submitted work. JB reports personal fees from Chiesi, Cipla, Hikma, Menarini, Mundipharma, Mylan, Novartis, Purina, Sanofi-Aventis, Takeda, Teva and Uriach and other from Kyomed-Innov, outside the submitted work.

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J Allergy Clin Immunol Pract

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. 2023 Oct 31:S2213-2198(23)01199-6.

Work-related asthma and its impact on quality of life and work productivity

[Eva Suarhana](#)¹, [Nicole Le Moual](#)², [Catherine Lemièrè](#)³, [Jean Bousquet](#)⁴, [Stephie Pierre](#)⁵, [Bernardo Sousa Pinto](#)⁶, [Alfi Afadiyanti Parfi](#)⁵, [Philippe Van Brussel](#)⁷, [Hormoz Nassiri Kigloo](#)⁸, [Olivier Vandenas](#)⁹, [Paul K Henneberger](#)¹⁰

Affiliations expand

- PMID: 37918649
- DOI: [10.1016/j.jaip.2023.10.044](https://doi.org/10.1016/j.jaip.2023.10.044)

Abstract

Background: The impact of Work-related asthma (WRA) on quality of life (QoL) and work productivity remains largely neglected/uncertain despite its high prevalence.

Objective: We aimed to investigate the association of WRA with QoL and work productivity as compared to subjects with asthma unrelated to work and those without asthma and rhinitis.

Methods: A cross-sectional survey was carried out among workers during their periodic occupational health visit in Belgium. The mini Asthma QoL Questionnaire (mAQLQ), Medical Outcome Study Short Form-8 (SF-8), and Work Productivity and Activity Impairment-General Health questionnaires were administered. Survey participants were divided into three groups: 1) WRA (current asthma with ≥ 2 respiratory symptoms at work, $n=89$); 2) non-WRA (current asthma without work-related respiratory symptoms, $n=119$); and 3) the reference group (no asthma and no lower respiratory, nasal, or eye symptoms; $n=815$). Associations of QoL and work productivity with WRA were evaluated by multivariable regression analyses.

Results: WRA and having poor asthma control were significantly associated with lower global mAQLQ scores compared to non-WRA. Asthmatic subjects had significantly lower physical and mental health components of the SF-8 instrument and overall work productivity compared to the reference group, with greater impairment in WRA than non-WRA. Moreover, workers with WRA had higher percentages of doctor visits and income reduction due to respiratory symptoms than non-WRA. Work-related rhinitis and depression were associated with reduced QoL, independent of the effect of WRA.

Conclusions: Comprehensive management of WRA should be done to reduce the worsening of QoL and work productivity of those affected.

Keywords: Quality of life; Socioeconomic burden; Work productivity; Work-related asthma.

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Review

S Afr Fam Pract (2004)

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. 2023 Oct 30;65(1):e1-e11.

doi: 10.4102/safp.v65i1.5806.

[Allergic rhinitis: Review of the diagnosis and management: South African Allergic Rhinitis Working Group](#)

[Guy A Richards](#)¹, [Marinda McDonald](#), [Claudia L Gray](#), [Pieter De Waal](#), [Ray Friedman](#), [Maurice Hockman](#), [Sarah J Karabus](#), [Cornelia M Lodder](#), [Tshegofatso Mabelane](#), [Sylvia M Mosito](#), [Ashen Nanan](#), [Jonny G Peter](#), [Traugott H C Quitter](#), [Riaz Seedat](#), [Sylvia Van den Berg](#), [Andre Van Niekerk](#), [Eftyhia Vardas](#), [Charles Feldman](#)

Affiliations expand

- PMID: 37916698

- PMID: [PMC10623625](#)
- DOI: [10.4102/safp.v65i1.5806](#)

Abstract

Background: Allergic rhinitis (AR) has a significant impact on the community as a whole with regard to quality of life and its relationship to allergic multi-morbidities. Appropriate diagnosis, treatment and review of the efficacy of interventions can ameliorate these effects. Yet, the importance of AR is often overlooked, and appropriate therapy is neglected. The availability of effective medications and knowledge as to management are often lacking in both public and private health systems.

Methods: This review is based on a comprehensive literature search and detailed discussions by the South African Allergic Rhinitis Working Group (SAARWG).

Results: The working group provided up-to-date recommendations on the epidemiology, pathology, diagnosis and management of AR, appropriate to the South African setting.

Conclusion: Allergic rhinitis causes significant, often unappreciated, morbidity. It is a complex disease related to an inflammatory response to environmental allergens. Therapy involves education, evaluation of allergen sensitisation, pharmacological treatment, allergen immunotherapy (AIT) and evaluation of the success of interventions. Regular use of saline; the important role of intranasal corticosteroids, including those combined with topical antihistamines and reduction in the use of systemic steroids are key. Practitioners should have a thorough knowledge of associated morbidities and the need for specialist referral. **Contribution:** This review summarises the latest developments in the diagnosis and management of AR such that it is a resource that allows easy access for family practitioners and specialists alike.

Keywords: allergic rhinitis; antihistamines; immunotherapy; intranasal corticosteroids; saline rinse.

Conflict of interest statement

C.F. has received speakers fees from Aspen, MSD, Astra Zeneca, Aurogen, Procter and Gamble. G.A.R. has received speakers fees from Glenmark, Aspen, MSD, Astra Zeneca, Novartis, Cipla, Acino, Sandoz, and consultative fees from Cipla. C.M.L. has received speakers fees from Glenmark, Astra Zeneca, Norvartis, Cipla, Acino, Sandoz, and consultative fees from Cipla. R.F. has received speakers fees from Aspen and Glenmark. M.H. has received speakers fees from GSK, Aspen, Pharmacare, Glenmark, Medel and

SouthernENT. J.P. has received support for pollen monitoring across South Africa from Novartis, Glenmark, Clicks, Pharmadynamics, Dr Reddy's, Thermofischer Scientific, Twinsaver and A Vogel Echinaforce and speakers fees from Glenmark, Johnson and Johnson, Sanofi and Astra Zeneca. T.M. has received speakers fees from Aspen, Astra Zeneca and Cipla. A.v.N. has received speakers fees from Acino, Actor Pharma, Aspen, Astra Zeneca and Glenmark, MSD, Organon, Sanofi and Takeda. C.L.G. has received speaker's fees from Aspen, Astra Zeneca, Cipla, Glenmark and Organon. M.M. has received speakers fees from Glenmark, Cipla, Aspen, Sanofi, Proctor and Gamble, Thermo Scientific, Lancet laboratories and Immunospec. A.N., P.d.W., S.K., R.S., S.v.d.B., C.Q., S.M. and E.V. have no disclosures.

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

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Allergy

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. 2023 Nov 2.

doi: 10.1111/all.15927. Online ahead of print.

[Natural course of pollen-induced allergic rhinitis from childhood to adulthood: A 20-year follow up](#)

[Magnus Lindqvist](#)¹, [Katja Biering Leth-Møller](#)², [Allan Linneberg](#)^{2,3}, [Inger Kull](#)⁴, [Anna Bergström](#)^{5,6}, [Antonios Georgellis](#)^{5,6}, [Magnus P Borres](#)⁷, [Agneta Ekeboom](#)⁸, [Marianne van Hage](#)¹, [Erik Melén](#)⁴, [Marit Westman](#)^{1,9}

Affiliations expand

- PMID: 37916606
- DOI: [10.1111/all.15927](https://doi.org/10.1111/all.15927)

Abstract

Background: Allergic rhinitis (AR) is one of the most common chronic diseases worldwide. There are limited prospective long-term data regarding persistency and remission of AR. The objective of this study was to investigate the natural course of pollen-induced AR (pollen-AR) over 20 years, from childhood into early adulthood.

Methods: Data from 1137 subjects in the Barn/Children Allergi/Allergy Milieu Stockholm Epidemiologic birth cohort (BAMSE) with a completed questionnaire regarding symptoms, asthma, treatment with allergen immunotherapy (AIT) and results of allergen-specific IgE for inhalant allergens at 4, 8, 16 and 24 years were analyzed. Pollen-AR was defined as sneezing, runny, itchy or blocked nose; and itchy or watery eyes when exposed to birch and/or grass pollen in combination with allergen-specific IgE $\geq 0.35\text{kU}_A/\text{L}$ to birch and/or grass.

Results: Approximately 75% of children with pollen-AR at 4 or 8 years had persistent disease up to 24 years, and 30% developed asthma. The probability of persistency was high already at low levels of pollen-specific IgE. The highest rate of remission from pollen-AR was seen between 16 and 24 years (21.5%); however, the majority remained sensitized. This period was also when pollen-specific IgE-levels stopped increasing and the average estimated annual incidence of pollen-AR decreased from 1.5% to 0.8% per year.

Conclusion: Children with pollen-AR are at high risk of persistent disease for at least 20 years. Childhood up to adolescence seems to be the most dynamic period of AR progression. Our findings underline the close cross-sectional and longitudinal relationship between sensitization, AR and asthma.

Keywords: BAMSE; IgE; allergic rhinitis; asthma; pollen allergy.

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Ann Allergy Asthma Immunol



. 2023 Oct 30:S1081-1206(23)01392-3.

doi: 10.1016/j.anai.2023.10.029. Online ahead of print.

[Efficacy and Safety of Intratonsillar Immunotherapy for Allergic Rhinitis: A Randomized, Double-blind, Placebo-Controlled Clinical Trial](#)

[Junyan Zhang](#)¹, [Xiaobin Yang](#)¹, [Guangui Chen](#)¹, [Jintao Hu](#)¹, [Ying He](#)¹, [Jinxiang Ma](#)², [Zhaoen Ma](#)¹, [Huifang Chen](#)¹, [Yuyi Huang](#)¹, [Qirong Wu](#)¹, [Yongping Liu](#)¹, [Lu Yu](#)¹, [Hong Zhang](#)¹, [He Lai](#)¹, [Jianguo Zhang](#)¹, [Jinming Zhai](#)¹, [Minqi Huang](#)¹, [Zehong Zou](#)¹, [Ailin Tao](#)³

Affiliations expand

- PMID: 37913839
- DOI: [10.1016/j.anai.2023.10.029](https://doi.org/10.1016/j.anai.2023.10.029)

Abstract

Background: A lower adherence rate existed in patients received allergen specific immunotherapy (AIT) due to its lengthy period and side effects even though it is the only curative treatment for IgE-mediated allergies. Therefore, exploring innovative AIT routes are necessary.

Objective: This study was designed to explore the efficacy and safety of the intratonsillar injection of house dust mite (HDM) extract in patients with HDM-induced allergic rhinitis.

Methods: A randomized double-blind placebo-controlled clinical trial was conducted. Eighty patients with HDM-induced AR were randomized to receive 6 intratonsillar injections with HDM extract or placebo over 3 months. The total nasal symptom score (TNSS), Visual Analogue Scale (VAS) of nasal symptoms, combined symptom and medication score (CSMS), Mini Rhinoconjunctivitis Quality of Life Questionnaire (MiniRQLQ), and serum allergen-specific IgG4 to *D. pteronyssinus* were all monitored at baseline, 3, 6, and 12 months after the treatment finished. The intent-to-treat (ITT) and per protocol set (PPS) are both analyzed.

Results: The primary endpoints TNSS and Δ TNSS were improved significantly at 3 months after AR patients finished a 3-month 6-injection intratonsillar immunotherapy (ITIT) by comparing to the placebo treatment in both ITT and PPS. VAS, CSMS and MiniRQLQ were also improved significantly at 3 months after treatment in PPS. However, the improvement effect of ITIT at 6 and 12 months was limited and uncertain based on the data. The increase of serum Der p IgG4 in the active group was significantly higher than that in the placebo group at 3, 6, and 12 months after the treatment finished. Adverse events were monitored, and no systemic adverse reactions were observed.

Conclusion: The clinical trial showed that intratonsillar injection with HDM extract was safe and effective in patients with AR. Optimizing the protocol and allergen formulations is expected to increase and maintain the efficacy of this novel approach.

Keywords: allergic rhinitis; house dust mite; intratonsillar immunotherapy; randomized controlled trial; specific immunotherapy.

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. 2023 Nov;37(11):878-885.

doi: 10.13201/j.issn.2096-7993.2023.11.005.

[The efficacy and safety of glucocorticoid stent implantation compared with oral glucocorticoid during perioperative period in chronic rhinosinusitis with nasal polyps]

[Article in Chinese]

[Rong Xiang](#)¹, [Yu Xu](#)¹

Affiliations expand

- PMID: 37905482
- DOI: [10.13201/j.issn.2096-7993.2023.11.005](https://doi.org/10.13201/j.issn.2096-7993.2023.11.005)

Abstract

in [English](#), [Chinese](#)

Objective:To compare the perioperative efficacy and safety of postoperative oral glucocorticoid and glucocorticoid stent implantation in patients with chronic rhinosinusitis with nasal polyps (CRSwNP) undergoing functional endoscopic sinus surgery (FESS). **Methods:**Sixty patients with bilateral CRSwNP with similar degree of lesions were selected and divided into three groups: conventional surgical treatment group (20 cases), glucocorticoid stent group (20 cases), and oral glucocorticoid group (20 cases). All three groups underwent routine FESS, patients in the sinus glucocorticoid stent group receiving sinus glucocorticoid stent placed in the ethmoid sinuses (one on each side) during surgery, and patients in the oral glucocorticoid group received postoperative oral methylprednisolone at a dose of 0.4 mg/kg per day for 7 days, followed by a tapering of 8

mg per week to 8 mg followed by maintenance therapy for 1 week, for a total of 3-4 weeks. Visual analog scale (VAS) scores were used to evaluate nasal congestion, rhinorrhea, olfaction, and facial pressure symptoms before surgery, as well as at 2, 4, 8, and 12 weeks after surgery. Nasal endoscopic Lund-Kennedy scores were recorded, and adverse reactions such as stent detachment, stent-related allergic reactions, sleep disorders, edema, gastrointestinal symptoms, rash/acne, behavioral/cognitive changes, weight gain, limb pain, and infection risk were documented. **Results:**The nasal congestion symptom scores at 2, 4, 8, and 12 weeks after surgery were significantly lower than those before operation in all three groups, and the differences were statistically significant ($P < 0.05$). The sinus glucocorticoid stent group exhibited significantly lower nasal congestion symptom scores at 4 and 8 weeks after surgery compared to the conventional surgical treatment group. The rhinorrhea symptom scores at 2, 8, and 12 weeks after surgery were significantly lower than preoperative scores in all three groups. Additionally, the sinus glucocorticoid stent group had significantly lower rhinorrhea scores than the conventional surgical treatment group at 2 weeks postoperatively. Concerning olfaction, the sinus glucocorticoid stent group showed a significant reduction in scores at 12 weeks postoperatively, while the oral glucocorticoid group exhibited significant improvement starting from 8 weeks after surgery. There were no statistically significant differences in nasal congestion, rhinorrhea, facial pressure, and olfaction scores between the sinus glucocorticoid stent and oral glucocorticoid groups at 2, 4, 8, and 12 weeks postoperatively. Nasal endoscopy scores revealed lower polyp scores and edema at 2, 4, 8, and 12 weeks postoperatively for all three groups compared to preoperative scores. The conventional surgical treatment group exhibited a significant reduction in nasal secretion scores starting from 8 weeks after surgery, while both the sinus glucocorticoid stent and oral glucocorticoid groups showed significant reductions starting from 2 weeks postoperatively, with scores significantly lower than those of the conventional surgical treatment group at 2 weeks. Scab/scar scores in the conventional surgical treatment group significantly decreased from 8 weeks after surgery, while both the sinus glucocorticoid stent and oral glucocorticoid groups exhibited significant reductions starting from 4 weeks. No statistically significant differences were observed in endoscopy scores (including polyps, edema, nasal secretion, scars, and scabs) between the sinus glucocorticoid stent and oral glucocorticoid groups at 2, 4, 8, and 12 weeks postoperatively. Regarding adverse reactions, no postoperative complications related to sinus glucocorticoid stent were observed in the sinus glucocorticoid stent group. In the oral glucocorticoid group, 1 patient experienced irritability, and 1 patient experienced weight gain. **Conclusion:**The glucocorticoid stent implantation has comparable effects to oral glucocorticoid in improving postoperative nasal symptoms, reducing nasal mucosal edema, scar formation, and nasal secretion in patients with CRSwNP undergoing FESS, with a better safety profile.

Keywords: chronic sinusitis with nasal polyps; endoscopic sinus surgery; glucocorticoid stent; oral glucocorticoid.

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Conflict of interest statement

The authors of this article and the planning committee members and staff have no relevant financial relationships with commercial interests to disclose.

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Medicine (Baltimore)

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. 2023 Oct 27;102(43):e35711.

doi: 10.1097/MD.00000000000035711.

[Nasal microbes in allergic rhinitis children with or without sublingual immunotherapy](#)

[Xiao-Fei Shen](#)¹, [Zhi-Pan Teng](#)¹, [Qi Li](#)¹, [Zhen-Kun Yu](#)²

Affiliations expand

- PMID: 37904472
- PMCID: [PMC10615503](#)

- DOI: [10.1097/MD.00000000000035711](https://doi.org/10.1097/MD.00000000000035711)

Free PMC article

Abstract

The mechanism of allergic rhinitis (AR) remains unclear. Most researchers believe that AR is the result of a combination of environmental and genetic factors. Sublingual immunotherapy (SLIT) is a treatment that can change the natural course of AR through immunomodulatory mechanism and maintain efficacy after the treatment. Nasal cavity is the main site where AR patients contact with external allergens, produce inflammatory reactions and nasal symptoms. Therefore, in this study, we investigate the nasal microbiome in AR patients, and the changes after SLIT. In this cross-sectional study, nasal swabs for microbiome analysis were collected from 3 groups: SLIT-naïve AR patients (AR group), AR patients undergoing SLIT treatment over 2 years (SLIT group) and a control group (CG). The characteristics of nasal microbiome of each groups were produced by 16s-rDNA sequencing technology. The Simpson index of AR group was significantly higher than that of CG and SLIT groups, but not different between SLIT group and CG group. The abundance of Bacteroidete and Firmicutes remarkably increased in the AR group, but Bacteroidete reduced to CG level after SLIT. AR patients have different nasal microbiome composition, but we do not know how it happened and whether the AR condition affected nasal microbiome composition or nasal microbiome affected AR.

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Conflict of interest statement

The authors have no funding and conflicts of interest to disclose.

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

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Review

Eur Arch Otorhinolaryngol

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. 2023 Oct 30.

doi: 10.1007/s00405-023-08307-z. Online ahead of print.

Pediatric chronic rhinosinusitis

[Hassan H Ramadan](#)¹

Affiliations expand

- PMID: 37899371
- DOI: [10.1007/s00405-023-08307-z](https://doi.org/10.1007/s00405-023-08307-z)

Abstract

Purpose: An up-to-date overview of diagnosis, differential diagnosis, comorbidities, and current medical and surgical management of pediatric chronic rhinosinusitis (PCRS).

Methods: Review of current evidence-based literature on PCRS.

Results: Diagnosis of PCRS seems to be improving based on recent evidence using nasal endoscopy as well as computed tomography scanning. Recent literature supports the fact that chronic adenoiditis can be an independent etiology of symptoms of chronic sinusitis, that are very similar to chronic adenoiditis. Allergic rhinitis and immune deficiency play important roles in the management of PCRS. Surgery for PCRS has evolved significantly in the last 15-20 years to include adenoidectomy as well as endoscopic sinus surgery.

Conclusions: PCRS is very common in children causing poor QOL for these children. Medical management remains the main stay of treatment with attention to management of co-morbidities that may contribute to the disease severity. Making the correct diagnosis will help with the choice of surgical intervention if medical management fails.

Keywords: Adenoidectomy; Chronic adenoiditis; Chronic rhinosinusitis; Endoscopic sinus surgery; Pediatric.

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J Allergy Clin Immunol Pract

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. 2023 Oct 26:S2213-2198(23)01193-5.

doi: 10.1016/j.jaip.2023.10.039. Online ahead of print.

[The Art of Immunotherapy](#)

[Harold S Nelson](#)¹

Affiliations [expand](#)

- PMID: 37898175
- DOI: [10.1016/j.jaip.2023.10.039](https://doi.org/10.1016/j.jaip.2023.10.039)

Abstract

Selection of a patient with rhinitis/conjunctivitis or asthma for allergy immunotherapy (AIT) requires several decisions. First, does the patient's sensitization, pattern of exposure to an allergen and degree of exposure to that allergen reasonably suggest a causal relationship? Does the level and duration of symptoms warrant the cost and inconvenience of immunotherapy, or is the patient motivated by the disease modifying potential of AIT? If AIT is selected, is the choice to be greater safety and convenience with SLIT-tablets, but with treatment probably limited to two or three allergens, or for SCIT where multiple allergen therapy is the rule and efficacy may be somewhat greater, at least initially, or does the physician go off-label into the unknowns of liquid SLIT? Are there extracts of sufficient potency to achieve likely effective doses? How does the physician deal with large local or systemic reactions, with gaps in treatment, with pollen seasons and the use of premedication or cautionary prescription of epinephrine autoinjectors? How can adherence to AIT be improved? These and other questions are addressed in this paper.

Keywords: AIT; Allergic asthma; SCIT; SLIT; allergic rhinitis/conjunctivitis; allergy immunotherapy; dosing; multi-allergic; patient selection; subcutaneous; sublingual.

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Indian J Pediatr

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. 2023 Oct 28.

doi: 10.1007/s12098-023-04907-z. Online ahead of print.

[Managing Children with Allergic Rhinitis: A Preliminary Experience with a New Multicomponent Nasal Spray](#)

[Maria Angela Tosca](#)¹, [Attilio Varricchio](#)², [Irene Schiavetti](#)³, [Giorgio Ciprandi](#)⁴

Affiliations expand

- PMID: 37897589
- DOI: [10.1007/s12098-023-04907-z](https://doi.org/10.1007/s12098-023-04907-z)

No abstract available

- [2 references](#)

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Review

Int J Mol Med

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. 2023 Dec;52(6):117.

doi: 10.3892/ijmm.2023.5320. Epub 2023 Oct 27.

[Role of dendritic cell-derived exosomes in allergic rhinitis \(Review\)](#)

[Chenglin Kang](#)¹, [Haipeng He](#)², [Peng Liu](#)¹, [Yue Liu](#)¹, [Xiaomei Li](#)³, [Jin Zhang](#)¹, [Hong Ran](#)¹, [Xianhai Zeng](#)¹, [Hailiang Zhao](#)¹, [Jiangqi Liu](#)¹, [Shuqi Qiu](#)¹

Affiliations expand

- PMID: 37888754
- DOI: [10.3892/ijmm.2023.5320](https://doi.org/10.3892/ijmm.2023.5320)

Abstract

Allergic rhinitis (AR) is a common pathological condition in otorhinolaryngology. Its prevalence has been increasing worldwide and is becoming a major burden to the world population. Dendritic cells (DCs) are typically activated and matured after capturing, phagocytosing, and processing allergens during the immunopathogenesis of AR. In addition, the process of DC activation and maturation is accompanied by the production of exosomes, which are cell-derived extracellular vesicles (EVs) that can carry proteins, lipids, nucleic acids, and other cargoes involved in intercellular communication and material transfer. In particular, DC-derived exosomes (Dex) can participate in allergic immune responses, where the biological substances carried by them can have potentially important implications for both the pathogenesis and treatment of AR. Dex can also be exploited to carry anti-allergy agents to effectively treat AR. This provides a novel method to explore the pathogenesis of and treatment strategies for AR further. Therefore, the present review focuses on the origin, composition, function, and biological characteristics of DCs, exosomes, and Dex, in addition to the possible relationship between Dex and AR.

Keywords: allergic rhinitis; dendritic cells; exosomes; extracellular vesicles; intercellular communication.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances expand

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. 2023 Oct 26.

doi: 10.1007/s11356-023-30559-9. Online ahead of print.

Associations of allergy-related outcomes with depression in the US adults

[Tenglong Yan](#)^{#1}, [Xin Song](#)^{#2}, [Xiaowen Ding](#)¹, [Ziyi Guan](#)³, [Dongsheng Niu](#)¹, [Jue Li](#)¹, [Mengyang Wang](#)⁴, [Minghui Wang](#)⁵

Affiliations expand

- PMID: 37884722
- DOI: [10.1007/s11356-023-30559-9](https://doi.org/10.1007/s11356-023-30559-9)

Abstract

Evidences showed the link between allergy and depression, while the relationships of depression with allergy-related outcomes is insufficient. The objective of this study is to evaluate and compare the relationship of depression with allergy-related outcomes assessed using two different outcome indicators, in a population-based study. A cross-sectional study was performed of 1094 participants in the 2005-2006 National Health and Nutrition Examination Survey (NHANES). The self-reported allergic symptoms of allergic rhinitis (AR) status and immunoglobulin E (IgE) were used to evaluate the allergy-related outcomes. The depression disorder was defined as the ≥ 10 points on the Patient Health Questionnaire-9. Logistic and linear regression models were performed to illustrate the associations of depression and allergy-related outcomes. The prevalence of AR and depression was 34.2% and 6.8%, respectively. The odds of depression were 8.6% higher in participants with AR patients compared those without AR [odds ratio (OR) = 1.739, 95% confidence interval (CI): (1.034, 2.933)], while the odds of depression in participants with allergic sensitization and without allergic sensitization were not found significant difference. Allergy is positively associated with depression disorder, and patients with allergy-related outcomes, such as AR, may be at higher risk of depression, while the IgE level was not founded to be related with depression. In the treatment of AR patients with

depression symptoms, early detection and management of mental problems are of importance.

Keywords: Allergic rhinitis (AR); Allergic sensitization; Allergy-related outcomes; Depression.

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Meta-Analysis

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. 2023 Oct 26;13(1):18361.

doi: 10.1038/s41598-023-44932-8.

[Cesarean section and the risk of allergic rhinitis in children: a systematic review and meta-analysis](#)

[Zixin Liu](#) ^{#1,2}, [Li Xie](#) ^{#1}, [Xiaohua Liu](#) ^{1,3}, [JunRong Chen](#) ¹, [Yaqian Zhou](#) ⁴, [Jialin Zhang](#) ¹, [Honghui Su](#) ², [Yide Yang](#) ¹, [Mei Tian](#) ¹, [Jian Li](#) ^{#5,6,7}, [Yunpeng Dong](#) ^{#8}

Affiliations expand

- PMID: 37884557
- PMCID: [PMC10603136](#)
- DOI: [10.1038/s41598-023-44932-8](#)

Free PMC article

Abstract

Multiple evidence indicates that perinatal factors make impact on immune development and affect offspring allergic rhinitis (AR) risk. In this systematic review and meta-analysis, we examined available published studies to clarify the relationship between cesarean section (C-section) and offspring AR in children. To explore the relationship between C-section, especially the special attention was paid to different cesarean delivery mode, and the risk of AR in children. Articles were searched using PubMed, Web of Science, EMBASE, Cochrane Library, China knowledge Network, Wanfang, and China Science and Technology Journal databases. A meta-analysis of 22 studies published before August 1, 2022, which included 1,464,868 participants, was conducted for statistical analysis with RevMan5.4. The correlation strength between C-section and offspring AR was determined by combining odds ratio (OR) and 95% confidence interval (95% CI). Meta-regression and subgroup analyses were used to explore potential sources of heterogeneity. Publication bias was detected using the funnel chart and Egger tests. Meta-analysis revealed that there was a significant correlation between C-section and children AR (OR = 1.19, 95% CI: 1.12-1.27, $P < 0.001$), especially C-section with a family history of allergy (OR = 1.82, 95% CI: 1.36-2.43, $P < 0.001$). Moreover, elective C-section (without genital tract microbe exposure) had the higher risk of offspring AR (OR = 1.24, 95% CI: 1.05-1.46, $P = 0.010$) compared with the whole study. Meta-regression demonstrated that sample size explained 38.0% of the variability between studies, and year of publication explained 18.8%. Delivery by C-section, particularly elective C-section and C-section with a family history of allergy can increase the risk of AR in children.

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Conflict of interest statement

The authors declare no competing interests.

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

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Publication types, MeSH termsexpand

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nature portfolio 

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Review

Int Immunopharmacol

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. 2023 Nov;124(Pt B):111003.

doi: 10.1016/j.intimp.2023.111003. Epub 2023 Oct 6.

[Effect of mesenchymal stem cell therapy in animal models of allergic rhinitis: A systematic review and meta-analysis](#)

[Dongdong Hong](#)¹, [Zhen Hu](#)¹, [Juanling Weng](#)¹, [Long Yang](#)¹, [Yalan Xiong](#)¹, [Yuanxian Liu](#)²

Affiliations expand

- PMID: 37806104

- DOI: [10.1016/j.intimp.2023.111003](https://doi.org/10.1016/j.intimp.2023.111003)

Free article

Abstract

Background: Allergic rhinitis (AR) is a worldwide problem that affects people of all ages, impairing patients' physical and mental health and causing great social expenditure. Animal studies have suggested the potential efficacy of mesenchymal stem cell (MSC) therapy in treating AR. Our meta-analysis was performed to evaluate the effect of MSC therapy in animal models of AR by pooling animal studies.

Methods: The search was executed in PubMed, Embase, Web of Science, OVID, and the Cochrane Library for relevant studies up to February 2023. The applicable data were extracted from the eligible studies, and the risk of bias was assessed for each study. The meta-analysis was conducted using Review Manager (version 5.4.1) and Stata (version 15.1).

Results: A total of 12 studies were included in the final analysis. Compared to the model control group, the MSC therapy group presented lower frequency of sneezing [(Standardized mean difference (SMD) -1.87, 95% CI -2.30 to -1.43)], nasal scratching (SMD -1.41, 95% CI -1.83 to -0.99), and overall nasal symptoms (SMD -1.88, 95% CI -3.22 to -0.54). There were also remarkable reductions after transplantation with MSCs in the levels of total immunoglobulin E (IgE) (SMD -1.25, 95% CI -1.72 to -0.79), allergen-specific IgE (SMD -1.79, 95% CI -2.25 to -1.32), and allergen-specific immunoglobulin G1 (SMD -1.29, 95% CI -2.03) in serum, as well as the count of eosinophils (EOS) in nasal mucosa (SMD -3.48, 95% CI -4.48 to -2.49). In terms of cytokines, MSC therapy significantly decreased both protein and mRNA levels of T helper cell 2 (Th2)-related cytokines, including interleukin (IL)-4, IL-5, IL-10, and IL-13.

Conclusion: MSC therapy has the potential to be an effective clinical treatment for AR patients by attenuating Th2 immune responses, reducing secretion of IgE and nasal infiltration of EOS, and consequently alleviating nasal symptoms.

Keywords: Allergic rhinitis; Animal study; Mesenchymal stem cells; Meta-analysis.

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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 types, MeSH terms, Substancesexpand

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J Allergy Clin Immunol Glob



. 2023 Jul 3;2(4):100134.

doi: 10.1016/j.jacig.2023.100134. eCollection 2023 Nov.

[Chronic rhinosinusitis with nasal polyps and allergic rhinitis as different multimorbid treatable traits in asthma](#)

[José Antonio Castillo](#)^{1,2,3}, [Vicente Plaza](#)⁴, [Gustavo Rodrigo](#)⁵, [Berta Juliá](#)⁶, [César Picado](#)^{2,7}, [Cristina Fernández](#)⁸, [Joaquim Mullol](#)^{2,3,9}

Affiliations expand

- PMID: 37781668
- PMCID: [PMC10510007](#)
- DOI: [10.1016/j.jacig.2023.100134](#)

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Abstract

Background: Respiratory multimorbidities are linked to asthma, such as allergic rhinitis (AR) with early allergic asthma and chronic rhinosinusitis (CRS) with nasal polyps (CRSwNP) with late nonallergic asthma.

Objective: Our aim was to investigate the association of asthma severity and control with specific upper airway phenotypes.

Method: Patients with asthma were prospectively recruited from 23 pulmonology and ear, nose, and throat clinics. Asthma severity and control, as well as upper airway comorbidities (AR and non-AR [NAR], CRSwNP, and CRS without nasal polyps [CRSsNP]) were assessed according to international consensus guidelines definitions.

Results: A total of 492 asthmatic patients were included. Half of the asthmatic patients (49.6%) had associated rhinitis (37.0% had AR and 12.6% had NAR) and 36.2% had CRS (16.7% had CRSsNP and 19.5% had CRSwNP), whereas 14.2% had no sinonasal symptoms. Most cases of AR (78%) and NAR (84%) were present in patients with mild-to-moderate asthma, whereas CRSwNP was more frequent in patients with severe asthma (35% [$P < .001$]), mainly nonatopic asthma (44% [$P < .001$]). Patients with severe asthma with CRSwNP had worse asthma control, which was correlated ($r = 0.249$ [$P = .034$]) with sinus occupancy. Multiple logistic regression analysis showed that late-onset asthma, intolerance of aspirin and/or nonsteroidal anti-inflammatory drugs, and CRSwNP were independently associated with severe asthma.

Conclusion: Severe asthma is associated with CRSwNP, with sinus occupancy affecting asthma control. This study has identified 2 main different upper airway treatable traits, AR and CRSwNP, which need further evaluation to improve management and control of patients with asthma.

Keywords: Asthma; allergic rhinitis; asthma control; asthma severity; chronic rhinosinusitis with nasal polyps; united airway disease.

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- [5 figures](#)

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J Allergy Clin Immunol Glob



. 2023 Jul 19;2(4):100149.

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Neonatal rhinorrhea, heart rate variability, and childhood exercise-induced wheeze

[Sophie Berger](#)¹, [Nicolò Pini](#)^{2,3}, [Maristella Lucchini](#)^{2,3}, [J David Nugent](#)^{2,3}, [Luis Acosta](#)⁴, [Jyoti Angal](#)⁵, [Virginia A Rauh](#)⁶, [Amy J Elliott](#)⁵, [Michael M Myers](#)^{2,7}, [William P Fifer](#)^{2,3,7}, [Matthew S Perzanowski](#)⁴

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- PMCID: [PMC10509928](#)
- DOI: [10.1016/j.jacig.2023.100149](#)

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Abstract

Background: There is increasing evidence linking infant rhinorrhea to school-age exercise-induced wheeze (EIW) via a parasympathetic nervous system pathway. The ratio of the root mean square of successive differences in heart beats (RMSSD) measured in quiet sleep versus active sleep (RMSSD_{QS:AS}) is a novel biomarker in asthma.

Objective: We tested the hypotheses that (1) neonatal rhinorrhea predicts childhood EIW independent of other neonatal respiratory symptoms, (2) neonatal RMSSD_{QS:AS} predicts childhood EIW, and (3) RMSSD_{QS:AS} mediates the association between neonatal rhinorrhea and childhood EIW.

Methods: Participants from the Safe Passage/Environmental Influences on Child Health Outcomes (PASS/ECHO) prospective birth cohort had heart rate variability extracted from electrocardiogram traces acquired in the first month of life. Parents reported on rhinorrhea in their child at age 1 month and on EIW in their child at ages 4 to 11 years.

Results: In models (N = 831) adjusted for potential confounders and covariates, including neonatal wheeze, cough and fever, neonatal rhinorrhea-predicted childhood EIW (relative risk [RR] = 2.22; $P = .040$), specifically, among females (RR = 3.38; $P = .018$) but not males (RR = 1.39; $P = .61$). Among participants contributing data in both active and quiet sleep (n = 231), $RMSSD_{QS:AS}$ predicted EIW (RR = 2.36; $P = .003$) and mediated the effect estimate of neonatal rhinorrhea predicting EIW among females. Half of the females with a higher $RMSSD_{QS:AS}$ and neonatal rhinorrhea (n = 5 of 10) developed EIW as compared with 1.8% of the other females (n = 2 of 109) ($P < .001$).

Conclusions: Our findings support dysregulation of the parasympathetic nervous system in infancy as one of the possible underlying mechanisms for the development of EIW later in childhood among females, which could aid in the development of future interventions.

Keywords: Asthma; exercise induced asthma; heart rate variability and sleep states; parasympathetic nervous system; rhinitis; watery eyes.

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J Allergy Clin Immunol Glob

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. 2023 Jul 19;2(4):100150.

Prevalence and risk factors for allergic sensitization: 3 cross-sectional studies among schoolchildren from 1996 to 2017

[Eva Rönmark](#)¹, [Joakim Bunne](#)¹, [Anders Bjerg](#)², [Matthew Perzanowski](#)³, [Anna Winberg](#)⁴, [Martin Andersson](#)¹, [Thomas Platts-Mills](#)⁵, [Linnea Hedman](#)¹

Affiliations expand

- PMID: 37781648
- PMCID: [PMC10510014](#)
- DOI: [10.1016/j.jacig.2023.100150](#)

Free PMC article

Abstract

Background: The prevalence of allergic sensitization and allergic diseases has increased for decades in Northern Europe, but recent studies are lacking.

Objective: We sought to study the prevalence trends of allergic sensitization, associated risk factors, and the association with asthma and allergic rhinitis (AR) among children in Northern Sweden.

Methods: Three cohorts of children aged 7 to 8 years participated in a skin prick test (SPT) with 10 airborne allergens in 1996, 2006, and 2017, with 2148, 1693, and 1762 participants tested, respectively, representing 87% to 90% of schoolchildren in the catchment communities. Adjusted Poisson regression was used to identify risk factors for allergic sensitization and the association with asthma and AR.

Results: The prevalence of any positive SPT response increased from 21% in 1996 to 30% in 2006 and remained at 30% in 2017 ($P < .001$). Sensitization to cat was the most common for all the years. The risk factor pattern for a positive SPT response was similar in all examinations, with positive and significant associations with a family history of allergy (risk

ratio, 1.4-1.5) and negative and significant associations with having a cat at home (risk ratio, 0.7-0.8). The prevalence of physician-diagnosed asthma increased, but the association with allergic sensitization weakened. The opposite trends were found for AR- decreasing prevalence and strengthened association with allergic sensitization.

Conclusions: The prevalence of allergic sensitization increased from 1996 to 2006 but plateaued in the next decade, whereas the risk factor pattern remained stable. The diverging trends of associations between allergic sensitization and asthma and AR suggest secular trends in the clinical management of allergic diseases.

Keywords: Allergic sensitization; OLIN; allergic rhinitis; asthma; epidemiology; schoolchildren; skin prick test.

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- [3 figures](#)

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Eur Respir J

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. 2023 Nov 2;62(5):2300558.

doi: 10.1183/13993003.00558-2023. Print 2023 Nov.

[Dupilumab leads to better-controlled asthma and quality of life in children: the VOYAGE study](#)

[Alessandro G Fiocchi](#)¹, [Wanda Phipatanakul](#)², [Robert S Zeiger](#)³, [Sandy R Durrani](#)⁴, [Jeremy Cole](#)⁵, [Jérôme Msihid](#)⁶, [Rebecca Gall](#)⁴, [Juby A Jacob-Nara](#)⁷, [Yamo Deniz](#)⁴, [Paul J Rowe](#)⁷, [David J Lederer](#)⁴, [Megan Hardin](#)⁸, [Yi Zhang](#)⁴, [Asif H Khan](#)⁶

Affiliations expand

- PMID: 37734856
- PMCID: [PMC10620476](#)
- DOI: [10.1183/13993003.00558-2023](#)

Free PMC article

Abstract

Background: Dupilumab has shown long-term treatment benefits in children with uncontrolled asthma. We assessed in more detail the impact of dupilumab on asthma control and health-related quality of life (HRQoL) in children and their caregivers.

Methods: Children aged 6-11 years with uncontrolled moderate-to-severe type 2 asthma (baseline blood eosinophils ≥ 150 cells· μL^{-1} or fractional exhaled nitric oxide ≥ 20 ppb; n=350) were treated with dupilumab or placebo for 52 weeks in the VOYAGE study. Primary outcomes of these analyses were asthma control (change from baseline in Asthma Control Questionnaire 7 Interviewer-Administered (ACQ-7-IA) and achieving a clinically meaningful response of ≥ 0.5 points); proportion of patients achieving well-controlled asthma or better (ACQ-7-IA ≤ 0.75 points); effect on patients' (Standardised Paediatric Asthma Quality of Life Questionnaire Interviewer-Administered (PAQLQ(S)-IA)) and caregivers' (Paediatric Asthma Caregiver's Quality of Life Questionnaire (PACQLQ)) HRQoL; and allergic rhinitis-related QoL.

Results: Dupilumab *versus* placebo significantly improved children's ACQ-7-IA scores by week 4 with sustained improvements through week 52 (least squares mean difference at week 52: -0.44, 95% CI -0.59- -0.30; $p < 0.0001$); a higher proportion achieved a clinically meaningful response (week 52: 86% *versus* 75%; $p = 0.0051$). At weeks 24 and 52, more children who received dupilumab achieved well-controlled asthma (ACQ-7-IA ≤ 0.75 points: 61% *versus* 43%; $p = 0.0001$ and 70% *versus* 46%; $p < 0.0001$, respectively). Significant improvements in PAQLQ(S)-IA and PACQLQ scores were observed by week 52.

Conclusions: In children aged 6-11 years with moderate-to-severe type 2 asthma, dupilumab treatment was associated with rapid, sustained improvements in asthma control. HRQoL was significantly improved for children and their caregivers.

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Conflict of interest statement

Conflict of interest: A.G. Fiocchi has served as an advisory board member for Abbott, Danone, DBV Technologies, HiPP Organic, Novartis and Stallergenes Greer, and reports research sponsorship from Danone, Ferrero, HiPP Organic and Sanofi. W. Phipatanakul has served as a consultant and has received clinical trial support/medication support from Genentech, GSK for Asthma Therapeutics, Merck, Regeneron Pharmaceuticals Inc. and Sanofi. R.S. Zeiger has served as a deputy editor for the AAAAI and a consultant for the ACAAI, received research support from ALK and the NIH, received research support from and served as an advisory board member for AstraZeneca, Genentech/Novartis, GSK and Teva, served as an advisory board member for Sanofi-Regeneron Pharmaceuticals Inc., and reports royalties from UpToDate. J. Cole has no conflicts of interest to disclose. J. Msihid, J.A. Jacob-Nara, P.J. Rowe, M. Hardin and A.H. Khan are Sanofi employees and may hold stock and/or stock options in the company. S.R. Durrani, R. Gall, Y. Deniz and D.J. Lederer are employees and shareholders of Regeneron Pharmaceuticals Inc. Y. Zhang is a former employee of Regeneron Pharmaceuticals Inc. and may hold shares and/or share options in the company.

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- [3 figures](#)

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Immunotherapy

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. 2023 Nov;15(16):1401-1414.

doi: 10.2217/imt-2023-0100. Epub 2023 Sep 20.

Safety and effectiveness of a 300 IR house dust mite sublingual tablet: descriptive 4-year final analysis of a post-marketing surveillance in Japan

[Yoshitaka Okamoto](#)¹, [Moe Kato](#)², [Kiyonori Ishii](#)², [Yumi Sato](#)³, [Tomohisa Hata](#)⁴, [Yuta Asaka](#)⁴

Affiliations expand

- PMID: 37727966
- DOI: [10.2217/imt-2023-0100](https://doi.org/10.2217/imt-2023-0100)

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Abstract

Background: Data are limited for clinical outcomes with house dust mite (HDM) allergen immunotherapy beyond 2 years' observation. **Materials & methods:** A post-marketing drug-use survey assessed the safety and effectiveness of the 300 index of reactivity (IR) HDM tablet during use for up to 4 years in Japan. **Results:** 538 patients were evaluable for safety and 383 for effectiveness. Most adverse drug reactions (ADRs) occurred early and were local reactions; 5.6% of 249 total events were reported during years 2 to 4 as new ADRs after the interim analysis. The CAP-RAST score was identified as a potential risk factor for ADRs. The proportion of evaluable patients with severe allergic rhinitis symptoms decreased from 46.4% at baseline (n = 317) to 1.0% at 4 years (n = 104). Patients (n = 16) who discontinued 300 IR HDM tablet due to symptomatic improvement had sustained improvement relative to baseline 1 to 2 years later. **Conclusion:** Long-term use of the 300 IR HDM tablet is safe and effective.

Keywords: Actair; allergic rhinitis; effectiveness and safety; house dust mite; post-marketing survey; sublingual immunotherapy tablet.

Plain language summary

The 300 index of reactivity house dust mite (HDM) sublingual tablet (Actair®) is a treatment option for people with HDM allergy. A Japanese study investigated the safety and effectiveness of the HDM sublingual tablet during its use for up to 4 years. Less than a third of patients (29%) reported adverse effects, mainly itching or irritation in the mouth. The percentage of patients with no allergic rhinitis symptoms increased from 0.3% before

treatment to 57.7% after 4 years of use. The percentage of patients who perceived that their allergic rhinitis had improved 'substantially' compared with before treatment increased from 22.3% at 6 months to 73.5% at 4 years. Patients who ended treatment with the HDM sublingual tablet because their symptoms had improved continued to perceive benefit 1 to 2 years later. **Clinical Trial Registration:** University hospital Medical Information Network (UMIN) Clinical Trials Registry identifier: UMIN000042840.

SUPPLEMENTARY INFO

MeSH terms, Substances expand

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Pediatr Pulmonol

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. 2023 Nov;58(11):3083-3094.

doi: 10.1002/ppul.26626. Epub 2023 Aug 22.

Phenotypic characteristics, healthcare use, and treatment in children with night cough compared with children with wheeze

[Maria C Mallet](#)^{1,2}, [Rebeca Mozun](#)^{1,3}, [Cristina Ardura-Garcia](#)¹, [Eva S L Pedersen](#)¹, [Maja Jurca](#)^{1,4}, [Philipp Latzin](#)⁵, [LUIS Study Group](#); [Alexander Moeller](#)⁶, [Claudia E Kuehni](#)^{1,5}

Affiliations expand

- PMID: 37606206

- DOI: [10.1002/ppul.26626](https://doi.org/10.1002/ppul.26626)

Free article

Abstract

Objectives: Population-based studies of children with dry night cough alone compared with those who also wheeze are few and inconclusive. We compared how children with dry night cough differ from those who wheeze.

Methods: LuftiBus in the school is a population-based study of schoolchildren conducted between 2013 and 2016 in Zurich, Switzerland. We divided children into four mutually exclusive groups based on reported dry night cough (henceforth referred as "cough") and wheeze and compared parent-reported symptoms, comorbidities, exposures, FeNO, spirometry, and healthcare use and treatment.

Results: Among 3457 schoolchildren aged 6-17 years, 294 (9%) reported "cough," 181 (5%) reported "wheeze," 100 (3%) reported "wheeze and cough," and 2882 (83%) were "asymptomatic." Adjusting for confounders in a multinomial regression, children with "cough" reported more frequent colds, rhinitis, and snoring than "asymptomatic" children; children with "wheeze" or "wheeze and cough" more often reported hay fever, eczema, and parental histories of asthma. FeNO and spirometry were similar among "asymptomatic" and children with "cough," while children with "wheeze" or "wheeze and cough" had higher FeNO and evidence of bronchial obstruction. Children with "cough" used healthcare less often than those with "wheeze," and they attended mainly primary care. Twenty-two children (7% of those with "cough") reported a physician diagnosis of asthma and used inhalers. These had similar characteristics as children with wheeze.

Conclusion: Our representative population-based study confirms that children with dry night cough without wheeze clearly differed from those with wheeze. This suggests asthma is unlikely, and they should be investigated for alternative aetiologies, particularly upper airway disease.

Keywords: FeNO; asthma; healthcare; spirometry.

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- [43 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Review

Am J Rhinol Allergy

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. 2023 Nov;37(6):766-776.

doi: 10.1177/19458924231193528. Epub 2023 Aug 9.

[Efficacy of Sublingual Immunotherapy in Allergic Rhinitis Patients with Asthma: A Systematic Review and Meta-Analysis](#)

[Dijiang Ma](#)¹, [Qiling Zheng](#)¹, [Jianing Sun](#)¹, [Shenjun Tang](#)¹, [Wudan He](#)¹

Affiliations expand

- PMID: 37559376
- DOI: [10.1177/19458924231193528](https://doi.org/10.1177/19458924231193528)

Abstract

Objective: Sublingual immunotherapy (SLIT) has been widely applied to treat patients with allergic rhinitis (AR). However, meta-analyses on the efficacy of SLIT in AR patients with asthma are still limited.

Methods: Literature without language limitation published before October 28, 2022, were retrieved from PubMed, EMBASE, and Cochrane Library. STATA 16.0 software was used for the meta-analysis of the extracted data. The results reported were symptom scores, drug scores, adverse effects rates, and cost of treatment.

Results: Ten studies involving 1722 patients met the inclusion criteria. The total rhinitis score (TRSS) (weighted mean difference [WMD] = -1.23, 95% CI: -1.39--1.06, $P < .001$) and total asthma symptom score (TASS) (WMD = -1.00, 95% CI: -1.12-0.89, $P < .001$) were significantly lower in the SLIT group than the placebo group. The SLIT group had higher rates of treatment-related adverse events (relative risk [RR] = 2.82, 95% CI: 1.77-4.48, $P < .001$) and total costs of treatment (standardized mean difference [SMD] = 0.71, 95% CI: 0.45-0.97, $P < .001$). There was no significant difference in inhaled corticosteroids (ICS) dose ($P = .195$), fractional exhaled nitric oxide (FeNO) ($P = .158$), forced expiratory volume in 1 s (FEV1) ($P = .237$), and direct costs of treatment ($P = .630$) between the SLIT and placebo groups.

Conclusion: SLIT may be a therapeutic method for improving rhinitis symptoms and asthma symptoms in AR patients with asthma. However, as there was significant heterogeneity in results, more high-quality and well-designed studies are needed in the future to elucidate the efficacy of SLIT.

Keywords: allergic rhinitis; asthma; efficacy; meta-analysis; sublingual immunotherapy.

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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Am J Rhinol Allergy

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. 2023 Nov;37(6):751-757.

doi: 10.1177/19458924231193156. Epub 2023 Aug 8.

Glucocorticoid-Induced Transcript 1 (GLCCI1) SNP rs37937 Is Associated With the Risk of Developing Allergic Rhinitis and the Response to Intranasal Corticosteroids in a Chinese Han Population

[Xu Liang](#)¹, [Peng Jin](#)¹, [Changcui Zhan](#)², [Li Zhao](#)¹, [Xiaoxue Zi](#)¹, [Lili Zhi](#)³, [Kena Yu](#)¹

Affiliations expand

- PMID: 37553950
- DOI: [10.1177/19458924231193156](https://doi.org/10.1177/19458924231193156)

Abstract

Background: Evidence has shown that glucocorticoid-induced transcript 1 (GLCCI1) single nucleotide polymorphism (SNP) rs37937 is associated with asthma.

Objectives: The objective of this study was to investigate whether the GLCCI1 SNP rs37937 is a risk factor for allergic rhinitis (AR) in a Chinese Han population.

Methods: A total of 220 individuals including 109 AR patients and 111 healthy subjects were included. The genotyping of GLCCI1 rs37937 was performed by the SNaPshot method. The correlations of rs37937 polymorphism, AR risk, and clinical characteristics were further analyzed, as well as the treatment response to intranasal corticosteroids (INCS) in AR patients of different genotypes.

Results: Three GLCCI1 rs37973 SNP genotypes were identified in both AR patients and healthy subjects. Significant association between rs37973 polymorphism and AR under allele model, dominant model, heterozygote model, and homozygote model were shown. The A allele frequency of SNP rs37973 in AR was significantly higher than that in controls. The serum total immunoglobulin E (IgE) in AR patients of AA genotype was significantly higher than in patients of GA and GG genotype, and the serum total IgE in GA genotype was significantly higher than in GG genotype. Interestingly, after 4 weeks of INCS treatment for AR patients, the improvement of the nasal itching score, sneezing score, runny nose score, total nasal symptom score, and visual analog scale score of the GG genotype were worse than the AA or GA genotype.

Conclusion: The GLCCI1 rs37937 polymorphism is associated with the risk of developing AR and the response to INCS treatment in the Chinese Han population.

Keywords: Chinese Han population; GLCCI1; IgE; allele; allergic rhinitis; clinical characteristics; gene; genotype; intranasal corticosteroids; single nucleotide polymorphism.

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

MeSH terms, Substances, Supplementary conceptsexpand

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Am J Rhinol Allergy

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. 2023 Nov;37(6):739-750.

doi: 10.1177/19458924231193154. Epub 2023 Aug 3.

TSLP Induces Epithelial–Mesenchymal Transition in Nasal Epithelial Cells From Allergic Rhinitis Patients Through TGF- β 1/Smad2/3 Signaling

[Hong Wei Yu](#)¹, [Wei Wei Wang](#)¹, [Qian Jing](#)¹, [Yong Liang Pan](#)¹

Affiliations expand

- PMID: 37537875
- DOI: [10.1177/19458924231193154](https://doi.org/10.1177/19458924231193154)

Abstract

Background: Airway remodeling is demonstrated in Asian patients with allergic rhinitis (AR). The epithelial-mesenchymal transition (EMT) is one of the key mechanisms underlying airway remodeling. Thymic stromal lymphopoietin (TSLP) is an important contributor to airway remodeling. Although increased TSLP is found in AR, little is known about whether TSLP is involved in airway remodeling through induction of the EMT.

Objective: We investigated the effect of TSLP on the EMT in human nasal epithelial cells (HNECs) from AR patients.

Methods: Human nasal epithelial cells from AR patients were stimulated with TSLP in the absence or presence of the preincubation with a selective inhibitor of transforming growth factor beta 1 (TGF- β 1) receptor (SB431542). The expression of TGF- β 1 in the cells was evaluated by using real-time polymerase chain reaction, Western blotting, and immunocytochemistry. Western blotting and immunocytochemistry were used to assay EMT markers including vimentin, fibroblast-specific protein 1 (FSP1) and E-cadherin, small mothers against decapentaplegic homolog2/3 (Smad2/3), and phosphorylated Smad2/3 in the cells. The levels of extracellular matrix components such as collagens I and III in supernatants were measured by enzyme-linked immunoassay. Morphological changes of the cells were observed under inverted phase-contrast microscope.

Results: A concentration-dependent increase of TGF- β 1 mRNA and protein was observed following stimulation with TSLP. Furthermore, TSLP decreased the expression of E-cadherin protein, but upregulated the production of FSP1 and vimentin proteins along with increased levels of collagens I and III, and the morphology of the cells was transformed

into fibroblast-like shape. Additionally, a significant increase was found in phosphorylation of Smad2/3 protein. However, these effects were reversed by SB431542 preincubation.

Conclusion: TSLP-induced HNECs to undergo the EMT process via TGF- β 1-mediated Smad2/3 activation. TSLP is an activator of the EMT in HNECs and might be a potential target for inhibiting EMT and reducing airway remodeling in AR.

Keywords: allergic rhinitis; epithelial–mesenchymal transition; human nasal epithelial cells; small mothers against decapentaplegic homolog; thymic stromal lymphopoietin; transforming growth factor beta 1.

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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Environ Res

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. 2023 Nov 1;236(Pt 1):116754.

doi: 10.1016/j.envres.2023.116754. Epub 2023 Jul 26.

[Airborne grass pollen and thunderstorms influence emergency](#)

department asthma presentations in a subtropical climate

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

Affiliations expand

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

Abstract

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

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

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

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

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

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Conflict of interest statement

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

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Am J Rhinol Allergy

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. 2023 Nov;37(6):705-729.

doi: 10.1177/19458924231190568. Epub 2023 Jul 25.

Systematic Review of Protein Biomarkers in Adult Patients With Chronic Rhinosinusitis

[Shyam A Gokani](#)^{1,2}, [Andreas Espehana](#)¹, [Ana C Pratas](#)¹, [Louis Luke](#)², [Ekta Sharma](#)³, [Jennifer Mattock](#)¹, [Jelena Gavrilovic](#)⁴, [Allan Clark](#)¹, [Tom Wileman](#)^{1,5}, [Carl M Philpott](#)^{1,2}

Affiliations expand

- PMID: 37491901
- PMCID: [PMC10548774](#)
- DOI: [10.1177/19458924231190568](#)

Free PMC article

Abstract

Background: Chronic rhinosinusitis (CRS) is a heterogeneous condition characterized by differing inflammatory endotypes. The identification of suitable biomarkers could enable personalized approaches to treatment selection.

Objective: This study aimed to identify and summarize clinical studies of biomarkers in adults with CRS in order to inform future research into CRS endotypes.

Methods: We conducted systematic searches of MEDLINE and Web of Science from inception to January 30, 2022 and included all clinical studies of adult CRS patients and healthy controls measuring biomarkers using enzyme-linked immunosorbent assays or Luminex immunoassays. Outcomes included the name and tissue type of identified biomarkers and expression patterns within CRS phenotypes. Study quality was assessed using the National Institutes of Health quality assessment tool for observational cohort and cross-sectional studies. A narrative synthesis was performed.

Results: We identified 78 relevant studies involving up to 9394 patients, predominantly with CRS with nasal polyposis. Studies identified 80 biomarkers from nasal tissue, 25 from nasal secretions, 14 from nasal lavage fluid, 24 from serum, and one from urine. The majority of biomarkers found to distinguish CRS phenotypes were identified in nasal tissue, especially in nasal polyps. Serum biomarkers were more commonly found to differentiate CRS from controls. The most frequently measured biomarker was IL-5, followed by IL-13

and IL-4. Serum IgE, IL-17, pentraxin-3 and nasal phospho-janus kinase 2, IL-5, IL-6, IL-17A, granulocyte-colony stimulating factor, and interferon gamma were identified as correlated with disease severity.

Conclusion: We have identified numerous potential biomarkers to differentiate a range of CRS phenotypes. Future studies should focus on the prognostic role of nasal tissue biomarkers or expand on the more limited studies of nasal secretions and nasal lavage fluid. We registered this study in PROSPERO (CRD42022302787).

Keywords: CRSsNP; CRSwNP; ECRS; biomarkers; chronic rhinosinusitis; cytokines; endotypes; interleukin; nasal polyps; phenotypes.

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.

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

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Randomized Controlled Trial

Am J Rhinol Allergy

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. 2023 Nov;37(6):638-645.

The Effect of Corticosteroids on Sinus Microbiota in Chronic Rhinosinusitis Patients with Nasal Polyposis

[Yousif Alammam](#)^{1,2}, [Simon Rousseau](#)³, [Martin Desrosiers](#)⁴, [Marc A Tewfik](#)¹

Affiliations expand

- PMID: 37475202
- PMCID: [PMC10548776](#)
- DOI: [10.1177/19458924231183848](#)

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Abstract

Background: Chronic rhinosinusitis with nasal polyposis (CRSwNP) is a multifactorial disease with no known single cause, but it is thought that bacteria play a role in the disease process.

Objective: This pilot study aims to assess the longitudinal effect of corticosteroid therapy on sinus microbiota in chronic rhinosinusitis patients with nasal polyposis (CRSwNP).

Methods: A longitudinal prospective case-control study was done on patients with CRSwNP and healthy controls. Patients with CRSwNP were randomly allocated to a corticosteroids and antibiotics treatment group (CRSwNP-SA) or a corticosteroid-only treatment group (CRSwNP-S). Data were collected at three-time points (before treatment, 1, and 3 months after treatment). Specimens were cultured and matrix-assisted laser desorption ionization-time of flight (MALDI-TOF) mass spectrometry (MS) was used as a bacterial detection method.

Results: Data from 29 patients with CRSwNP (16 CRSwNP-SA and 13 CRSwNP-S) was compared to 15 healthy subjects. Patients reported significant symptom improvement initially (1 month), but not in the long-term (3 months). This result was found in both treatment groups, whether or not antibiotics were used. After 3 months from treatment, the prevalence of *Corynebacterium* genera tended to increase in the CRSwNP-SA, while

Staphylococcus and Gram-negative genera (*Pseudomonas*) tended to increase in the CRSwNP-S. Smoking, aspirin sensitivity, and previous endoscopic sinus surgery were found to be co-factors significantly associated with the response to systemic corticosteroid therapy.

Conclusion: In this pilot study, both treatment options were effective to improve symptoms in the short-term but not in the long-term, and were not linked to any clear sinus microbiota response. As a result, this study supports the avoidance of systemic antibiotics without evidence of active infection.

Keywords: SNOT-22; antibiotics; chronic rhinosinusitis; corticosteroids; microbiota; nasal polyps.

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.

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

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[Review](#)

Eur Arch Otorhinolaryngol

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. 2023 Nov;280(11):4751-4758.

doi: 10.1007/s00405-023-08117-3. Epub 2023 Jul 18.

General classification of rhinopathies: the need for standardization according to etiology and nasal cytology

[M Gelardi](#)¹, [V Fiore](#)¹, [R Giancaspro](#)², [F M Di Canio](#)¹, [C Fiorentino](#)¹, [S Patruno](#)¹, [A Ruzza](#)¹, [M Cassano](#)¹

Affiliations expand

- PMID: 37462742
- PMCID: [PMC10562500](#)
- DOI: [10.1007/s00405-023-08117-3](#)

Free PMC article

Abstract

Background: Rhinitis is as an inflammation of the nasal mucosa, characterized by high prevalence, widespread morbidity, and a significant financial burden on health care systems. Nevertheless, it is often considered as no more than a mere annoyance. This point of view has progressively led to underestimate and trivialize the disease. Therefore, there are numerous, mostly overlapping classifications of rhinopathies, but clear and standardized guidelines for diagnosis and treatment are still lacking. In the context of Precision Medicine, the development of a classification system focused on the endotypes of rhinitis to be widely adopted appears of utmost importance, also by virtue of study of the nasal immunophlogosis that, thanks to nasal cytology (NC), has recently allowed to better define the different forms of rhinitis, giving a new nosological dignity to several rhinopathies.

Aim: We aimed to summarize the current knowledge regarding rhinitis and to propose a systematic classification of rhinitis, based on both etiology and cytological findings.

Keywords: Allergic rhinitis; Classification of rhinopathies; Nasal cytology; Rhinitis; Rhinopathies; Vasomotor rhinitis.

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Conflict of interest statement

The authors declare no conflicts of interest.

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

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29

J Asthma

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. 2023 Nov;60(11):2014-2020.

doi: 10.1080/02770903.2023.2209175. Epub 2023 May 31.

[Efficacy and safety of fixed-dose combination of Bilastine-Montelukast in adult patients with allergic rhinitis: a phase III, randomized, multi-center, double-blind, active controlled clinical study](#)

[Shubhadeep D Sinha](#)¹, [Sridevi Perapogu](#)², [Sreenivasa Chary S](#)¹, [S Ramesh](#)³, [Jaimanti Bakshi](#)⁴, [Ajit Singh](#)⁵, [Abdul Khabeer Ahmed](#)⁶, [B Mohan Reddy](#)¹, [Muralidhar Panapakam](#)¹, [Leela Talluri](#)¹, [Ramya Vattipalli](#)¹

Affiliations expand

- PMID: 37140964
- DOI: [10.1080/02770903.2023.2209175](https://doi.org/10.1080/02770903.2023.2209175)

Abstract

Background: Histamine and cysteinyl leukotrienes (CysLTs) are potent inflammatory mediators in allergic rhinitis (AR). Studies involving other combinations of antihistaminics (Levocetirizine) and highly selective leukotriene receptor antagonist (LTA) (Montelukast) combination have shown additive benefits and are widely prescribed for AR.

Objective: Evaluate the efficacy and safety of Bilastine 20 mg and Montelukast 10 mg fixed-dose combination (FDC) therapy in patients with AR.

Methods: A randomized, double-blind, comparative, parallel, phase III study was conducted to evaluate efficacy and safety of Bilastine 20 mg and Montelukast 10 mg FDC at 16 tertiary care otolaryngology centres in India. Adult patients with AR for one year with IgE antibody positive and 12-h NSS score >36 in 3 days were randomized to receive either Bilastine 20 mg and Montelukast 10 mg or Montelukast 10 mg & Levocetirizine 5 mg tablets for 4 weeks. The change in total symptom score (nasal symptom scores (NSS) & non-nasal symptom scores (NNS)) from baseline to week 4 was assessed as primary endpoint. Secondary endpoints included changes in TSS, NSS, NNS, individual symptom scores (ISS), Rhinoconjunctivitis Quality of Life (RQLQ), discomfort due to rhinitis (VAS), and clinical global impression (CGI) scores.

Results: The change in mean TSS from baseline to week 4 in Test group (16.6 units) was comparable to reference group (17 units) ($p= 0.8876$). The difference in change in mean NSS, NNS and ISS from baseline to day 7, 14, 28 were comparable. RQLQ improved from baseline to Day 28. Significant improvements were observed in discomfort due to AR measured by VAS and CGI scores from baseline to day 14 and 28. The safety and tolerability of patients were comparable between the groups. All adverse events (AEs) were mild to moderate in severity. No patient discontinued due to AEs.

Conclusions: The FDC of Bilastine 20 mg and Montelukast 10 mg was efficacious and well tolerated in Indian patients with AR.

Keywords: Second-generation antihistamine; allergic rhinitis; clinical trial; fixed-dose combination; leukotriene receptor antagonist; safety; total symptom score.

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Otolaryngol Head Neck Surg

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. 2023 Nov;169(5):1329-1334.

doi: 10.1002/ohn.361. Epub 2023 May 3.

[The Role of Nasal Endoscopy in the Preoperative Evaluation of Nasal Airway Obstruction](#)

[Lauren A Gardiner](#)¹, [Lindsey K Goyal](#)¹, [Jennifer L McCoy](#)^{2,3}, [Grant S Gillman](#)¹

Affiliations expand

- PMID: 37132657

- DOI: [10.1002/ohn.361](https://doi.org/10.1002/ohn.361)

Abstract

Objective: To examine the prevalence and nature of nasal endoscopic findings in patients referred for structural nasal obstruction, and analyze how such findings influence the preoperative evaluation or operative plan.

Study design: Cross-sectional study.

Setting: University-based academic otolaryngology practice.

Methods: Nasal endoscopy was performed by a single surgeon and the exam findings were documented. Patient demographics, variables in the patient history, Nasal Obstruction Symptom Evaluation scores, and an Ease-of-Breathing Likert Scale were tested for associations with findings on endoscopy.

Results: A total of 82 of 346 patients (23.7%) had findings on rigid nasal endoscopy not appreciable on anterior rhinoscopy. Prior nasal surgery ($p = .001$) and positive allergy testing ($p = .013$) were significantly associated with findings on nasal endoscopy. Endoscopic findings prompted additional preoperative studies in 50 (14.5%) patients, and a change in the operative plan in 26 (7.5%) patients.

Conclusion: In patients referred for surgical management of nasal obstruction, findings on nasal endoscopy otherwise undetected with anterior rhinoscopy are most common in but certainly not limited to those with prior nasal surgery or allergic rhinitis. Routine nasal endoscopy should be considered for all patients being evaluated for nasal airway surgery. These results may benefit future updates of the clinical consensus statements regarding the role of nasal endoscopy in the evaluation of nasal valve compromise and septoplasty.

Keywords: nasal airway obstruction; nasal endoscopy; practice guidelines.

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Ann Otol Rhinol Laryngol

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. 2023 Nov;132(11):1400-1403.

Long-term Follow-up of Pediatric Chronic Rhinosinusitis After Surgical Treatment

[Chadi A Makary](#)¹, [Maximilian Bonnici](#)², [Garrett Jones](#)¹, [Patrick Sullivan](#)², [Cara Stokes](#)³, [Hassan H Ramadan](#)¹

Affiliations expand

- PMID: 36951071
- DOI: [10.1177/00034894231161417](https://doi.org/10.1177/00034894231161417)

Abstract

Objective: To study the long-term outcomes of pediatric chronic rhinosinusitis (CRS) after surgical treatment.

Methods: Cross-sectional survey of patients who were treated surgically for CRS as children more than 10 years ago. Survey included SNOT-22 questionnaire, additional functional endoscopic sinus surgery (FESS) since last treatment, status of allergic rhinitis and asthma, and availability of any CT scan sinus/face for review.

Results: About 332 patients were contacted by phone or email. Seventy-three patients filled the survey (22.5% response rate). Current age was 26 years (\pm 4.7, 15.3-37.8 years). Age at initial treatment was 6.8 years (\pm 3.1, 1.7-14.7 years). Fifty-two patients (71.2%) had FESS and adenoidectomy, and 21 patients (28.8%) had adenoidectomy only. Follow-up since surgical treatment was 19.3 years (\pm 4.1). SNOT-22 score was 34.5 (\pm 22.2). None of the patients had any additional FESS for the duration of the follow-up, and only 3 patients had septoplasty and inferior turbinoplasty as adults. Twenty-four patients had CT scan sinuses/face available for review. Scans were obtained at an average of 14 years after surgical intervention (\pm 5.2). CT LM score was 0.9 (\pm 1.9), compared to 9.3 at time of their surgery (\pm 5.9) ($P < .0001$). Currently 45.8% and 36.9% of patients have asthma and AR, compared to 35.6% and 40.6% respectively as kids ($P = .897$ and $P = .167$).

Conclusion: Children who had surgery for CRS do not seem to have CRS as adults. However, patients continue to have active allergic rhinitis that may affect their quality of life.

Keywords: adenoidectomy; chronic rhinosinusitis; miscellaneous; otolaryngology; outcome; pediatric sinusitis; quality of life; rhinology.

- [Cited by 1 article](#)

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Laryngoscope

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. 2023 Nov;133(11):2898-2909.

doi: 10.1002/lary.30642. Epub 2023 Mar 13.

[Upper Airway Disease in Adults with Cystic Fibrosis in the Era of CFTR Modulators](#)

[Saartje Uyttebroek](#)^{1,2}, [Lieven Dupont](#)^{3,4}, [Mark Jorissen](#)^{1,2}, [Laura Van Gerven](#)^{1,2,5}

Affiliations expand

- PMID: 36912358
- DOI: [10.1002/lary.30642](https://doi.org/10.1002/lary.30642)

Abstract

Objectives: Chronic rhinosinusitis (CRS) is prevalent in people with cystic fibrosis (PwCF) and is often refractory to treatments. Uncontrolled CRS might negatively impact the lower airways and the quality of life. The aim of this study is to evaluate the burden of cystic fibrosis (CF)-related CRS in the era of CF transmembrane conductance regulator (CFTR) modulators.

Methods: Adult PwCF were asked to fill in a questionnaire on sinonasal complaints, they underwent a nasal endoscopy, bacteriological sampling, and a CT scan. Afterwards, these outcome measures were compared between patients treated with and without modulators.

Results: In the 122 included patients, CRS was present in 83%. CFTR modulators were prescribed in 48% of the patients, with a median of 10 months since the start of the treatment. Subjectively, the median SNOT-22 score was 16/110. Objectively, a median Lund-Kennedy score of 6/12 and modified Lund-Mackay score of 10/24 were observed. No correlation could be found between SNOT-22 score and other outcome measures including endoscopy and radiology. Altogether, 21% of the patients had controlled disease. When comparing patients treated with and without modulators, significantly lower CT scores ($p = 0.0018$) and less bacterial colonization ($p = 0.0082$) were observed in patients receiving modulators.

Conclusion: CF-CRS is highly prevalent in our cohort and only the minority of PwCF has a well-controlled disease. A multidisciplinary ENT-pneumology clinic would be beneficial, as there is a high discrepancy between patient-reported symptoms and the extent of the disease. CFTR modulators are promising, as lower CT scores and less bacterial colonization were observed in the modulator group.

Level of evidence: Level 3 Laryngoscope, 133:2898-2909, 2023.

Keywords: CFTR modulator; chronic rhinosinusitis; nasal polyps; upper airway disease.

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- [Cited by 1 article](#)
- [31 references](#)

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Am J Rhinol Allergy



. 2023 Nov;37(6):623-629.

doi: 10.1177/19458924231160596. Epub 2023 Mar 7.

Co-treatment with Fexofenadine and Budesonide Increases FoxP3 Gene Expression in Patients with Allergic Rhinitis

[Elham Bagherinia](#)¹, [Sara Falahi](#)¹, [Seyed Hamidreza Mortazavi](#)², [Farhad Salari](#)³, [Alireza Rezaeiemanesh](#)³, [Ali Gorgin Karaji](#)³

Affiliations expand

- PMID: 36882993
- DOI: [10.1177/19458924231160596](https://doi.org/10.1177/19458924231160596)

Abstract

Background: T helper type 2 (Th2), Th17, and regulatory T cells (Tregs) play essential roles in the pathogenesis and control of allergic rhinitis (AR). Fexofenadine and budesonide are first-line treatments for AR. This study aimed to investigate the effect of co-treatment with fexofenadine and budesonide on the expression of Th2, Th17, and Treg-specific transcription factors (GATA-binding protein 3 [GATA-3], RAR-related orphan receptor gamma [RORγt], and forkhead box P3 [FoxP3], respectively) in AR patients.

Methods: In this study, 29 AR patients were co-treated with fexofenadine and budesonide for 1 month. Blood was collected from AR patients before and after 1 month of treatment.

The gene expression levels of GATA-3, ROR γ t, and FoxP3 transcription factors in blood samples were measured. In addition, serum immunoglobulin E (IgE) levels and eosinophil percentages in blood samples were determined.

Findings: The expression level of FoxP3 increased significantly after treatment compared with that before treatment ($P < .001$). In contrast, GATA-3 and ROR γ t expression levels did not show any noticeable changes. In addition, the percentage of peripheral blood eosinophils significantly decreased ($P < .01$). Serum IgE levels decreased compared with those before treatment, but the difference was not statistically significant. Furthermore, the clinical symptoms of the patients improved compared with those before treatment.

Conclusion: Our results showed that combined treatment with fexofenadine and budesonide increased the expression level of the FoxP3 gene, decreased the percentage of peripheral blood eosinophils, and improved the clinical symptoms of AR patients. This regimen appears to improve disease symptoms, at least in part by increasing the Treg population and decreasing the eosinophil population.

Keywords: budesonide, fexofenadine, FoxP3, allergic rhinitis, eosinophils, Treg.

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

MeSH terms, Substancesexpand

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Laryngoscope

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. 2023 Nov;133(11):2885-2890.

Postoperative Polyp Scale (POPS): Development of a New Sinonasal Polyp Grading Scale

[Arthur W Wu](#)^{1,2}, [Akaber M Halawi](#)^{1,3}, [Elisa A Illing](#)^{1,4}, [Dennis M Tang](#)^{1,2}, [Philip G Chen](#)^{1,5}, [Edward C Kuan](#)^{1,6}, [Jonathan Y Ting](#)^{1,4}, [Daniel A Norez](#)⁷, [Stacey A Kim](#)⁸, [Dhruv Sharma](#)^{1,4}, [Douglas D Reh](#)^{1,9}, [Sanjeet V Rangarajan](#)^{1,10}, [Kent K Lam](#)^{1,11}, [Randall A Ow](#)^{1,12}, [J Wesley Sublett](#)^{1,13}, [Thomas S Higgins](#)^{1,14,15}

Affiliations expand

- PMID: 36866689
- DOI: [10.1002/lary.30623](https://doi.org/10.1002/lary.30623)

Abstract

Objective: Commonly used endoscopic grading scales, such as the nasal polyp scale, inadequately describe the degree of polyposis found postoperatively in the paranasal sinus cavities. The purpose of this study was to create a novel grading system that more accurately characterizes polyp recurrence in postoperative sinus cavities, the Postoperative Polyp Scale (POPS).

Methods: A modified Delphi method was utilized to establish the POPS using consensus opinion among 13 general otolaryngologists, rhinologists, and allergists. Postoperative endoscopy videos from 50 patients with chronic rhinosinusitis with nasal polyps were reviewed by 7 fellowship-trained rhinologists and scored according to the POPS. Videos were rated again 1 month later by the same reviewers, and scores were assessed for test-retest and inter-rater reliability.

Results: Overall inter-rater reliability for the first and second reviews of the 52 videos was $K_f = 0.49$ (95% CI 0.42-0.57) and $K_f = 0.50$ (95% CI 0.42-0.57) for the POPS. Intra-rater reliability showed near-perfect test-retest reliability for the POPS with $K_f = 0.80$ (95% CI 0.76-0.84).

Conclusion: The POPS is an easy-to-use, reliable, and novel objective endoscopic grading scale that more accurately describes polyp recurrence in the postoperative state which will be useful in the future for measuring the efficacy of various medical and surgical interventions.

Level of evidence: 5 Laryngoscope, 133:2885-2890, 2023.

Keywords: chronic rhinosinusitis; endoscopic grading; endoscopic sinus surgery; nasal polyps; outcomes.

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SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS



Chronic cough

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Pediatr Pulmonol

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. 2023 Nov 3.

doi: 10.1002/ppul.26744. Online ahead of print.

The Habit Cough Syndrome

[Miles Weinberger](#)^{1,2}, [Dennis Buettner](#)³

Affiliations expand

- PMID: 37921546
- DOI: [10.1002/ppul.26744](https://doi.org/10.1002/ppul.26744)

No abstract available

Keywords: behavioral therapy; chronic cough; habit cough; speech and language therapy; suggestion therapy.

- [20 references](#)

SUPPLEMENTARY INFO

Grants and funding [expand](#)

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Allergy Asthma Proc

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. 2023 Nov 1;44(6):382-394.

doi: [10.2500/aap.2023.44.230059](https://doi.org/10.2500/aap.2023.44.230059).

Evaluation and management of chronic cough in adults

[Dana V Wallace](#)

- PMID: 37919844
- DOI: [10.2500/aap.2023.44.230059](https://doi.org/10.2500/aap.2023.44.230059)

Abstract

Background: Chronic cough (CC), a cough that lasts > 8 weeks, has an overall prevalence of 5-11% in adults, peaking between 60 and 80 years of age. Of the 15% of patients who remain undiagnosed or refractory to treatment, two thirds are women. **Objective:** The objective was to present an updated evidence-based algorithmic approach for evaluating and managing CC, with emphasis on treatment modalities for refractory CC. **Methods:** A

literature search was conducted of medical literature data bases for guidelines, position papers, systematic reviews, and clinical trials from January 2022 to June 2023, on the evaluation and management of CC. **Results:** The initial assessment should be limited to a detailed history, physical examination, chest radiograph, spirometry, exhaled nitric oxide, blood eosinophil count, and measurement of cough severity and quality of life by using validated instruments. The top diagnoses to consider are asthma, chronic obstructive pulmonary disease, nonasthmatic eosinophilic bronchitis, gastroesophageal reflux disease, and upper airway cough syndrome. Additional studies are only obtained when red flags are present or the patient fails to respond after avoidance of high-risk factors, e.g., smoking and angiotensin-converting enzyme inhibitors, and 4-6 weeks of empiric treatment for the most likely respiratory and gastrointestinal diseases. When diagnostic tests and/or specific directed treatments fail to control CC, low-dose morphine (preferred), gabapentin, pregabalin, and/or cough control therapy are recommended. Non-narcotic purinergic 2×3 (P2×3) receptor antagonists, gafapixant and campilixant, are currently being studied for CC. **Conclusion:** For the evaluation and management of patients with CC, clinicians should use an algorithmic approach and identify "red flags," reduce high-risk factors, and use empiric treatment for the five top diagnoses before extensive diagnostic testing. Current treatment for refractory cough is limited to symptomatic management.

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[Review](#)

MMW Fortschr Med

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. 2023 Nov;165(19):61-63.

doi: 10.1007/s15006-023-3099-1.

[Chronic cough – Stepchild of diagnostics]

[Article in German]

[Thomas Hering](#)¹

Affiliations expand

- PMID: 37919591
- DOI: [10.1007/s15006-023-3099-1](https://doi.org/10.1007/s15006-023-3099-1)

No abstract available

- [5 references](#)

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Laryngoscope

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. 2023 Nov 2.

doi: 10.1002/lary.31120. Online ahead of print.

Two-Year Outcomes After Radiofrequency Neurolysis of Posterior Nasal Nerve in Chronic Rhinitis

[Jivianne T Lee](#)¹, [Gregory M Abbas](#)², [Daniel D Charous](#)³, [Mandy Cuevas](#)⁴, [Önder Göktas](#)⁵, [Patricia A Loftus](#)⁶, [Nathan E Nachlas](#)⁷, [Elina M Toskala](#)⁸, [Jeremy P Watkins](#)⁹, [Detlef Brehmer](#)^{10 11 12}

Affiliations expand

- PMID: 37916848
- DOI: [10.1002/lary.31120](https://doi.org/10.1002/lary.31120)

Abstract

Objective: To assess the long-term safety and effectiveness of temperature-controlled radiofrequency (TCRF) neurolysis of the posterior nasal nerve (PNN), a minimally invasive treatment for chronic rhinitis.

Methods: A prospective, single-arm study of 129 patients at 16 centers (United States, Germany) was conducted. Patient-reported outcome measures were the 24-h reflective total nasal symptom score (rTNSS) and mini rhinoconjunctivitis quality of life questionnaire (MiniRQLQ). Postnasal drip and cough symptoms were assessed using a 4-point scale.

Results: The mean pretreatment rTNSS was 7.8 (95% CI, 7.5-8.1). The significant rTNSS treatment effect at 3 months (-4.2 [95% CI, -4.6 to -3.8]; $p < 0.001$) was sustained through 2 years (-4.5 [95% CI, -5.0 to -3.9]; $p < 0.001$), a 57.7% improvement. At 2 years, the proportion of patients with a minimal clinically important difference (MCID) of $\geq 30\%$ improvement in rTNSS from baseline was 80.0% (95% CI, 71.4%-86.5%). Individual postnasal drip and cough symptom scores were significantly improved from baseline through 2 years. The proportion of patients who reached the MCID for the MiniRQLQ (≥ 0.4 -point improvement) at 2 years was 77.4% (95% CI, 68.5%-84.3%). Of 81 patients using chronic rhinitis medications at baseline, 61.7% either stopped all medication use (28.4%) or stopped or decreased (33.3%) use of ≥ 1 medication class at 2 years. No device/procedure-related serious adverse events were reported throughout 2 years.

Conclusion: TCRF neurolysis of the PNN resulted in sustained improvements in chronic rhinitis symptom burden and quality of life through 2 years, accompanied by a substantial decrease in medication burden.

Level of evidence: 4 Laryngoscope, 2023.

Keywords: MiniRQLQ; chronic rhinitis; neurolysis; posterior nasal nerve; quality of life; rTNSS; radiofrequency; temperature-controlled.

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- [29 references](#)

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BMC Pulm Med

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. 2023 Oct 31;23(1):416.

doi: 10.1186/s12890-023-02709-9.

[Understanding the economic burden of chronic cough: a systematic literature review](#)

[Vishal Bali](#)^{1,2}, [Ada Adriano](#)³, [Aidan Byrne](#)³, [Katherine G Akers](#)⁴, [Andrew Frederickson](#)⁴, [Jonathan Schelfhout](#)⁵

Affiliations [expand](#)

- PMID: 37907889

- PMID: [PMC10619292](#)
- DOI: [10.1186/s12890-023-02709-9](#)

Free PMC article

Abstract

Chronic cough (CC) is associated with high healthcare resource utilization (HCRU) due to challenges in diagnosis and treatment and is anticipated to have a substantial economic impact. This systematic literature review (SLR) sought to identify evidence on the cost-effectiveness of treatments and the economic burden associated with CC. Electronic database searches were supplemented with searches of conference proceedings and health technology assessment body websites. Two independent reviewers assessed all citations for inclusion based on predefined inclusion/exclusion criteria. Key inclusion criteria were patient population with CC, and outcomes related to cost-effectiveness and HCRU and costs. After screening, one cost-effectiveness analysis was identified, alongside eight studies reporting HCRU and costs related to CC. Though evidence was limited, studies suggest that patients with CC incur higher costs and use more resources than those with acute cough. Types of resource use reported included healthcare contacts and prescriptions, diagnostic tests, referrals and specialist evaluations, and treatment use. There is a paucity of literature on HCRU and costs in CC, and very limited cost-effectiveness analyses. The economic burden appears higher in these patients however, without direct comparison to the general population it is difficult to determine the total impact. The increased burden is expected to be a result of the challenges with diagnosis and lack of approved treatments. However, limited conclusions can be drawn in the absence of further data. Future studies should endeavor to quantify the HCRU and cost attributable to patients with CC.

Keywords: Burden; Chronic cough; Economic burden; Refractory chronic cough; Unexplained chronic cough.

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Conflict of interest statement

The authors declare no competing interests.

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

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Publication types, MeSH termsexpand

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Review

Respiration

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. 2023 Oct 31:1-13.

doi: 10.1159/000534370. Online ahead of print.

[Airway Mucosal Remodeling: Mechanism of Action and Preclinical Data of Pulsed Electric Fields for Chronic Bronchitis and Mucus Hypersecretion](#)

[William Krinsky](#)¹, [Robert E Neal li](#)¹, [Victor Kim](#)²

Affiliations expand

- PMID: 37906995
- DOI: [10.1159/000534370](https://doi.org/10.1159/000534370)

Abstract

Patients living with chronic bronchitis (CB) suffer from physical limitations and poor quality of life. In general, treatment options that directly address the mucus hypersecretion component of CB are quite limited. Chronic airway inflammation and the associated hypersecretion and cough that are pathognomonic for CB generally result from long-term exposure to airway irritants such as tobacco use and other environmental insults. This, in turn, results in an increase in the quantity and change in composition of the airway mucosa as a consequence of altered goblet cells, club cells, and submucosal glands. Pulsed electric fields (PEFs) provide a method for eradicating the cellular constituents of tissue with limited impact on the stromal proteins. Preclinical evidence in porcine airways demonstrated that particular PEF waveforms allowed for salutary remodeling of the epithelial and submucosal airway tissue layers and appeared to foster rapid regeneration and recovery of the tissue. Therefore, a therapeutic opportunity might exist whereby the application of a specific form of PEF may result in a reduction of the cellular secretory constituents of the airway while also reducing airway mucosal inflammation. This review discusses the use of such PEF to address the underlying disease processes in CB including challenges around device design, dosing, and appropriate delivery methods. Further, we outline considerations for the transition to human airways along with a brief examination of the initial work treating CB patients, suggesting that the therapy is well tolerated with limited adverse events.

Keywords: Airway mucosa; Chronic bronchitis; Chronic obstructive pulmonary disease; Non-pharmacologic treatment; Pulsed electric fields; RheOx.

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Respir Med



. 2023 Nov:218:107396.

doi: 10.1016/j.rmed.2023.107396. Epub 2023 Aug 30.

Predictors of treatment response to pregabalin in unexplained or refractory chronic cough

[Mathieu D Saint-Pierre](#)¹

Affiliations expand

- PMID: 37657533
- DOI: [10.1016/j.rmed.2023.107396](https://doi.org/10.1016/j.rmed.2023.107396)

Abstract

Background: Patients with chronic cough (>8 weeks) often remain symptomatic after appropriate investigations and therapeutic trials. Prior research has shown a benefit in certain individuals from pregabalin, but clinical improvement is quite unpredictable and variable.

Objective: The main objective of this study was to identify the demographic and clinical characteristics associated with a higher likelihood of cough improvement with a trial of pregabalin therapy.

Methods: 50 consecutive patients with chronic cough were enrolled in this prospective cohort study. Subjects were prescribed pregabalin 75 mg oral qhs for 4 weeks followed by 75 mg oral bid. Leicester Cough Questionnaire (LCQ) was completed at treatment initiation and after 3 months of therapy. A comparison was performed between treatment responders (LCQ total score improvement ≥ 1.3) and non-responders.

Results: 56% of patients reported a LCQ total score improvement ≥ 1.3 (minimal clinically important difference). Responders to pregabalin therapy were more likely to have refractory (with underlying pulmonary disease) versus unexplained chronic cough ($p = 0.01$). Patients with significant improvement were also on average more symptomatic at baseline (mean LCQ total score 10.2 versus 13.0, $p < 0.01$). No significant relationship was identified with age, gender, body mass index, history of anxiety and/or depression,

cigarette smoking history, or cough duration ($p > 0.05$). The unexplained chronic cough group had a strong female predominance (85.7% versus 40.9% for refractory cough, $p < 0.01$).

Conclusion: This is the first study that has investigated clinical predictors of treatment response to pregabalin in chronic cough patients. Further research is needed to develop therapies for subjects who do not improve with currently available neuromodulating medications.

Keywords: Chronic cough; Cough; Pregabalin; Treatment response.

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Conflict of interest statement

Declaration of competing interest No conflict of interest.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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8

Ann Am Thorac Soc

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. 2023 Nov;20(11):1578-1586.

doi: 10.1513/AnnalsATS.202301-0500C.

[Longitudinal Changes and Association of Respiratory Symptoms with](#)

Preserved Ratio Impaired Spirometry (PRISm): The Nagahama Study

[Mariko Kogo](#)¹, [Susumu Sato](#)^{1,2}, [Shigeo Muro](#)³, [Hisako Matsumoto](#)^{1,4}, [Natsuko Nomura](#)¹, [Tsuyoshi Oguma](#)¹, [Hironobu Sunadome](#)², [Tadao Nagasaki](#)², [Kimihiko Murase](#)², [Takahisa Kawaguchi](#)⁵, [Yasuharu Tabara](#)^{5,6}, [Fumihiko Matsuda](#)⁵, [Kazuo Chin](#)^{5,7}, [Toyohiro Hirai](#)¹

Affiliations expand

- PMID: 37560979
- DOI: [10.1513/AnnalsATS.202301-050OC](https://doi.org/10.1513/AnnalsATS.202301-050OC)

Abstract

Rationale: Subjects with preserved ratio impaired spirometry (PRISm) experience increased respiratory symptoms, although they present heterogeneous characteristics. However, the longitudinal changes in these symptoms and respiratory function are not well known. **Objectives:** To investigate PRISm from the viewpoint of respiratory symptoms in a longitudinal, large-scale general population study. **Methods:** The Nagahama study included 9,789 inhabitants, and a follow-up evaluation was conducted after 5 years. Spirometry and self-administered questionnaires regarding respiratory symptoms, including prolonged cough, sputum and dyspnea, and comorbidities were conducted. **Results:** In total, 9,760 subjects were analyzed, and 438 subjects had PRISm. Among the subjects with PRISm, 53% presented with respiratory symptoms; dyspnea was independently associated with PRISm. Follow-up assessment revealed that 73% of the subjects with PRISm with respiratory symptoms were consistently symptomatic, whereas 39% of the asymptomatic subjects with PRISm developed respiratory symptoms within 5 years. In addition, among subjects with respiratory symptoms without airflow limitation at baseline, PRISm was a risk factor for the development of airflow limitation independent of smoking history and comorbidities. **Conclusions:** This study demonstrated that 53% of the subjects with PRISm had respiratory symptoms; dyspnea was a distinct characteristic of PRISm. Approximately three-fourths of the symptomatic subjects with PRISm consistently complained of respiratory symptoms within 5 years. Together with our result that PRISm itself is an independent risk factor for the development of chronic obstructive pulmonary disease among subjects with respiratory symptoms, the clinical course of subjects with PRISm with symptoms requires careful monitoring.

Keywords: airflow limitation; dyspnea; pulmonary function test.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Heart Lung



. 2023 Nov-Dec;62:168-174.

doi: 10.1016/j.hrtlng.2023.07.008. Epub 2023 Aug 2.

[Relationship between nighttime symptoms and clinical features in COPD patients: A cross-sectional multicenter study in China](#)

[Jiankang Wu](#)¹, [Weiwei Meng](#)¹, [Huihui Zeng](#)¹, [Yiming Ma](#)¹, [Yan Chen](#)²

Affiliations expand

- PMID: 37541136
- DOI: [10.1016/j.hrtlng.2023.07.008](https://doi.org/10.1016/j.hrtlng.2023.07.008)

Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a chronic respiratory disease that causes breathing difficulties, coughing, and other symptoms. Nighttime symptoms, such as coughing, wheezing, and shortness of breath, can significantly impact the quality of life for people with COPD.

Objective: To investigate the relationship between nighttime symptoms and other clinical features in patients with COPD, and identify potential risk factors associated with nighttime symptoms.

Methods: This cross-sectional study was conducted from October 1, 2022 to November 30, 2022 in 24 hospital outpatient departments in different cities of Hunan Province, China. The COPD Nighttime Symptom Instrument (NiSCI) was used to measure the severity of night time symptoms in COPD patients. Descriptive and inferential statistics were used to express patient socio-demographics and factors influencing nighttime symptoms.

Results: The study included 2219 COPD patients. The results showed that nighttime symptom scores differed significantly based on gender, whether the patient had experienced acute exacerbation in the past year, mMRC and CAT scores, the duration of home oxygen therapy and home non-invasive ventilation (all $P < 0.0001$). Multiple linear regression analysis revealed that CAT score ($P < 0.0001$) was significantly associated with nighttime symptom scores.

Conclusion: Nighttime symptoms are prevalent in Chinese COPD patients and correlate with disease severity. The assessment and management of nighttime symptoms in COPD patients must take into account gender, CAT and mMRC scores, history of acute exacerbations, and duration of home oxygen therapy and home non-invasive ventilation to enable tailoring of treatment strategies to individual needs.

Keywords: COPD; Clinical features; Nighttime symptoms; Related factors.

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Conflict of interest statement

Declaration of Competing Interest The authors declare that they have no competing interests.

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Respir Med



. 2023 Nov:218:107372.

doi: 10.1016/j.rmed.2023.107372. Epub 2023 Jul 27.

Dysfunctional mucociliary clearance in asthma and airway remodeling - New insights into an old topic

[Milos Jesenak](#)¹, [Peter Durdik](#)², [Dasa Oppova](#)², [Sona Franova](#)³, [Zuzana Diamant](#)⁴, [Kornel Golebski](#)⁵, [Peter Banovcin](#)², [Jarmila Vojtkova](#)⁶, [Elena Novakova](#)⁷

Affiliations expand

- PMID: 37516275
- DOI: [10.1016/j.rmed.2023.107372](https://doi.org/10.1016/j.rmed.2023.107372)

Abstract

Bronchial asthma is a heterogeneous respiratory condition characterized by chronic airway inflammation, airway hyperresponsiveness and airway structural changes (known as remodeling). The clinical symptoms can be evoked by (non)specific triggers, and their intensity varies over time. In the past, treatment was mainly focusing on symptoms' alleviation; in contrast modern treatment strategies target the underlying inflammation, even during asymptomatic periods. Components of airway remodeling include epithelial cell shedding and dysfunction, goblet cell hyperplasia, subepithelial matrix protein deposition, fibrosis, neoangiogenesis, airway smooth muscle cell hypertrophy and hyperplasia. Among the other important, and frequently forgotten aspects of airway remodeling, also loss of epithelial barrier integrity, immune defects in anti-infectious defence and mucociliary clearance (MCC) dysfunction should be pointed out. Mucociliary clearance represents one of the most important defence airway mechanisms. Several studies in asthmatics demonstrated various dysfunctions in MCC - e.g., ciliated cells displaying intracellular disorientation, abnormal cilia and cytoplasmic blebs. Moreover, excessive mucus production and persistent cough are one of the well-recognized features of severe asthma and are also associated with defects in MCC. Damaged airway epithelium and impaired function of the ciliary cells leads to MCC dysfunction resulting in higher susceptibility to infection and inflammation. Therefore, new strategies aimed on restoring the remodeling changes and MCC dysfunction could present a new therapeutic approach for the management of asthma and other chronic respiratory diseases.

Keywords: Airway defence mechanisms; Airway remodeling; Bronchial asthma; Chronic inflammation; Epithelial dysfunction; Mucociliary clearance.

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Conflict of interest statement

Declaration of competing interest No conflict of interest.

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MeSH termsexpand

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Randomized Controlled Trial

Laryngoscope

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. 2023 Nov;133(11):3068-3074.

doi: 10.1002/lary.30739. Epub 2023 May 11.

[The Efficacy of Superior Laryngeal Nerve Block for Neurogenic Cough: A Placebo-Controlled Trial](#)

[Courtney B Tipton](#)¹, [Rameen Walters](#)¹, [Rachana Gudipudi](#)¹, [Drasti Smyre](#)¹, [Shaun Nguyen](#)¹, [Ashli K O'Rourke](#)¹

Affiliations expand

- PMID: 37166167
- DOI: [10.1002/lary.30739](https://doi.org/10.1002/lary.30739)

Abstract

Objectives: Chronic cough is a common and debilitating problem. The objective of this study is to assess the efficacy and safety of superior laryngeal nerve (SLN) block for neurogenic cough through a placebo-controlled, prospective trial.

Methods: Patients were recruited in an outpatient tertiary care center. Inclusion criteria included a history consistent with neurogenic cough and age ≥ 18 . Exclusion criteria included patients with untreated other etiologies of chronic cough (i.e., uncontrolled reflux) and current neuromodulating medication use. Patients were randomized into the treatment (1-2 mL of a 1:1 triamcinolone 40 mg: 1% lidocaine with 1:200,000 epinephrines) or placebo (saline) group and received two unilateral injections at approximately 2-week intervals. Outcomes were measured primarily by the Leicester Cough Questionnaire (LCQ) and a patient symptom log including a visual analog scale of cough severity.

Results: 17 patients completed the study, including 10 in the treatment group and seven in the placebo group. Eight (80%) patients in the treatment group reported improvement with at least one of the injections, whereas only 1 (14.3%) patient reported improvement in the placebo group ($p < 0.0001$). Average total LCQ scores increased in the treatment group from 10.09 to 13.15 ($p = 0.03$), with the most change occurring in the social domain. There was no statistically significant change in LCQ scores for the placebo group. There were no serious adverse events.

Conclusion: An SLN block is a safe and efficacious procedure for the treatment of neurogenic cough. Further studies are needed to optimize treatment protocol and assess long-term follow-up of patient outcomes.

Level of evidence: 2 Laryngoscope, 133:3068-3074, 2023.

Keywords: cough; superior laryngeal nerve block.

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- [26 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS



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

1

Am J Respir Crit Care Med



. 2023 Nov 2.

doi: 10.1164/rccm.202310-1827ED. Online ahead of print.

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

Keywords: Bronchiectasis; inflammation; microbiome.

FULL TEXT LINKS



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Correspondence on "Efficacy and safety of macrolides in the treatment of children with bronchiectasis: a meta-analysis"

[Qifang Zheng](#)¹

Affiliations expand

- PMID: 37898704
- DOI: [10.1038/s41390-023-02872-z](https://doi.org/10.1038/s41390-023-02872-z)

No abstract available

- [5 references](#)

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Publication types expand

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nature portfolio **UNIMORE** 

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. 2023 Oct 26;10(4):450-516.

doi: 10.15326/jcopdf.2023.0464.

The 6th World Bronchiectasis and Nontuberculous Mycobacteria Conference Abstract Presentations

[Timothy R Aksamit](#)¹, [Elizabeth J Emery](#)², [Ashwin Basavaraj](#)², [Mark L Metersky](#)³, [Anne E O'Donnell](#)⁴, [Doreen J Addrizzo-Harris](#)²

Affiliations expand

- PMID: 37879732
- DOI: [10.15326/jcopdf.2023.0464](https://doi.org/10.15326/jcopdf.2023.0464)

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No abstract available

Keywords: 6th World Bronchiectasis and NTM Conference; bronchiectasis; nontuberculous mycobacteria.

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. 2023 Nov 1;107(11):e292-e304.

doi: 10.1097/TP.0000000000004726. Epub 2023 Oct 21.

Prognostic Value of Chest CT Findings at BOS Diagnosis in Lung Transplant Recipients

[Anke Van Herck](#)¹, [Hanne Beeckmans](#)¹, [Pieterjan Kerckhof](#)¹, [Annelore Sacreas](#)¹, [Saskia Bos](#)², [Janne Kaes](#)¹, [Arno Vanstapel](#)¹, [Bart M Vanaudenaerde](#)¹, [Jan Van Slambrouck](#)^{1,3}, [Michaela Orlitová](#)^{1,3}, [Xin Jin](#)¹, [Laurens J Ceulemans](#)^{1,3}, [Dirk E Van Raemdonck](#)^{1,3}, [Arne P Neyrinck](#)⁴, [Laurent Godinas](#)^{1,5}, [Lieven J Dupont](#)^{1,5}, [Geert M Verleden](#)^{1,5}, [Adriana Dubbeldam](#)⁶, [Walter De Wever](#)⁶, [Robin Vos](#)^{1,5}

Affiliations expand

- PMID: 37870882
- DOI: [10.1097/TP.0000000000004726](https://doi.org/10.1097/TP.0000000000004726)

Abstract

Background: Bronchiolitis obliterans syndrome (BOS) after lung transplantation is characterized by fibrotic small airway remodeling, recognizable on high-resolution computed tomography (HRCT). We studied the prognostic value of key HRCT features at BOS diagnosis after lung transplantation.

Methods: The presence and severity of bronchiectasis, mucous plugging, peribronchial thickening, parenchymal anomalies, and air trapping, summarized in a total severity score, were assessed using a simplified Brody II scoring system on HRCT at BOS diagnosis, in a cohort of 106 bilateral lung transplant recipients transplanted between January 2004 and January 2016. Obtained scores were subsequently evaluated regarding post-BOS graft survival, spirometric parameters, and preceding airway infections.

Results: A high total Brody II severity score at BOS diagnosis ($P = 0.046$) and high subscores for mucous plugging ($P = 0.0018$), peribronchial thickening ($P = 0.0004$), or parenchymal involvement ($P = 0.0121$) are related to worse graft survival. A high total Brody II score was associated with a shorter time to BOS onset ($P = 0.0058$), lower forced expiratory volume in 1 s ($P = 0.0006$) forced vital capacity (0.0418), more preceding airway

infections ($P = 0.004$), specifically with *Pseudomonas aeruginosa* ($P = 0.002$), and increased airway inflammation ($P = 0.032$).

Conclusions: HRCT findings at BOS diagnosis after lung transplantation provide additional information regarding its underlying pathophysiology and for future prognosis of graft survival.

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Conflict of interest statement

The authors declare no conflicts of interest.

- [Cited by 1 article](#)
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Pediatr Pulmonol

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. 2023 Nov;58(11):3038-3039.

doi: 10.1002/ppul.26637. Epub 2023 Aug 18.

Deterioration of FEV₁ in primary ciliary dyskinesia: What about the conditional change score?

[Helmi Ben Saad](#)¹

Affiliations expand

- PMID: 37594152
- DOI: [10.1002/ppul.26637](https://doi.org/10.1002/ppul.26637)

No abstract available

Keywords: conditional change score; pediatric population; spirometry; z-score.

Comment on

- [Risk factors for the deterioration of pulmonary function in primary ciliary dyskinesia.](#) Fein V, Maier C, Schlegtendal A, Denz R, Koerner-Rettberg C, Brinkmann F. *Pediatr Pulmonol.* 2023 Jul;58(7):1950-1958. doi: 10.1002/ppul.26417. Epub 2023 Apr 25. PMID: 37096790
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SUPPLEMENTARY INFO

Publication types, MeSH terms expand

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Respirology



. 2023 Nov;28(11):1053-1059.

doi: 10.1111/resp.14568. Epub 2023 Aug 7.

Safety and efficacy of bronchial thermoplasty in Australia 5 years post-procedure

[Monica Hatch](#)¹, [Paul Lilburn](#)^{2,3}, [Caroline Scott](#)⁴, [Alvin Ing](#)³, [David Langton](#)^{1,5}

Affiliations [expand](#)

- PMID: 37550800
- DOI: [10.1111/resp.14568](https://doi.org/10.1111/resp.14568)

Free article

Abstract

Background and objective: Outside clinical trials, there is limited long-term data following bronchial thermoplasty (BT). In a cohort of real-world severe asthmatics in an era of biological therapy, we sought to evaluate the safety and efficacy of BT 5 years post-treatment.

Methods: Every patient treated with BT at two Australian tertiary centres were recalled at 5 years, and evaluated by interview and record review, Asthma Control Questionnaire (ACQ), spirometry and high-resolution CT Chest. CT scans were interpreted using the modified Reiff and BRICS CT scoring systems for bronchiectasis.

Results: Fifty-one patients were evaluated. At baseline, this cohort had a mean age of 59.0 ± 11.8 years, mean ACQ of 3.0 ± 1.0 , mean FEV1 of $55.5 \pm 18.8\%$ predicted, and 53% were receiving maintenance oral steroids in addition to triple inhaler therapy. At 5 years, there was a sustained improvement in ACQ scores to 1.8 ± 1.0 ($p < 0.001$). Steroid requiring exacerbation frequency was reduced from 3.8 ± 3.6 to 1.0 ± 1.6 exacerbations per annum ($p < 0.001$). 44% of patients had been weaned off oral steroids. No change in spirometry was observed. CT scanning identified minor degrees of localized radiological bronchiectasis in 23/47 patients with the modified Reiff score increasing from 0.6 ± 2.6 at

baseline to 1.3 ± 2.5 ($p < 0.001$). However, no patients exhibited clinical features of bronchiectasis, such as recurrent bacterial infection.

Conclusion: Sustained clinical benefit from BT at 5 years was demonstrated in this cohort of very severe asthmatics. Mild, localized radiological bronchiectasis was identified in a portion of patients without clinical features of bronchiectasis.

Keywords: BT; asthma; bronchial thermoplasty; bronchoscopy and interventional techniques; cohort study; radiological bronchiectasis.

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- [23 references](#)

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Pediatr Res

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. 2023 Nov;94(5):1600-1608.

doi: 10.1038/s41390-023-02591-5. Epub 2023 May 26.

[Efficacy and safety of macrolides in the treatment of children with bronchiectasis: a meta-analysis](#)

[Guihua Song](#)¹, [Yan Zhang](#)², [Suping Yu](#)², [Mengmeng Sun](#)², [Bingxue Zhang](#)², [Minghao Peng](#)², [Weigang Lv](#)², [Hongyun Zhou](#)²

Affiliations expand

- PMID: 37237074
- DOI: [10.1038/s41390-023-02591-5](https://doi.org/10.1038/s41390-023-02591-5)

Abstract

Background: This study summarized the available randomized controlled trials (RCTs) to assess the efficacy and safety of macrolides on pathogens, lung function, laboratory parameters, and safety in children with bronchiectasis.

Methods: PubMed, EMBASE, and the Cochrane Library were searched for available papers published up to June 2021. The outcomes were the pathogens, adverse events (AEs), and the forced expiratory volume in one second (FEV1%) predicted.

Results: Seven RCTs (633 participants) were included. The long-term use of macrolides reduced the risk of the presence of *Moraxella catarrhalis* (RR = 0.67, 95% CI: 0.30-1.50, P = 0.001; I² = 0.0%, P_{heterogeneity} = 0.433), but not *Haemophilus influenzae* (RR = 0.19, 95% CI: 0.08-0.49, P = 0.333; I² = 57.0%, P_{heterogeneity} = 0.040), *Streptococcus pneumoniae* (RR = 0.91, 95% CI: 0.61-1.35, P = 0.635; I² = 0.0%, P_{heterogeneity} = 0.515), *Staphylococcus aureus* (RR = 1.01, 95% CI: 0.36-2.84, P = 0.986; I² = 61.9%, P_{heterogeneity} = 0.033), and any pathogens present (RR = 0.61, 95% CI: 0.29-1.29, P = 0.195; I² = 80.3%, P_{heterogeneity} = 0.006). Long-term macrolides had no effect on FEV1% predicted (WMD = 2.61, 95% CI: -1.31, 6.53, P = 0.192; I² = 0.0%, P_{heterogeneity} = 0.896). Long-term macrolides did not increase the risk of AEs or serious AEs.

Conclusion: Macrolides do not significantly reduce the risk of pathogens present (except for *Moraxella catarrhalis*) or increase FEV1% predicted among children with bronchiectasis. Moreover, macrolides were not associated with AEs. Considering the limitations of the meta-analysis, further larger-scale RCTs are needed to confirm the findings.

Impact: Macrolides do not significantly reduce the risk of pathogens present (except for *Moraxella catarrhalis*) among children with bronchiectasis. Macrolides do not significantly increase FEV1% predicted among children with bronchiectasis. This meta-analysis reports on the efficacy and safety of macrolides in the treatment of children with bronchiectasis, providing evidence for the management of children with bronchiectasis. This meta-analysis does not support the use of macrolides in the management of children with bronchiectasis unless the presence of *Moraxella catarrhalis* is proven or suspected.

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Does asthma-bronchiectasis overlap syndrome (ABOS) really exist?

[Angelica Tiotiu](#)^{1,2}, [Miguel-Angel Martinez-Garcia](#)^{3,4}, [Paula Mendez-Brea](#)⁵, [Iria Roibas-Veiga](#)⁵, [Francisco-Javier Gonzalez-Barcala](#)^{4,6,7,8}

Affiliations [expand](#)

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Abstract

Objective: To analyze the relationship between asthma and bronchiectasis, as well as the necessary conditions that this connection must meet for this group of patients to be considered a special phenotype.

Data sources: We performed a PubMed search using the MeSH terms "asthma" and "bronchiectasis." The literature research was limited to clinical trials, meta-analyses, randomized controlled trials, cohort studies, and systematic reviews, involving adult patients, published until November 30th, 2022.

Study selections: Selected papers were initially evaluated by the Authors, to assess their eligibility in contributing to the statements.

Results: The prevalence of bronchiectasis is higher than expected in patients with asthma, particularly in those with more severe disease, and in some patients, between 1.4% and 7% of them, asthma alone could be the cause of bronchiectasis. Both diseases share etiopathogenic mechanisms, such as neutrophilic and eosinophilic inflammation, altered airway microbiota, mucus hypersecretion, allergen sensitization, immune dysfunction, altered microRNA, dysfunctional neutrophilic activity, and variants of the HLA system. Besides that, they also share comorbidities, such as gastroesophageal reflux disease and psychiatric illnesses. The clinical presentation of asthma is very similar to patients with bronchiectasis, which could cause mistakes with diagnoses and delays in being prescribed the correct treatment. The coexistence of asthma and bronchiectasis also poses difficulties for the therapeutic focus.

Conclusions: The evidence available seems to support that the asthma-bronchiectasis phenotype really exists although longitudinal studies which consistently demonstrate that asthma is the cause of bronchiectasis are still lacking.

Keywords: Asthma; bronchiectasis; comorbidities; eosinophils; exacerbation; overlap; prognosis.

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