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HAPPY NEW YEAR

COPD

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BMJ Case Rep

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. 2023 Jan 2;16(1):e253186.

doi: 10.1136/bcr-2022-253186.

Pneumothorax in patients with COPD and emphysema receiving home chronic non-invasive ventilation: is it the emphysema phenotype or ventilator setting?

[Joanne M Sloots](#)^{1,2}, [Marieke L Duiverman](#)^{3,4}

Affiliations expand

- PMID: 36593077
- DOI: [10.1136/bcr-2022-253186](https://doi.org/10.1136/bcr-2022-253186)

Abstract

We describe three patients with chronic obstructive pulmonary disease (COPD) and emphysema who developed a pneumothorax while receiving chronic home non-invasive ventilation (NIV). These cases raise the question whether the high alveolar pressures given by NIV may have contributed to the development of their pneumothorax by barotrauma. Pneumothorax in patients with COPD receiving NIV is uncommon, the pressures in our patients with COPD who developed pneumothorax were not extremely high and time to development of pneumothorax was relatively long after the initiation of NIV. Further, in our patients, the CT scan showed paraseptal emphysema, a known risk factor for pneumothorax. This suggests that COPD/emphysema phenotype is probably a more important factor for indicating pneumothorax risk than ventilator settings. Better phenotyping of patients with COPD in whom benefits of NIV can be expected at minimal risk of serious side-effects is needed to inform our patients properly and bring the field of chronic NIV in COPD forward.

Keywords: Mechanical ventilation; Pneumothorax; Pulmonary emphysema; Respiratory medicine.

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Conflict of interest statement

Competing interests: None declared.

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J Allergy Clin Immunol

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. 2022 Dec 29;S0091-6749(22)02577-5.

doi: 10.1016/j.jaci.2022.12.810. Online ahead of print.

The gut microbiome is a significant risk factor for future chronic lung disease

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Affiliations expand

- PMID: 36587850
- DOI: [10.1016/j.jaci.2022.12.810](https://doi.org/10.1016/j.jaci.2022.12.810)

Abstract

Background: The gut-lung axis is generally recognized, but there are few large studies of the gut microbiome and incident respiratory disease in adults.

Objectives: To investigate the association and predictive capacity of the gut microbiome for incident asthma and chronic obstructive pulmonary disease (COPD).

Methods: Shallow metagenomic sequencing was performed for stool samples from a prospective, population-based cohort (FINRISK02; N=7,115 adults) with linked national administrative health register derived classifications for incident asthma and COPD up to 15 years after baseline. Generalised linear models and Cox regressions were utilised to assess associations of microbial taxa and diversity with disease occurrence. Predictive models were constructed using machine learning with extreme gradient boosting. Models considered taxa abundances individually and in combination with other risk factors, including sex, age, body mass index and smoking status.

Results: A total of 695 and 392 statistically significant associations were found between baseline taxonomic groups and incident asthma and COPD, respectively. Gradient boosting decision trees of baseline gut microbiome abundance predicted incident asthma and COPD in the validation datasets with mean area under the curves of 0.608 and 0.780, respectively. Cox analysis showed that the baseline gut microbiome achieved higher predictive performance than individual conventional risk factors, with C-indices of 0.623 for asthma and 0.817 for COPD. The integration of the gut microbiome and conventional risk factors further improved prediction capacities.

Conclusions: The gut microbiome is a significant risk factor for incident asthma and incident COPD and is largely independent of conventional risk factors.

Keywords: COPD; asthma; gut; metagenomics; microbiome.

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Allergol Int

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. 2022 Dec 29;S1323-8930(22)00139-3.

doi: 10.1016/j.alit.2022.11.012. Online ahead of print.

Blood eosinophil count variability in chronic obstructive pulmonary disease and severe asthma

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Affiliations expand

- PMID: 36586746
- DOI: [10.1016/j.alit.2022.11.012](https://doi.org/10.1016/j.alit.2022.11.012)

Free article

Abstract

Background: Blood eosinophils are essential biomarkers that vary substantially over time in patients with COPD and asthma. However, no study has identified the changes and effects in the changes of the blood eosinophil counts over time in both diseases. This study aimed to demonstrate blood eosinophil variability in patients with COPD and severe asthma based on these backgrounds.

Methods: A total of 172 patients with COPD from the Hokkaido COPD cohort study and 96 patients with severe asthma from the Hokkaido Severe Asthma Cohort Study, whose blood eosinophil counts were measured annually over a 3-year period, were analyzed. The factors contributing to consistently high or low blood eosinophil counts were examined in each cohort. The stability of the eosinophil classification (<150, 150-299, ≥300 cells/μL) was compared based on the number of asthma-like features in patients with COPD and the smoking status in patients with severe asthma.

Results: Among all the patients, the most stable range of baseline blood eosinophil counts differed between the two diseases, with <150 cells/ μL in COPD and ≥ 300 cells/ μL in severe asthma. In COPD, the number of asthma-like features (bronchodilator reversibility, blood eosinophilia, and atopy) affects the blood eosinophil count variation patterns. In severe asthma, smoking status did not affect the blood eosinophil count variation patterns.

Conclusions: We identified variations in the blood eosinophil counts and their contributing factors in patients with COPD and severe asthma.

Keywords: Asthma; Chronic obstructive pulmonary disease; Cohort studies; Eosinophils.

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Trials



. 2022 Dec 29;23(1):1060.

doi: 10.1186/s13063-022-06963-w.

[High-flow nasal cannula therapy with sequential noninvasive ventilation versus noninvasive ventilation alone as the initial ventilatory strategy in acute COPD exacerbations: study protocol for a randomized controlled trial](#)

[Shuai Liu](#)¹, [Joseph Harold Walline](#)², [Huadong Zhu](#)³, [Yan Li](#)¹, [Chunting Wang](#)¹, [Jihai Liu](#)¹

Affiliations expand

- PMID: 36581995
- PMCID: [PMC9798596](#)
- DOI: [10.1186/s13063-022-06963-w](#)

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Abstract

Background: Noninvasive ventilation (NIV) is the recommended mode of ventilation used in acute respiratory failure secondary to an acute exacerbation of chronic obstructive pulmonary disease (AECOPD). Recent data has shown that high-flow nasal cannula (HFNC) treatment can be an alternative for patients with hypercapnic respiratory failure. The purpose of this study is to evaluate HFNC with sequential NIV versus NIV alone as the initial ventilatory strategy in AECOPD.

Methods: This investigator-initiated, unblinded, single center, randomized controlled trial will be conducted in the emergency department, emergency intensive care unit, or respiratory intensive care unit of a tertiary-care urban teaching hospital. A total of 66 patients will be enrolled and randomized into the intervention group (HFNC with sequential NIV) or the control group (NIV group). The primary endpoint will be the mean difference in PaCO₂ from baseline to 24 h after randomization. Secondary endpoints include the mean difference in PaCO₂ from baseline to 6, 12, and 18 h, as well as the dyspnea score, overall discomfort score, rate of treatment failure, respiratory rate, rate of endotracheal intubation, length of hospital stay, and mortality.

Discussion: Taking the advantages of both HFNC and NIV on AECOPD patients into account, we designed this clinical trial to investigate the combination of these ventilatory strategies. This trial will help us understand how HFNC with sequential NIV compares to NIV alone in treating AECOPD patients.

Trial registration: ChiCTR2100054809.

Keywords: Chronic obstructive pulmonary disease; High-flow nasal cannula; Hospital emergency service; Intensive care units; Noninvasive ventilation; Respiratory insufficiency.

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Conflict of interest statement

The authors declare that they have no competing interests.

- [25 references](#)

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Aten Primaria

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. 2022 Dec 27;55(2):102550.

doi: 10.1016/j.aprim.2022.102550. Online ahead of print.

[Prevalence and characteristics of chronic obstructive pulmonary disease in non-smokers]

[Article in Spanish]

[Gabriela Mamani Trujillo](#)¹, [Kevin Clemente Chávez](#)¹, [Zulema Mansilla Sánchez](#)¹, [Carlos Andrés Mugruza-Vassallo](#)²

[Affiliations expand](#)

- PMID: 36580709
- DOI: [10.1016/j.aprim.2022.102550](https://doi.org/10.1016/j.aprim.2022.102550)

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Eur J Intern Med

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. 2022 Dec 26;S0953-6205(22)00451-4.

doi: 10.1016/j.ejim.2022.12.022. Online ahead of print.

Long-term prognostic capacity of multi-comorbid indices in chronic obstructive pulmonary disease

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Affiliations expand

- PMID: 36577566
- DOI: [10.1016/j.ejim.2022.12.022](https://doi.org/10.1016/j.ejim.2022.12.022)

No abstract available

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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7

Respir Res

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. 2022 Dec 28;23(1):380.

doi: 10.1186/s12931-022-02274-5.

Nebulization of risedronate alleviates airway obstruction and inflammation of chronic obstructive pulmonary diseases via suppressing prenylation-dependent RAS/ERK/NF- κ B and RhoA/ROCK1/MLCP signaling

[Di Liu](#) ^{#1,2}, [Wen Xu](#) ^{#3}, [Yuan Tang](#) ^{#1,4}, [Jingxue Cao](#) ^{1,5}, [Ran Chen](#) ¹, [Dingwei Wu](#) ⁶, [Hongpeng Chen](#) ⁶, [Bo Su](#) ^{7,8}, [Jinfu Xu](#) ⁹

Affiliations [expand](#)

- PMID: 36575527
- PMCID: [PMC9795678](#)
- DOI: [10.1186/s12931-022-02274-5](#)

Free PMC article

Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a progressive disorder that causes airway obstruction and lung inflammation. The first-line treatment of COPD is the bronchodilators of β 2-agonists and antimuscarinic drugs, which can help control the airway obstruction, but the long-term use might render the drug tolerance. Bisphosphonates are widely used in osteoclast-mediated bone diseases treatment for decades. For drug repurposing, can delivery of a third generation of nitrogen-containing bisphosphonate, risedronate (RIS) ameliorate the progression of COPD?

Methods: COPD rats or mice models have been established through cigarette-smoking and elastase injection, and then the animals are received RIS treatment via nebulization. Lung deposition of RIS was primarily assessed by high-performance liquid chromatography (HPLC). The respiratory parameters of airway obstruction in COPD rats and mice were documented using plethysmography method and resistance-compliance system.

Results: High lung deposition and bioavailability of RIS was monitored with 88.8% of RIS input dose. We found that RIS could rescue the lung function decline of airspace enlargement and mean linear intercept in the COPD lung. RIS could curb the airway obstruction by suppressing 60% of the respiratory resistance and elevating the airway's dynamic compliance, tidal volume and mid-expiratory flow. As an inhibitor of farnesyl diphosphate synthase (FDPS), RIS suppresses FDPS-mediated RAS and RhoA prenylation to obstruct its membrane localization in airway smooth muscle cells (ASMCs), leading to the inhibition of downstream ERK-MLCK and ROCK1-MLCP pathway to cause ASMCs relaxation. Additionally, RIS nebulization impeded pro-inflammatory cell accumulation, particularly macrophages infiltration in alveolar parenchyma. The NF- κ B, tumor necrosis factor- α , IL-1 β , IL-8, and IL-6 declined in microphages following RIS nebulization. Surprisingly, nebulization of RIS could overcome the tolerance of β 2-agonists in COPD-rats by increasing the expression of β 2 receptors.

Conclusions: Nebulization of RIS could alleviate airway obstruction and lung inflammation in COPD, providing a novel strategy for treating COPD patients, even those with β 2-agonists tolerance.

Keywords: Animal models; Chronic obstructive; Inflammation; Pulmonary disease; Risedronic acid.

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Conflict of interest statement

The authors declare no competing interest.

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- [6 figures](#)

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BMC Prim Care

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. 2022 Dec 27;23(1):340.

doi: 10.1186/s12875-022-01953-y.

Smoking quit rates among patients receiving pharmacotherapy who received general practitioner counselling versus intensive counselling: a retrospective cohort study

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Affiliations expand

- PMID: 36575392
- PMCID: [PMC9793508](#)
- DOI: [10.1186/s12875-022-01953-y](#)

Free PMC article

Abstract

Background: Behavioral treatments can augment the success of pharmacotherapy in smoking cessation. The aim of this study was to compare smoking quit rates between patients receiving individual counseling with their general practitioner during office visits or intensive counselling with behavioral support, both augmented by varenicline.

Methods: A nationwide retrospective cohort study conducted in a large Healthcare Maintenance Organization in Israel. We selected randomly patients who filled a prescription for varenicline and received either individual consulting by their general practitioner or intensive counselling with behavioural support, and asked them to answer a questionnaire. The outcome variables were smoking cessation 26-52 weeks following the beginning of treatment and satisfaction with the process.

Results: 870 patients were contacted and 604 agreed to participate (a response rate of 69%); 301 patients in the general practitioner group, 300 in the intensive counselling group and 3 were excluded due to missing data. The quit rate was 36.5% in the general practitioner group and 42.3% in the intensive counselling group ($P = 0.147$). In a logistic regression analysis, controlling for age, gender, socioeconomic status, ischemic heart disease, chronic obstructive pulmonary disease, pack years and duration of varenicline consumption, the adjusted OR for quitting in the general practitioner group was 0.79 (95% CI 0.56,1.13). The adjusted OR was higher in the group with the highest socioeconomic status at 2.06 (1.39,3.07) and a longer period of varenicline consumption at 1.30 (1.15,1.47). Age, gender and cigarette pack-years were not associated with quit rate. In the general practitioner group 68% were satisfied with the process, while 19% were not. In the intensive counselling group 64% were satisfied and 14% were not ($P = 0.007$).

Conclusion: We did not detect a statistically significant difference in smoking quit rates, though there was a trend towards higher quit rates with intensive counselling.

Keywords: Counselling; General practice; Smoking cessation; Varenicline.

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Conflict of interest statement

The authors declare that they have no competing interests.

- [31 references](#)

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NPJ Prim Care Respir Med



. 2022 Dec 27;32(1):59.

doi: 10.1038/s41533-022-00318-3.

Clinical recommendations for dry powder inhaler use in the management of COPD in primary care

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Affiliations expand

- PMID: 36575175
- PMCID: [PMC9794707](#)
- DOI: [10.1038/s41533-022-00318-3](#)

Free PMC article

Abstract

Over 1400 patients using dry powder inhalers (DPIs) to deliver COPD maintenance therapies were recruited across Europe and Australia. Their peak inspiratory flow (PIF) was measured, inhaler technique was observed, and adherence to treatment assessed. From relating the findings with patient health status, and thereby identifying critical errors, key clinical recommendations for primary care clinicians were determined, namely - measure PIF before prescribing a DPI to ensure inhalation manoeuvre ability is well-matched with

the device. Some patients could benefit from inhalation training whereas others should have their DPI changed for one better suited to their inspiratory ability or alternatively be prescribed an active device (such as a soft mist inhaler or pressurized metered dose inhaler). Observing the inhalation technique was valuable however this misses suboptimal PIF (approaching one fourth of patients with a satisfactory observed manoeuvre had a suboptimal PIF for their DPI). Assess adherence as deliberate non-adherence can point to a mismatch between a patient and their inhaler (deliberate non-adherence was significantly associated with PIFs below the minimum for the DPI). In-person observation of inhalation technique was found to be inferior to video rating based on device-specific checklists. Where video assessments are not possible, observation training for healthcare professionals would therefore be valuable particularly to improve the ability to identify the critical errors associated with health status namely 'teeth and lips sealed around mouthpiece', 'breathe in' and 'breathing out calmly after inhalation'. However, it is recommended that observation alone should not replace PIF measurement in the DPI selection process. Trial registration: <https://clinicaltrials.gov/ct2/show/NCT04532853> .

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Conflict of interest statement

M.T.L., J.v.C., L.D., I.v.d.H., Y.J., B.M., K.S., N.S. were employed by General Practitioners Research Institute (GPRI) at the time of the study. In the past three years (2019–2021), GPRI conducted investigator- and sponsor-initiated research funded by non-commercial organizations, academic institutes, and pharmaceutical companies (including AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Mundipharma, Novartis, and Teva). S.B.-A. has received grants from TEVA, and personal fees from TEVA, Boehringer Ingelheim, AstraZeneca, GSK, Sanofi and Mylan. J.C.d.S. reports or personal fees from AstraZeneca, Bial, Boehringer Ingelheim, GSK, Medinfar, Mundipharma and Sanofi. B.C. received honorarium from GSK and Sanofi. R.D. has received grants and personal fees from TEVA, Boehringer Ingelheim, AstraZeneca, GSK, Chiesi, Focus Care, and Glenmark. M.G.P. receives grants from AstraZeneca, GSK and Boehringer Ingelheim. A.G. and R.A.-E. are employees of Boehringer Ingelheim. R.G. has received personal fees from AstraZeneca, GSK and Chiesi. F.L. received grants and personal fees from GSK, personal fees from AstraZeneca, Boehringer Ingelheim, Chiesi, Menarini International, Novartis, Orion, and Trudell International, outside the submitted work. T.M. has no competing interests to declare. J.M. received grants from Boehringer Ingelheim, during the conduct of the study; and grants from AstraZeneca, Chiesi, Novartis, and GSK, outside the submitted work. D.P. reports grants and personal fees from AstraZeneca, Boehringer Ingelheim, Chiesi, Mylan, Novartis, Regeneron Pharmaceuticals, Sanofi Genzyme, Theravance and Zentiva (Sanofi Generics); grants from the British Lung Foundation, Respiratory Effectiveness Group, UK National Health Service, and AKL Research and Development Ltd; personal fees from Cipla, GlaxoSmithKline, Kyorin, Merck, Mundipharma, Airway Vista Secretariat, EPG Communication Holdings Ltd, FIECON Ltd, Fieldwork International, OM Pharma SA, PeerVoice, Phadia AB, Spirosure Inc, Strategic North Limited, Synapse Research Management Partners S.L., Talos Health Solutions, and WebMD Global LLC; non-financial support from Efficacy and Mechanism Evaluation

programme and Health Technology Assessment; stock/stock options from AKL Research and Development Ltd, which produces phytopharmaceuticals; owns 74% of the social enterprise Optimum Patient Care Ltd (Australia and UK) and 92.61% of Observational and Pragmatic Research Institute Pte Ltd (Singapore); and 5% shareholding in Timestamp, which develops adherence monitoring technology. M.R.-R. receives grants and personal fees from AstraZeneca and GSK; and personal fees from Boehringer Ingelheim, Chiesi, Menarini, Mundipharma, Novartis, Pfizer, TEVA and BIAL. I.T. reports grants and personal fees from GSK, AstraZeneca, Boehringer Ingelheim, Menarini, Novartis, Chiesi and Elpen. OU reports grants and personal fees from AstraZeneca, Boehringer Ingelheim, Edmond Pharma, Chiesi and GSK; grants from Edmond Pharma; and personal fees from Napp, Mundipharma, Sandoz, Takeda, Cipla, COVIS, Novartis, Mereobiopharma, Orion, and Menarini. J.W.H.K. reports grants, personal fees and non-financial support from AstraZeneca, GSK and Boehringer Ingelheim; grants and personal fees from Chiesi Pharmaceuticals and TEVA; grants from Mundipharma; personal fees from MSD and COVIS Pharma; and also holds 72.5% of shares in the General Practitioners Research Institute. IT is Editor-in-Chief of npj Primary Care Respiratory Medicine, and S.B.-A. and T.M. are Associate Editors. I.T., S.B.A., and TM were not involved in the journal's review of, or decisions related to, this manuscript.

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Life Sci Alliance

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. 2022 Dec 27;6(3):e202201609.

doi: 10.26508/lsa.202201609. Print 2023 Mar.

De novo discovery of traits co-occurring with chronic obstructive pulmonary disease

[Evgeniia Golovina](#)¹, [Tayaza Fadason](#)^{1,2}, [Rachel K Jaros](#)¹, [Haribalan Kumar](#)³, [Joyce John](#)³, [Kelly Burrowes](#)³, [Merryn Tawhai](#)³, [Justin M O'Sullivan](#)^{4,2,5,6,7}

Affiliations expand

- PMID: 36574990
- PMCID: [PMC9795035](#)
- DOI: [10.26508/lsa.202201609](#)

Free PMC article

Abstract

Chronic obstructive pulmonary disease (COPD) is a heterogeneous group of chronic lung conditions. Genome-wide association studies have identified single-nucleotide polymorphisms (SNPs) associated with COPD and the co-occurring conditions, suggesting common biological mechanisms underlying COPD and these co-occurring conditions. To identify them, we have integrated information across different biological levels (i.e., genetic variants, lung-specific 3D genome structure, gene expression and protein-protein interactions) to build lung-specific gene regulatory and protein-protein interaction networks. We have queried these networks using disease-associated SNPs for COPD, unipolar depression and coronary artery disease. COPD-associated SNPs can control genes involved in the regulation of lung or pulmonary function, asthma, brain region volumes, cortical surface area, depressed affect, neuroticism, Parkinson's disease, white matter microstructure and smoking behaviour. We describe the regulatory connections, genes and biochemical pathways that underlay these co-occurring trait-SNP-gene associations. Collectively, our findings provide new avenues for the investigation of the underlying biology and diverse clinical presentations of COPD. In so doing, we identify a collection of genetic variants and genes that may aid COPD patient stratification and treatment.

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Conflict of interest statement

The authors declare that they have no conflict of interest.

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Review

Eur Respir Rev

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. 2022 Dec 21;31(166):220134.

doi: 10.1183/16000617.0134-2022. Print 2022 Dec 31.

Role of autophagy in lung diseases and ageing

[Yan Zhang](#)¹, [Jin Zhang](#)¹, [Zhiling Fu](#)²

[Affiliations expand](#)

- PMID: 36543345
- DOI: [10.1183/16000617.0134-2022](https://doi.org/10.1183/16000617.0134-2022)

Free article

Abstract

The lungs face ongoing chemical, mechanical, biological, immunological and xenobiotic stresses over a lifetime. Advancing age progressively impairs lung function. Autophagy is a "housekeeping" survival strategy involved in numerous physiological and pathological

processes in all eukaryotic cells. Autophagic activity decreases with age in several species, whereas its basic activity extends throughout the lifespan of most animals. Dysregulation of autophagy has been proven to be closely related to the pathogenesis of several ageing-related pulmonary diseases. This review summarises the role of autophagy in the pathogenesis of pulmonary diseases associated with or occurring in the context of ageing, including acute lung injury, chronic obstructive pulmonary disease, asthma and pulmonary fibrosis, and describes its potential as a therapeutic target.

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Conflict of interest statement

Conflicts of interest: The authors declare no conflict of interest.

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Review

Respir Med



. 2023 Jan;206:107090.

doi: 10.1016/j.rmed.2022.107090. Epub 2022 Dec 13.

Readmission rate for acute exacerbation of chronic obstructive pulmonary

disease: A systematic review and meta-analysis

[Huanrong Ruan](#)¹, [Hailong Zhang](#)², [Jiajia Wang](#)³, [Hulei Zhao](#)³, [Weihong Han](#)¹, [Jiansheng Li](#)³

Affiliations expand

- PMID: 36528962
- DOI: [10.1016/j.rmed.2022.107090](https://doi.org/10.1016/j.rmed.2022.107090)

Free article

Abstract

Background: The readmission rate following hospitalization for chronic obstructive pulmonary disease (COPD) exacerbations is extremely high and has become a common and challenging clinical problem. This study aimed to systematically summarize COPD readmission rates for acute exacerbations and their underlying risk factors.

Methods: A comprehensive search was performed using PubMed, Embase, Cochrane Library, and Web of Science, published from database inception to April 2, 2022. Methodological quality was evaluated using the Newcastle-Ottawa Scale (NOS). We used a random-effects model or a fixed-effects model to estimate the pooled COPD readmission rate for acute exacerbations and underlying risk factors.

Results: A total of 46 studies were included, of which 24, 7, 17, 7, and 20 summarized the COPD readmission rates for acute exacerbations within 30, 60, 90, 180, and 365 days, respectively. The pooled 30-, 60-, 90-, 180-, and 365-day readmission rates were 11%, 17%, 17%, 30%, and 37%, respectively. The study design type, age stage, WHO region, and length of stay (LOS) were initially considered to be sources of heterogeneity. We also identified potential risk factors for COPD readmission, including male sex, number of hospitalizations in the previous year, LOS, and comorbidities such as heart failure, tumor or cancer, and diabetes, whereas obesity was a protective factor.

Conclusions: Patients with COPD had a high readmission rate for acute exacerbations, and potential risk factors were identified. Therefore, we should propose clinical interventions and adjust or targeted the control of avoidable risk factors to prevent and reduce the negative impact of COPD readmission.

Systematic review registration: PROSPERO, identifier CRD42022333581.

Keywords: Acute exacerbation; Chronic obstructive pulmonary disease; Meta-analysis; Readmission rate; Risk factors; Systematic review.

Conflict of interest statement

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

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Expert Opin Biol Ther

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. 2022 Dec 26;1-11.

doi: 10.1080/14712598.2022.2160238. Online ahead of print.

Biologic therapies for chronic obstructive pulmonary disease

[Maria Gabriella Matera](#)¹, [Luigino Calzetta](#)², [Mario Cazzola](#)³, [Josuel Ora](#)⁴, [Paola Rogliani](#)^{3,4}

Affiliations expand

- PMID: 36527286
- DOI: [10.1080/14712598.2022.2160238](https://doi.org/10.1080/14712598.2022.2160238)

Abstract

Introduction: Chronic obstructive pulmonary disease (COPD) is a disorder characterized by a complicated chronic inflammatory response that is resistant to corticosteroid therapy.

As a result, there is a critical need for effective anti-inflammatory medications to treat people with COPD. Using monoclonal antibodies (mAbs) to inhibit cytokines and chemokines or their receptors could be a potential approach to treating the inflammatory component of COPD.

Areas covered: The therapeutic potential that some of these mAbs might have in COPD is reviewed.

Expert opinion: No mAb directed against cytokines or chemokines has shown any therapeutic impact in COPD patients, apart from mAbs targeting the IL-5 pathway that appear to have statistically significant, albeit weak, effect in patients with eosinophilic COPD. This may reflect the complexity of COPD, in which no single cytokine or chemokine has a dominant role. Because the umbrella term COPD encompasses several endotypes with diverse underlying processes, mAbs targeting specific cytokines or chemokines should most likely be evaluated in limited and focused populations.

Keywords: COPD; chemokines; chronic inflammation; cytokines; monoclonal antibodies.

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Expert Opin Pharmacother

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. 2022 Dec 28;1-12.

doi: 10.1080/14656566.2022.2160239. Online ahead of print.

Current pharmacological strategies for symptomatic reduction of persistent breathlessness - a literature review

[Diana H Ferreira](#)¹, [Slavica Kochovska](#)^{1,2}, [Richard McNeill](#)^{3,4}, [David C Currow](#)¹

Affiliations expand

- PMID: 36525673
- DOI: [10.1080/14656566.2022.2160239](https://doi.org/10.1080/14656566.2022.2160239)

Abstract

Introduction: Persistent breathlessness is a debilitating symptom that is prevalent in the community, particularly in people with chronic and life-limiting illnesses. Treatment includes different steps, including pharmacological treatment aiming to improve the symptom and optimize people's wellbeing.

Areas covered: PubMed and Google Scholar were screened using 'chronic breathlessness' OR 'persistent breathlessness,' AND 'pharmacological treatment,' OR 'opioids.' This review focuses on pharmacological treatments to reduce persistent breathlessness and discusses possible mechanisms involved in the process of breathlessness reduction through pharmacotherapy. Research gaps in the field of persistent breathlessness research are outlined, and future research directions are suggested.

Expert opinion: Regular, low-dose (≤ 30 mg/day), sustained-release morphine is recommended as the first-line pharmacological treatment for persistent breathlessness. Inter-individual variation in response needs to be investigated in future studies in order to optimize clinical outcomes. This includes 1) better understanding the centrally mediated mechanisms associated with persisting breathlessness and response to pharmacological therapies, 2) understanding benefit from the perspective of people experiencing persistent breathlessness, small and meaningful gains in physical activity.

Keywords: Chronic obstructive pulmonary disease; evidence-based care; palliative care; persistent breathlessness; pharmacological treatment; quality of life; suffering; symptom control.

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Meta-Analysis

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. 2023 Jan;123:306-316.

doi: 10.1016/j.jes.2022.04.026. Epub 2022 May 2.

Fine particulate matter and cardiorespiratory health in China: A systematic review and meta-analysis of epidemiological studies

[Huihuan Luo](#)¹, [Qingli Zhang](#)¹, [Yue Niu](#)¹, [Haidong Kan](#)¹, [Renjie Chen](#)²

Affiliations expand

- PMID: 36521994
- DOI: [10.1016/j.jes.2022.04.026](https://doi.org/10.1016/j.jes.2022.04.026)

Abstract

This review aimed to systematically summarize the epidemiological literature on the cardiorespiratory effects of PM_{2.5} published during the 13th Five-Year Plan period (2016-2020) in China. Original articles published between January 1, 2016 and June 30, 2021 were searched in PubMed, Web of Science, the China National Knowledge Internet Database and Wanfang Database. Random- or fixed-effects models were used to pool effect estimates where appropriate. Of 8558 records identified, 145 met the full eligibility criteria. A 10 µg/m³ increase in short-term PM_{2.5} exposure was significantly associated with increases of 0.70%, 0.86%, 0.38% and 0.96% in cardiovascular mortality, respiratory mortality, cardiovascular morbidity, and respiratory morbidity, respectively. The specific diseases with significant associations included stroke, ischemic heart disease, heart failure, arrhythmia, chronic obstructive pulmonary disease, pneumonia and allergic rhinitis. The pooled estimates per 10 µg/m³ increase in long-term PM_{2.5} exposure were 15.1%, 11.9% and 21.0% increases in cardiovascular, stroke and lung cancer mortality, and 17.4%, 11.0% and 4.88% increases in cardiovascular, hypertension and lung cancer incidence respectively. Adverse changes in blood pressure, heart rate variability, systemic inflammation, blood lipids, lung function and airway inflammation were observed for either short-term or long-term PM_{2.5} exposure, or both. Collectively, we summarized representative exposure-response relationships between short- and long-term PM_{2.5} exposure and a wide range of cardiorespiratory outcomes applicable to China. The magnitudes of estimates were generally smaller in short-term associations and comparable in long-term associations compared with those in developed countries. Our findings are

helpful for future standard revisions and policy formulation. There are still some notable gaps that merit further investigation in China.

Keywords: Air pollution; Cardiovascular system; Epidemiological studies; Fine particulate matter; Mortality Morbidity; Respiratory system.

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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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Meta-Analysis

Lancet Glob Health

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. 2023 Jan;11(1):e69-e82.

doi: 10.1016/S2214-109X(22)00456-9.

Small airways obstruction and its risk factors in the Burden of Obstructive Lung

Disease (BOLD) study: a multinational cross-sectional study

[Ben Knox-Brown](#)¹, [Jaymini Patel](#)², [James Potts](#)², [Rana Ahmed](#)³, [Althea Aquart-Stewart](#)⁴, [Hamid Hacene Cherkaski](#)⁵, [Meriam Denquezli](#)⁶, [Mohammed Elbiaze](#)⁷, [Asma Elsony](#)³, [Frits M E Franssen](#)⁸, [Mohammed Al Ghobain](#)⁹, [Imed Harrabi](#)¹⁰, [Christer Janson](#)¹¹, [Rain Jõgi](#)¹², [Sanjay Juvekar](#)¹³, [Herve Lawin](#)¹⁴, [David Mannino](#)¹⁵, [Kevin Mortimer](#)¹⁶, [Asaad Ahmed Nafees](#)¹⁷, [Rune Nielsen](#)¹⁸, [Daniel Obaseki](#)¹⁹, [Stefanni Nonna M Paraguas](#)²⁰, [Abdul Rashid](#)²¹, [Li-Cher Loh](#)²¹, [Sundeep Salvi](#)²², [Terence Seemungal](#)²³, [Michael Studnicka](#)²⁴, [Wan C Tan](#)²⁵, [Emiel E F M Wouters](#)²⁶, [Cristina Barbara](#)²⁷, [Thorarinn Gislason](#)²⁸, [Kirthi Gunasekera](#)²⁹, [Peter Burney](#)², [Andre F S Amaral](#)², [BOLD Collaborative Research Group](#)

Affiliations expand

- PMID: 36521955
- DOI: [10.1016/S2214-109X\(22\)00456-9](https://doi.org/10.1016/S2214-109X(22)00456-9)

Free article

Abstract

Background: Small airways obstruction is a common feature of obstructive lung diseases. Research is scarce on small airways obstruction, its global prevalence, and risk factors. We aimed to estimate the prevalence of small airways obstruction, examine the associated risk factors, and compare the findings for two different spirometry parameters.

Methods: The Burden of Obstructive Lung Disease study is a multinational cross-sectional study of 41 municipalities in 34 countries across all WHO regions. Adults aged 40 years or older who were not living in an institution were eligible to participate. To ensure a representative sample, participants were selected from a random sample of the population according to a predefined site-specific sampling strategy. We included participants' data in this study if they completed the core study questionnaire and had acceptable spirometry according to predefined quality criteria. We excluded participants with a contraindication for lung function testing. We defined small airways obstruction as either mean forced expiratory flow rate between 25% and 75% of the forced vital capacity (FEF₂₅₋₇₅) less than the lower limit of normal or forced expiratory volume in 3 s to forced vital capacity ratio (FEV₃/FVC ratio) less than the lower limit of normal. We estimated the prevalence of pre-bronchodilator (ie, before administration of 200 µg salbutamol) and post-bronchodilator (ie, after administration of 200 µg salbutamol) small airways obstruction for each site. To identify risk factors for small airways obstruction, we performed multivariable regression analyses within each site and pooled estimates using random-effects meta-analysis.

Findings: 36 618 participants were recruited between Jan 2, 2003, and Dec 26, 2016. Data were collected from participants at recruitment. Of the recruited participants, 28 604

participants had acceptable spirometry and completed the core study questionnaire. Data were available for 26 443 participants for FEV₃/FVC ratio and 25 961 participants for FEF₂₅₋₇₅. Of the 26 443 participants included, 12 490 were men and 13 953 were women. Prevalence of pre-bronchodilator small airways obstruction ranged from 5% (34 of 624 participants) in Tartu, Estonia, to 34% (189 of 555 participants) in Mysore, India, for FEF₂₅₋₇₅, and for FEV₃/FVC ratio it ranged from 5% (31 of 684) in Riyadh, Saudi Arabia, to 31% (287 of 924) in Salzburg, Austria. Prevalence of post-bronchodilator small airways obstruction was universally lower. Risk factors significantly associated with FEV₃/FVC ratio less than the lower limit of normal included increasing age, low BMI, active and passive smoking, low level of education, working in a dusty job for more than 10 years, previous tuberculosis, and family history of chronic obstructive pulmonary disease. Results were similar for FEF₂₅₋₇₅, except for increasing age, which was associated with reduced odds of small airways obstruction.

Interpretation: Despite the wide geographical variation, small airways obstruction is common and more prevalent than chronic airflow obstruction worldwide. Small airways obstruction shows the same risk factors as chronic airflow obstruction. However, further research is required to investigate whether small airways obstruction is also associated with respiratory symptoms and lung function decline.

Funding: National Heart and Lung Institute and Wellcome Trust.

Translations: For the Dutch, Estonian, French, Icelandic, Malay, Marathi, Norwegian, Portuguese, Swedish and Urdu translations of the abstract see Supplementary Materials section.

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Conflict of interest statement

Declaration of interests DM declares being a consultant to and receiving royalties from GlaxoSmithKline, AstraZeneca, and the COPD Foundation (royalty payments are up to date) and acting as an expert witness for Schlesinger Law Firm, outside of the submitted work. RN reports grants and personal fees from AstraZeneca and GlaxoSmithKline and grants from Boehringer Ingelheim and Novartis, outside of the submitted work. All other authors declare no competing interests.

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Respir Med



. 2023 Jan;206:107086.

doi: 10.1016/j.rmed.2022.107086. Epub 2022 Dec 9.

The presence of extra-pulmonary treatable traits increases the likelihood of responding to pulmonary rehabilitation

[Sara Souto-Miranda](#)¹, [Vânia Rocha](#)², [Maria Aurora Mendes](#)³, [Paula Simão](#)⁴, [Vitória Martins](#)⁵, [Martijn A Spruit](#)⁶, [Alda Marques](#)⁷

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- PMID: 36516547
- DOI: [10.1016/j.rmed.2022.107086](https://doi.org/10.1016/j.rmed.2022.107086)

Free article

Abstract

Introduction: Studies suggest that people with chronic obstructive pulmonary disease (COPD) who are worse at baseline respond better to pulmonary rehabilitation (PR). Identifying treatable traits (TTs) may help to distinguish responders from non-responders. We explored the impact of PR on extra-pulmonary traits of people with COPD and whether the presence of TT influences the type of response to PR.

Methods: A comprehensive assessment of 9 TT including symptoms (dyspnoea, fatigue, anxiety and depression), functional capacity, deconditioning, balance, impact of the disease and health-related quality of life was conducted before and after a 12-week community-based PR programme. Pre-post differences between people with or without each TT at baseline were compared with independent samples t-tests or Mann-Whitney U tests. Proportion of responders between groups were explored with chi-square tests and odds ratio.

Results: 102 people with COPD were included (70 [65; 75] years old, 78% male, FEV₁ 47 [36; 60] %predicted). They had a median of 3 (out of 9) TTs per person and each patient responded on average to 5 (out of 9) outcomes of PR. People with TT were more responsive than those without them in all outcomes ($p < 0.05$) except for the 1-min sit-to-stand test. The presence of TT increased 4 to 20 times the likelihood of being a good responder.

Conclusions: Identification of baseline extra-pulmonary TT in people with COPD showed the potential to inform on PR responsiveness and might therefore be an important strategy for patient prioritization, treatment personalisation (i.e., activation of the most suitable components) and optimisation.

Keywords: COPD; Comprehensive assessment; Pulmonary rehabilitation; Responder analysis; Treatable traits.

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Conflict of interest statement

Declaration of competing interest None.

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Lancet Respir Med

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. 2023 Jan;11(1):13-14.

doi: 10.1016/S2213-2600(22)00476-3. Epub 2022 Dec 1.

Post-bronchodilator spirometry in chronic obstructive pulmonary disease

[Joan B Soriano](#)¹, [José M Marín](#)², [Bartolomé R Celli](#)³

Affiliations expand

- PMID: 36463911
- DOI: [10.1016/S2213-2600\(22\)00476-3](https://doi.org/10.1016/S2213-2600(22)00476-3)

No abstract available

Conflict of interest statement

BRC reports being a speaker at meetings and advisory boards for GlaxoSmithKline; a consultant of advisory boards and a speaker for AstraZeneca; a consultant and speaker at meetings for Menarini; a consultant and advisory board member for Sanofi Aventis; and a consultant for Axios. BRC also reports consulting fees from GlaxoSmithKline, AstraZeneca, and Sanofi Aventis; payment or honoraria from GlaxoSmithKline, AstraZeneca, Menarini, Chiesi, and Regeneron; support for meeting attendance or travel from GlaxoSmithKline and Sanofi Aventis; and participation on data safety monitoring boards or advisory boards for AZ Therapeutics, Sanofi Aventis, and Vertex. JBS and JMM declare no competing interests.

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Lancet Respir Med

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. 2023 Jan;11(1):18.

doi: 10.1016/S2213-2600(22)00494-5. Epub 2022 Nov 30.

GOLD COPD report: 2023 update

[Priya Venkatesan](#)

- PMID: 36462509
- DOI: [10.1016/S2213-2600\(22\)00494-5](https://doi.org/10.1016/S2213-2600(22)00494-5)

No abstract available

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Lancet Digit Health

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. 2023 Jan;5(1):e16-e27.

doi: 10.1016/S2589-7500(22)00187-X. Epub 2022 Nov 29.

Identifying and visualising multimorbidity and comorbidity patterns in patients in the English National Health Service: a population-based study

[Valerie Kuan](#)¹, [Spiros Denaxas](#)², [Praveetha Patalay](#)³, [Dorothea Nitsch](#)⁴, [Rohini Mathur](#)⁵, [Arturo Gonzalez-Izquierdo](#)⁶, [Reecha Sofat](#)⁷, [Linda Partridge](#)⁸, [Amanda Roberts](#)⁹, [Ian C K Wong](#)¹⁰, [Melanie](#)

[Hingorani¹¹](#), [Nishi Chaturvedi¹²](#), [Harry Hemingway¹³](#), [Aroon D Hingorani¹⁴](#); [Multimorbidity Mechanism and Therapeutic Research Collaborative \(MMTRC\)](#)

Collaborators, Affiliations expand

- PMID: 36460578
- DOI: [10.1016/S2589-7500\(22\)00187-X](https://doi.org/10.1016/S2589-7500(22)00187-X)

Free article

Abstract

Background: Globally, there is a paucity of multimorbidity and comorbidity data, especially for minority ethnic groups and younger people. We estimated the frequency of common disease combinations and identified non-random disease associations for all ages in a multiethnic population.

Methods: In this population-based study, we examined multimorbidity and comorbidity patterns stratified by ethnicity or race, sex, and age for 308 health conditions using electronic health records from individuals included on the Clinical Practice Research Datalink linked with the Hospital Episode Statistics admitted patient care dataset in England. We included individuals who were older than 1 year and who had been registered for at least 1 year in a participating general practice during the study period (between April 1, 2010, and March 31, 2015). We identified the most common combinations of conditions and comorbidities for index conditions. We defined comorbidity as the accumulation of additional conditions to an index condition over an individual's lifetime. We used network analysis to identify conditions that co-occurred more often than expected by chance. We developed online interactive tools to explore multimorbidity and comorbidity patterns overall and by subgroup based on ethnicity, sex, and age.

Findings: We collected data for 3 872 451 eligible patients, of whom 1 955 700 (50.5%) were women and girls, 1 916 751 (49.5%) were men and boys, 2 666 234 (68.9%) were White, 155 435 (4.0%) were south Asian, and 98 815 (2.6%) were Black. We found that a higher proportion of boys aged 1-9 years (132 506 [47.8%] of 277 158) had two or more diagnosed conditions than did girls in the same age group (106 982 [40.3%] of 265 179), but more women and girls were diagnosed with multimorbidity than were boys aged 10 years and older and men (1 361 232 [80.5%] of 1 690 521 vs 1 161 308 [70.8%] of 1 639 593). White individuals (2 097 536 [78.7%] of 2 666 234) were more likely to be diagnosed with two or more conditions than were Black (59 339 [60.1%] of 98 815) or south Asian individuals (93 617 [60.2%] of 155 435). Depression commonly co-occurred with anxiety, migraine, obesity, atopic conditions, deafness, soft-tissue disorders, and gastrointestinal disorders across all subgroups. Heart failure often co-occurred with hypertension, atrial fibrillation, osteoarthritis, stable angina, myocardial infarction, chronic kidney disease, type 2 diabetes, and chronic obstructive pulmonary disease. Spinal fractures were most strongly non-randomly associated with malignancy in Black individuals, but with osteoporosis in

White individuals. Hypertension was most strongly associated with kidney disorders in those aged 20-29 years, but with dyslipidaemia, obesity, and type 2 diabetes in individuals aged 40 years and older. Breast cancer was associated with different comorbidities in individuals from different ethnic groups. Asthma was associated with different comorbidities between males and females. Bipolar disorder was associated with different comorbidities in younger age groups compared with older age groups.

Interpretation: Our findings and interactive online tools are a resource for: patients and their clinicians, to prevent and detect comorbid conditions; research funders and policy makers, to redesign service provision, training priorities, and guideline development; and biomedical researchers and manufacturers of medicines, to provide leads for research into common or sequential pathways of disease and inform the design of clinical trials.

Funding: UK Research and Innovation, Medical Research Council, National Institute for Health and Care Research, Department of Health and Social Care, Wellcome Trust, British Heart Foundation, and The Alan Turing Institute.

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Conflict of interest statement

Declaration of interests DN is the UK Kidney Association Director of Informatics Research based at the UK Renal Registry and is on the steering committee for two GlaxoSmithKline-funded studies looking at kidney function markers in sub-Saharan Africa. ICKW was a member of the ISAC of CPRD and has received funding from Amgen, Bristol-Myers Squibb, Pfizer, Janssen, Bayer, GSK, and Novartis to conduct pharmacoepidemiological research outside the submitted work. RM has received consulting fees from Amgen. ADH is a co-investigator on a grant from Pfizer to identify potential therapeutic targets for heart failure using human genomics. NC is remunerated for her membership of a data safety and monitoring committee of a trial sponsored by AstraZeneca. All other authors declare no competing interests.

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Respir Med



. 2023 Jan;206:107064.

doi: 10.1016/j.rmed.2022.107064. Epub 2022 Nov 26.

Risk of hospitalization in a sample of COVID-19 patients with and without chronic obstructive pulmonary disease

[Laura C Myers](#)¹, [Richard Murray](#)², [Bonnie Donato](#)³, [Vincent X Liu](#)⁴, [Patricia Kipnis](#)⁴, [Asif Shaikh](#)⁵, [Jessica Franchino-Elder](#)³

Affiliations expand

- PMID: 36459955
- PMCID: [PMC9700393](#)
- DOI: [10.1016/j.rmed.2022.107064](#)

Free PMC article

Abstract

Background and objective: Patients with chronic obstructive pulmonary disease (COPD) may have worse coronavirus disease-2019 (COVID-19)-related outcomes. We compared COVID-19 hospitalization risk in patients with and without COPD.

Methods: This retrospective cohort study included patients ≥ 40 years, SARS-CoV-2 positive, and with Kaiser Permanente Northern California membership ≥ 1 year before COVID-19 diagnosis (electronic health records and claims data). COVID-19-related hospitalization risk was assessed by sequentially adjusted logistic regression models and stratified by disease severity. Secondary outcome was death/hospice referral after COVID-19.

Results and discussion: Of 19,558 COVID-19 patients, 697 (3.6%) had COPD. Compared with patients without COPD, COPD patients were older (median age: 69 vs 53 years); had

higher Elixhauser Comorbidity Index (5 vs 0) and more median baseline outpatient (8 vs 4), emergency department (2 vs 1), and inpatient (2 vs 1) encounters. Unadjusted analyses showed increased odds of hospitalization with COPD (odds ratio [OR]: 3.93; 95% confidence interval [CI]: 3.40-4.60). After full risk adjustment, there were no differences in odds of hospitalization (OR: 1.14, 95% CI: 0.93-1.40) or death/hospice referral (OR: 0.96, 95% CI: 0.72-1.27) between patients with and without COPD. Primary/secondary outcomes did not differ by COPD severity, except for higher odds of hospitalization in COPD patients requiring supplemental oxygen versus those without COPD (OR: 1.84, 95% CI: 1.02-3.33).

Conclusions: Except for hospitalization among patients using supplemental oxygen, no differences in odds of hospitalization or death/hospice referral were observed in the COVID-19 patient sample depending on whether they had COPD.

Keywords: COPD; COVID-19; Healthcare resource use; Pneumonia.

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Conflict of interest statement

Declaration of competing interest Dr. Bonnie Donato, Dr. Asif Shaikh, and Dr. Jessica Franchino-Elder are employees of BI. Dr. Richard Murray is the Chief Medical Officer of Spire Health and reports receiving consulting fees from BI; he serves as the Chairman of the Board for the Allergy and Asthma Foundation of America. Dr. Vincent Liu, Dr. Laura Myers, and Dr. Patricia Kipnis received funding from BI to perform the study.

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

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Review

Eur Respir Rev

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. 2022 Nov 29;31(166):220099.

doi: 10.1183/16000617.0099-2022. Print 2022 Dec 31.

Inhaled corticosteroids for the treatment of COVID-19

[Mona Bafadhel](#)¹, [Rosa Faner](#)², [Camille Taillé](#)³, [Richard E K Russell](#)⁴, [Tobias Welte](#)⁵, [Peter J Barnes](#)⁶, [Alvar Agustí](#)⁷

Affiliations expand

- PMID: 36450371
- PMCID: [PMC9724831](#)
- DOI: [10.1183/16000617.0099-2022](#)

Free PMC article

Abstract

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has caused severe illness and mortality for millions worldwide. Despite the development, approval and rollout of vaccination programmes globally to prevent infection by SARS-CoV-2 and the development of coronavirus disease 2019 (COVID-19), treatments are still urgently needed to improve outcomes. Early in the pandemic it was observed that patients with pre-existing asthma or COPD were underrepresented among those with COVID-19. Evidence from clinical studies indicates that the inhaled corticosteroids (ICS) routinely taken for asthma and COPD could have had a protective role in preventing severe COVID-19 and, therefore, may be a promising treatment for COVID-19. This review summarises the evidence supporting the beneficial effects of ICS on outcomes in patients with COVID-19 and explores the potential protective mechanisms.

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Conflict of interest statement

Conflict of interest: M. Bafadhel has unrestricted research grants from AstraZeneca and Roche, and has received honoraria to her institution for speaker's fees from AstraZeneca, Chiesi, Cipla and GlaxoSmithKline. She is a scientific adviser to Albus Health and ProAxis. Conflict of interest: R. Faner has received research funding, advisory board fees and lecture fees from AstraZeneca, Chiesi, GlaxoSmithKline and Menarini. Conflict of interest: C. Taillé has received grants to her institution, advisory board fees and lecture fees from AstraZeneca, Chiesi, GlaxoSmithKline, Novartis and Sanofi. Conflict of interest: R.E.K. Russell has received advisory board fees and lecture fees from AstraZeneca, Chiesi, Cipla and GlaxoSmithKline. Conflict of interest: T. Welte has received lecture fees from AstraZeneca, Basilea, Bayer, Berlin Chemie, Biotest, Boehringer Ingelheim, GlaxoSmithKline, MSD, Novartis, Pfizer, Roche and Sanofi-Aventis, and advisory board fees from AstraZeneca, Basilea, Bayer, Biotest, Boehringer Ingelheim, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer and Roche. Conflict of interest: P.J. Barnes has received research funding from AstraZeneca and Boehringer Ingelheim, and funding for consultancy, scientific advisory boards and talks from AstraZeneca, Boehringer Ingelheim, Covis, Epi-Endo, Novartis, Pieris and Teva. Conflict of interest: A. Agustí has unrestricted research grants from AstraZeneca and GlaxoSmithKline, and has received honoraria for speaker's fees from AstraZeneca, Chiesi, GlaxoSmithKline, Menarini, Orion Pharma and Zambon.

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

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Editorial

Arch Bronconeumol

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. 2023 Jan;59(1):5-6.

doi: 10.1016/j.arbres.2022.10.009. Epub 2022 Nov 1.

Home High-Flow Oxygen Therapy Should Be Considered in Patients With COPD and Chronic Respiratory Failure

[Article in English, Spanish]

[Manel Luján](#)¹

Affiliations expand

- PMID: 36402702
- DOI: [10.1016/j.arbres.2022.10.009](https://doi.org/10.1016/j.arbres.2022.10.009)

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24

Am J Ind Med

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. 2023 Jan;66(1):18-29.

doi: 10.1002/ajim.23445. Epub 2022 Nov 17.

How much have adverse occupational health outcomes among construction workers improved over time? Evidence from 25 years of medical screening

[Knut Ringen](#)¹, [John Dement](#)², [Laura Welch](#)¹, [Patricia Quinn](#)¹

Affiliations expand

- PMID: 36398410
- DOI: [10.1002/ajim.23445](https://doi.org/10.1002/ajim.23445)

Abstract

Background: Construction workers have always had a high risk of occupational illnesses. We used 25 years of data from a medical screening program serving older construction workers to determine how much health outcomes have improved over the past 60 years.

Methods: We investigated changes in relative risk for chest radiographs consistent with pneumoconiosis, COPD by spirometry, lung cancer mortality, and audiometry-assessed hearing impairment among workers participating in a medical screening program. Results were stratified by decade of first construction employment: before 1960, 1960-1969, 1970-1979, 1980-1989, and after 1990. Poisson and Cox regression analyses assessed relative risk by decade adjusted for age, sex, smoking, and years of construction trade work.

Results: Subjects were 94% male and, on average, 60 years old with 25 years of construction work. When compared to workers employed before 1960, those first employed after 1990 experienced the following reductions in model-adjusted relative risks: chronic obstructive pulmonary disease, 32%; all pneumoconiosis, 68%; parenchymal abnormalities, 35%; pleural abnormalities, 71%; hearing impairment, 20%; and lung cancer mortality, 48%. Risks started to decline in the 1960s with greatest reductions among workers first employed after 1970.

Conclusions: This study demonstrates the positive impact that adoption of occupational health protections have had over the past 60 years. The greatest risk reductions were observed for outcomes with strong regulatory and legal incentives to reduce exposures and associated risks, such as those associated with inhalation hazards (asbestos and silica), while lowest improvement was for hearing impairment, for which little regulatory enforcement and few prevention incentives have been adopted.

Keywords: BTMed; COPD; DOE; construction trades; hearing impairment; lung cancer; parenchymal changes; pneumoconiosis; surveillance.

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- [67 references](#)

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Meta-Analysis

Environ Res

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. 2023 Jan 1;216(Pt 4):114604.

doi: 10.1016/j.envres.2022.114604. Epub 2022 Nov 12.

Meta analysis of health effects of ambient air pollution exposure in low- and middle-income countries

[Pavanaditya Badida](#)¹, [Arun Krishnamurthy](#)², [Jayapriya Jayaprakash](#)³

Affiliations expand

- PMID: 36375501
- DOI: [10.1016/j.envres.2022.114604](https://doi.org/10.1016/j.envres.2022.114604)

Abstract

It is well established that exposure to ambient air pollution affects human health. A majority of literature concentrated on health effects of air pollution in high income countries. Only fewer studies analyzing health effects of air pollution in Low- and Middle-Income Countries (LMICs) are available. To bridge this gap in literature, this study investigated short term and long-term health impacts of ambient air pollutants focussed in LMICs. We evaluated Total Non-accidental mortality, Respiratory Mortality, Stroke Mortality, Cardio-vascular Mortality, Chronic Obstructive Pulmonary Disease (COPD), Ischemic Heart Disease (IHD) and Lung Cancer Mortality in LMICs particularly. Random Effects Model was utilised to derive overall risk estimate. Relative Risk (RR) estimates per 10 $\mu\text{g}/\text{m}^3$ was used as input for model. Subgroup and Sensitivity Analysis by Design and Country was conducted. A total of 152 studies were included for quantitative analysis. We found positive associations between pollutants and Total Non-accidental mortality for PM_{10} (RR:1.0043-1.0036), $\text{p} < 0.0001$), NO_2 (RR:1.0222 (1.0111-1.0336), $\text{p} < 0.0001$), SO_2 (RR:1.0107 - (1.0073-1.0140), $\text{p} < 0.0001$), O_3 (RR: 1.0038 (1.0023-1.0053), $\text{p} < 0.0001$) and $\text{PM}_{2.5}$ (RR: 1.0048 (1.0037-1.0059), $\text{p} < 0.0001$) for every 10 $\mu\text{g}/\text{m}^3$ increase. We found positive association between Long-term exposure to PM_{10} and Total Non-accidental mortality (RR: 1.0430 (1.0278-1.0583), $\text{p} < 0.0001$) We also found statistically significant positive associations between pollutants and Cardiorespiratory and Cardiovascular morbidity. The positive associations persisted when analysed amongst sub-groups. However, the high heterogeneity amongst studies persisted even after performing sub-group analysis. The study has found statistically significant positive associations between short-term and long-term exposure to Ambient air pollution with various health-outcome combinations.

Keywords: Air pollution; Case crossover study; Cohort study; Health effects; Meta analysis; Systematic review; Time series study.

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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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26

Environ Res



. 2023 Jan 1;216(Pt 4):114746.

doi: 10.1016/j.envres.2022.114746. Epub 2022 Nov 5.

Causal effect of PM₁ on morbidity of cause-specific respiratory diseases based on a negative control exposure

[Shiyun Lv](#)¹, [Xiangtong Liu](#)¹, [Zhiwei Li](#)¹, [Feng Lu](#)², [Moning Guo](#)², [Mengmeng Liu](#)³, [Jing Wei](#)⁴, [Zhiyuan Wu](#)¹, [Siqi Yu](#)¹, [Shihong Li](#)⁵, [Xia Li](#)⁶, [Wenkang Gao](#)⁷, [Lixin Tao](#)¹, [Wei Wang](#)⁸, [Jinyuan Xin](#)⁹, [Xiuhua Guo](#)¹⁰

Affiliations expand

- PMID: 36347395
- DOI: [10.1016/j.envres.2022.114746](https://doi.org/10.1016/j.envres.2022.114746)

Free article

Abstract

Background: Extensive studies have linked PM_{2.5} and PM₁₀ with respiratory diseases (RD). However, few is known about causal association between PM₁ and morbidity of RD. We aimed to assess the causal effects of PM₁ on cause-specific RD.

Methods: Hospital admission data were obtained for RD during 2014 and 2019 in Beijing, China. Negative control exposure and extreme gradient boosting with SHapley Additive exPlanation was used to explore the causality and contribution between PM₁ and RD. Stratified analysis by gender, age, and season was conducted.

Results: A total of 1,183,591 admissions for RD were recorded. Per interquartile range (28 µg/m³) uptick in concentration of PM₁ corresponded to a 3.08% [95% confidence interval (CI): 1.66%-4.52%] increment in morbidity of total RD. And that was 4.47% (95% CI: 2.46%-6.52%) and 0.15% (95% CI: 1.44%-1.78%), for COPD and asthma, respectively. Significantly

positive causal associations were observed for PM₁ with total RD and COPD. Females and the elderly had higher effects on total RD, COPD, and asthma only in the warm months ($Z = 3.03$, $P = 0.002$; $Z = 4.01$, $P < 0.001$; $Z = 3.92$, $P < 0.001$; $Z = 2.11$, $P = 0.035$; $Z = 2.44$, $P = 0.015$). Contribution of PM₁ ranked first, second and second for total RD, COPD, and asthma among air pollutants.

Conclusion: PM₁ was causally associated with increased morbidity of total RD and COPD, but not causally associated with asthma. Females and the elderly were more vulnerable to PM₁-associated effects on RD.

Keywords: Causal effect; Cause-specific respiratory diseases; Morbidity; PM(1).

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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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27

Heart Lung



. 2023 Jan-Feb;57:257-264.

doi: 10.1016/j.hrtlng.2022.10.007. Epub 2022 Oct 28.

Obstructive sleep apnea reduces functional capacity and impairs cardiac

autonomic modulation during submaximal exercise in patients with chronic obstructive pulmonary disease: A follow-up study

[Patrícia Faria Camargo¹](#), [Luciana Ditomaso-Luporini¹](#), [Luiz Carlos Soares de Carvalho Jr²](#), [Cássia da Luz Goulart¹](#), [Polliana Batista Dos Santos¹](#), [Rayane Sebold¹](#), [Meliza Goi Roscani³](#), [Renata Gonçalves Mendes¹](#), [Audrey Borghi-Silva⁴](#)

Affiliations expand

- PMID: 36332349
- DOI: [10.1016/j.hrtlng.2022.10.007](https://doi.org/10.1016/j.hrtlng.2022.10.007)

Abstract

Background: Functional capacity and heart rate variability (HRV) are important prognostic markers in chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea syndrome (OSA). However, the impact of the overlap of these diseases and the one-year clinical follow-up has not yet been evaluated.

Objectives: To assess whether the presence of OSA can impair functional performance and cardiac autonomic control during exercise in patients with COPD; and to verify whether the overlap of these diseases could lead to worse clinical outcomes during the one-year follow-up.

Methods: Thirty-four patients underwent pulmonary function tests, echocardiography and polysomnography for diagnostic confirmation, disease staging, exclusion of any cardiac changes, and allocation between groups. The patients underwent the six-minute walk test (6MWT) to assess functional capacity and HRV during exercise. Subsequently, patients were followed up for 12 months to record outcomes such as exacerbation, hospitalization, and deaths. At the end of this period, the patients were reevaluated to verify the hypotheses of the study.

Results: The OSA-COPD group showed greater functional impairment when compared to the COPD group ($p=0.003$) and showed worse cardiac autonomic responses during the 6MWT with greater parasympathetic activation ($p=0.03$) and less complexity of the autonomic nervous system, in addition to being more likely to exacerbate ($p=0.03$) during one year of follow-up.

Conclusion: OSA-COPD produces deleterious effects on functional performance and a greater autonomic imbalance that impairs clinical outcomes.

Keywords: COPD; Clinical outcomes; Heart rate variability; OSA; Six-minute walk test.

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Conflict of interest statement

Declaration of Competing Interests None.

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28

Review

Eur Respir Rev

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. 2022 Nov 2;31(166):220098.

doi: 10.1183/16000617.0098-2022. Print 2022 Dec 31.

Prognostic factors for mortality, intensive care unit and hospital admission due to SARS-CoV-2: a systematic review and meta-analysis of cohort studies in Europe

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Affiliations expand

- PMID: 36323422
- PMCID: [PMC9724816](#)
- DOI: [10.1183/16000617.0098-2022](#)

Free PMC article

Abstract

Background: As mortality from coronavirus disease 2019 (COVID-19) is strongly age-dependent, we aimed to identify population subgroups at an elevated risk for adverse outcomes from COVID-19 using age-/gender-adjusted data from European cohort studies with the aim to identify populations that could potentially benefit from booster vaccinations.

Methods: We performed a systematic literature review and meta-analysis to investigate the role of underlying medical conditions as prognostic factors for adverse outcomes due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), including death, hospitalisation, intensive care unit (ICU) admission and mechanical ventilation within three separate settings (community, hospital and ICU). Cohort studies that reported at least age and gender-adjusted data from Europe were identified through a search of peer-reviewed articles published until 11 June 2021 in Ovid Medline and Embase. Results are presented as odds ratios with 95% confidence intervals and absolute risk differences in deaths per 1000 COVID-19 patients.

Findings: We included 88 cohort studies with age-/gender-adjusted data from 6 653 207 SARS-CoV-2 patients from Europe. Hospital-based mortality was associated with high and moderate certainty evidence for solid organ tumours, diabetes mellitus, renal disease, arrhythmia, ischemic heart disease, liver disease and obesity, while a higher risk, albeit with low certainty, was noted for chronic obstructive pulmonary disease and heart failure. Community-based mortality was associated with a history of heart failure, stroke, diabetes and end-stage renal disease. Evidence of high/moderate certainty revealed a strong association between hospitalisation for COVID-19 and solid organ transplant recipients, sleep apnoea, diabetes, stroke and liver disease.

Interpretation: The results confirmed the strong association between specific prognostic factors and mortality and hospital admission. Prioritisation of booster vaccinations and the implementation of nonpharmaceutical protective measures for these populations may contribute to a reduction in COVID-19 mortality, ICU and hospital admissions.

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Conflict of interest statement

Conflicts of 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.

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

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Review

Heart Lung

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. 2023 Jan-Feb;57:236-242.

doi: 10.1016/j.hrtlng.2022.09.021. Epub 2022 Oct 19.

Effects of Kinesio Taping® on pulmonary function of individuals with COPD: A systematic review and meta-analysis

[Luana de Campos](#)¹, [Rafaela Neves](#)¹, [Karoliny Dos Santos Isoppo](#)²

Affiliations [expand](#)

- PMID: 36272221
- DOI: [10.1016/j.hrtlng.2022.09.021](https://doi.org/10.1016/j.hrtlng.2022.09.021)

Abstract

Background: Currently, there is no consensus regarding indication and benefits of Kinesio Taping® on pulmonary function of individuals with chronic obstructive pulmonary disease (COPD).

Objectives: To identify the effects of Kinesio Taping® on pulmonary function of individuals with COPD through a systematic review and meta-analysis.

Methods: Systematic review including experimental or quasi-experimental studies in English, Portuguese, or Spanish. Searches were conducted on LILACS, Scielo, Medline, Web of Science, and Scopus databases. Two reviewers independently conducted study selection, data extraction, and analysis. Methodological quality was assessed using PEDro scale, while meta-analyses were conducted using RevMan software. This review was registered (PROSPERO CRD42020223752).

Results: Five studies were included. Forced expiratory volume in the first second (FEV₁), forced vital capacity (FVC), FEV₁/FVC ratio, and peak expiratory flow were not different between Kinesio Taping® group and control group.

Conclusion: Results suggest that Kinesio Taping® does not improve pulmonary function of individuals with COPD.

Keywords: Athletic tape; Chronic obstructive; Pulmonary disease; Respiratory function tests; Respiratory muscles; Spirometry.

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Conflict of interest statement

Declaration of Competing Interest None.

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J Appl Physiol (1985)

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. 2023 Jan 1;134(1):20-27.

doi: 10.1152/jappphysiol.00385.2022. Epub 2022 Oct 21.

Physiological impacts of computed tomography airway dysanapsis, fractal dimension, and branch count in asymptomatic never smokers

[Tomoki Maetani](#)¹, [Naoya Tanabe](#)¹, [Satoru Terada](#)¹, [Yusuke Shiraishi](#)¹, [Hiroshi Shima](#)¹, [Shizuo Kaji](#)², [Ryo Sakamoto](#)³, [Tsuyoshi Oguma](#)¹, [Susumu Sato](#)^{1,4}, [Izuru Masuda](#)⁵, [Toyohiro Hirai](#)¹

Affiliations expand

- PMID: 36269294
- DOI: [10.1152/jappphysiol.00385.2022](https://doi.org/10.1152/jappphysiol.00385.2022)

Abstract

Dysanapsis, a mismatch between airway tree caliber and lung size, contributes to a large variation in lung function on spirometry in healthy subjects. However, it remains unclear whether other morphological features of the airway tree could be associated with the variation in lung function independent of dysanapsis. This study used lung cancer screening chest computed tomography (CT) and spirometry data from asymptomatic never smokers. Dysanapsis and the complexity of airway tree geometry were quantified on CT by measuring airway to lung ratio (ALR) and airway fractal dimension (AFD). Moreover, total airway count (TAC), ratio of airway luminal surface area to volume (SA/V), longitudinal tapering and irregularity of the radius of the internal lumen from the central to peripheral airways (Tapering index and Irregularity index) were quantified. In 431 asymptomatic never smokers without a history of lung diseases, lower ALR was associated with lower forced expiratory volume in 1 s (FEV₁) and FEV₁/forced vital capacity (FEV₁/FVC). The associations of ALR with AFD and TAC ($r = 0.41$ and 0.13) were weaker than the association between

TAC and AFD ($r = 0.64$). In multivariable models adjusted for age, sex, height, and mean lung density, lower AFD and TAC were associated with lower FEV₁ and FEV₁/FVC independent of ALR, whereas SA/V and Tapering index were not. These results suggest that the smaller airway tree relative to a given lung size and the lower complexity of airway tree shape, including lower branch count, are independently associated with lower lung function in healthy subjects. **NEW & NOTEWORTHY** This study showed that fractal dimension and total airway count of the airway tree on computed tomography are associated with lung function on spirometry independent of a smaller airway for a given lung size (dysanapsis) in asymptomatic never smokers without a history of lung diseases. In addition to dysanapsis, the morphometric complexity of the airway tree and the airway branch count may cause a substantial variation of lung function in these subjects.

Keywords: airway fractal dimension; airway morphology; dysanapsis; lung function; total airway count.

Comment in

- [Airway trees in the Anthropocene.](#)
Smith BM. *J Appl Physiol* (1985). 2023 Jan 1;134(1):18-19. doi: 10.1152/jappphysiol.00666.2022. Epub 2022 Nov 23. PMID: 36417199 No abstract available.

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31

Review

J Thorac Imaging

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. 2023 Jan 1;38(1):W1-W18.

A Computer-based Analysis for Identification and Quantification of Small Airway Disease in Lung Computed Tomography Images: A Comprehensive Review for Radiologists

[Mohammad Mehdi Baradaran Mahdavi](#)¹, [Masoud Arabfard](#)¹, [Mehravat Rafati](#)², [Mostafa Ghanei](#)¹

Affiliations expand

- PMID: 36206107
- DOI: [10.1097/RTI.0000000000000683](https://doi.org/10.1097/RTI.0000000000000683)

Abstract

Computed tomography (CT) imaging is being increasingly used in clinical practice for detailed characterization of lung diseases. Respiratory diseases involve various components of the lung, including the small airways. Evaluation of small airway disease on CT images is challenging as the airways cannot be visualized directly by a CT scanner. Small airway disease can manifest as pulmonary air trapping (AT). Although AT may be sometimes seen as mosaic attenuation on expiratory CT images, it is difficult to identify diffuse AT visually. Computer technology advances over the past decades have provided methods for objective quantification of small airway disease on CT images. Quantitative CT (QCT) methods are being rapidly developed to quantify underlying lung diseases with greater precision than subjective visual assessment of CT images. A growing body of evidence suggests that QCT methods can be practical tools in the clinical setting to identify and quantify abnormal regions of the lung accurately and reproducibly. This review aimed to describe the available methods for the identification and quantification of small airway disease on CT images and to discuss the challenges of implementing QCT metrics in clinical care for patients with small airway disease.

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Conflict of interest statement

The authors declare no conflicts of interest.

- [107 references](#)

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Am J Respir Cell Mol Biol

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. 2023 Jan;68(1):90-102.

doi: 10.1165/rcmb.2022-0131OC.

Chronic Obstructive Pulmonary Disease and Cigarette Smoke Lead to Dysregulated Mucosal-associated Invariant T-Cell Activation

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Affiliations expand

- PMID: 36174211
- DOI: [10.1165/rcmb.2022-0131OC](https://doi.org/10.1165/rcmb.2022-0131OC)

Abstract

Chronic obstructive pulmonary disease (COPD) is associated with airway inflammation, increased infiltration by CD8⁺ T lymphocytes, and infection-driven exacerbations. Although cigarette smoke is the leading risk factor for COPD, the mechanisms driving the development of COPD in only a subset of smokers are incompletely understood. Lung-resident mucosal-associated invariant T (MAIT) cells play a role in microbial infections and

inflammatory diseases. The role of MAIT cells in COPD pathology is unknown. Here, we examined MAIT cell activation in response to cigarette smoke-exposed primary human bronchial epithelial cells (BECs) from healthy, COPD, or smoker donors. We observed significantly higher baseline MAIT cell responses to COPD BECs than healthy BECs. However, infected COPD BECs stimulated a smaller fold increase in MAIT cell response despite increased microbial infection. For all donor groups, cigarette smoke-exposed BECs elicited reduced MAIT cell responses; conversely, cigarette smoke exposure increased ligand-mediated MR1 surface translocation in healthy and COPD BECs. Our data demonstrate that MAIT cell activation is dysregulated in the context of cigarette smoke and COPD. MAIT cells could contribute to cigarette smoke- and COPD-associated inflammation through inappropriate activation and reduced early recognition of bacterial infection, contributing to microbial persistence and COPD exacerbations.

Keywords: MAIT cells; MR1; *Streptococcus pneumoniae*; chronic obstructive pulmonary disease; cigarette smoke.

Comment in

- [Breaching the Defenses? Mucosal-associated Invariant T Cells, Smoking, and Chronic Obstructive Pulmonary Disease.](#)

Staples KJ. *Am J Respir Cell Mol Biol*. 2023 Jan;68(1):9-10. doi: 10.1165/rcmb.2022-0393ED.PMID: 36256956 No abstract available.

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33

Respir Care

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. 2023 Jan;68(1):92-100.

doi: 10.4187/respcare.10091. Epub 2022 Sep 27.

Continuous Monitoring of Pulse Oximetry During the 6-Minute Walk Test Improves Clinical Outcomes Prediction in COPD

[Kellen S Batista](#)¹, [Igor Dossin Cézar](#)¹, [Igor G Benedetto](#)¹, [Ravena M C da Silva](#)¹, [Litiele Evelin Wagner](#)¹, [Danton Pereira da Silva](#)¹, [Paulo R Sanches](#)¹, [Marcelo B Gazzana](#)¹, [Marli M Knorst](#)¹, [Juan P de-Torres](#)², [J Alberto Neder](#)², [Danilo C Berton](#)³

Affiliations expand

- PMID: 36167849
- DOI: [10.4187/respcare.10091](https://doi.org/10.4187/respcare.10091)

Abstract

Background: Continuous monitoring of S_{pO_2} throughout the 6-min walk test (6MWT) unveiled that some patients with respiratory diseases may present values across the test lower than S_{pO_2} measured at the end of the test. Nevertheless, it remains unclear whether this approach improves the yield of walk-induced desaturation detection in predicting mortality and hospitalizations in patients with COPD.

Methods: Four hundred twenty-one subjects (51% males) with mild-very severe COPD underwent a 6MWT with continuous measurement of S_{pO_2} . Exercise desaturation was defined as a fall in $S_{pO_2} \geq 4\%$. All-cause mortality was assessed up to 6 y of follow-up and the rate of hospitalizations in the year succeeding the 6MWT.

Results: One hundred forty-nine subjects (35.4%) died during a mean (interquartile) follow-up of 55.5 (30.2-64.1) months. Desaturation was observed in 299/421 (71.0%). S_{pO_2} along the test was $< \text{end } S_{pO_2}$ (88 [82-92]% vs 90 [84-93]%, $P < .001$). Desaturation detected only during (but not at the end of) the test was found in 81/421 (19.2%) participants. Multivariate Cox regression model adjusted for sex, body composition, FEV_1 , residual volume/total lung capacity ratio, walk distance, O_2 supplementation during the test, and comorbidities retained the presence of desaturation either at the end (1.85 [95% CI 1.02-3.36]) or only along the test (2.08 [95% CI 1.09-4.01]) as significant predictors of mortality. The rate of hospitalizations was higher in those presenting with any kind of desaturation compared to those without exercise desaturation. Logistic regression analysis revealed that walking interruption and diffusing capacity of the lung for carbon monoxide predicted desaturation observed only during the test.

Conclusions: O_2 desaturation missed by end-exercise S_{pO_2} but exposed by measurements during the test was independently associated with all-cause mortality and hospitalizations in subjects with COPD.

Keywords: 6-min walk test; COPD; hospitalization; oxygen saturation; prognosis; survival analysis.

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Conflict of interest statement

The authors have disclosed no conflicts of interest.

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Arch Gerontol Geriatr

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. 2023 Jan;104:104822.

doi: 10.1016/j.archger.2022.104822. Epub 2022 Sep 20.

Admission high-sensitivity cardiac troponin levels as a prognostic indicator for in-hospital mortality rates in the elderly and very elderly COVID-19 patients

[Alessio Menditto](#)¹, [Olga Protic](#)², [Mirko Di Rosa](#)³, [Anna Rita Bonfigli](#)⁴, [Fabrizia Lattanzio](#)⁴, [Roberto Antonicelli](#)²

Affiliations expand

- PMID: 36156408
- PMCID: [PMC9484855](#)
- DOI: [10.1016/j.archger.2022.104822](#)

Free PMC article

Abstract

Background: Elevation of cardiac troponin (cTn) is associated with the worst prognosis not only in cardiovascular disease but also in non-cardiovascular disease. The aim of this study is to verify if cTn has a prognostic role in elderly and very elderly coronavirus disease 2019 (COVID-19) patients.

Methods: This study enrolled consecutive COVID-19 elderly patients hospitalized at INRCA hospital, with available admission high sensitivity cardiac troponin T (HS-cTnT) level. Patients were divided into three groups based on HS-cTnT level: group A (Hs-cTnT \leq 40 pg/ml), group B (Hs-cTnT 41-100 pg/ml), and group C (Hs-cTnT \geq 101 pg/ml). The correlation between HS-cTnT levels and mortality rates was analyzed.

Results: 461 patients (mean age 86 years; 59% female) were divided into group A (261 patients), group B (129 patients), and group C (71 patients). Group C resulted significantly older, more affected by heart failure, chronic obstructive pulmonary disease, chronic kidney disease, and dementia, and with higher levels of creatinine, C-reactive protein, pro-calcitonin, interleukin-6, ferritin, NT-proBNP, D-dimer than group A and group B. Mortality rate increased significantly across groups (group A: 18.4%; group B: 36.4%; group C: 62.0%; $p < 0.001$). Group C had a significant increase in mortality risk compared to group A, both univariate analysis (HR 3.78) and multivariate analysis (model 2 HR 3.10; model 3 HR 3.59; model 4 HR 1.72).

Conclusion: HS-cTnT has demonstrated a prognostic role in elderly and very elderly COVID-19 patients. HS-cTnT is a simple and inexpensive laboratory exam that gives clinicians important information on mortality risk stratification.

Keywords: COVID-19; Elderly; High-sensitivity cardiac troponin assay; Mortality; SARSCov2; Troponin.

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Conflict of interest statement

Declaration of Competing Interest None to declare

- [31 references](#)

- [1 figure](#)

[supplementary info](#)

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Editorial

[Respirology](#)

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. 2023 Jan;28(1):11-12.

doi: 10.1111/resp.14369. Epub 2022 Sep 15.

COPD-related incidence, mortality, and disability: An illustrative summary of the GBD study (1990-2019)

[Jennifer L Perret](#)^{1,2}, [Shyamali C Dharmage](#)¹

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

- PMID: 36106405
- DOI: [10.1111/resp.14369](https://doi.org/10.1111/resp.14369)

Free article

No abstract available

Keywords: COPD; chronic obstructive pulmonary disease; disability; epidemiology; global; incidence; mortality.

- [14 references](#)

supplementary info

Publication types, MeSH termsexpand

full text links

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36

Respirology

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. 2023 Jan;28(1):47-55.

doi: 10.1111/resp.14345. Epub 2022 Aug 10.

Respiratory admissions before and during the COVID-19 pandemic with mediation analysis of air pollutants, mask-wearing and influenza rates

[Fanny Wai San Ko¹](#), [Louis Ho Shing Lau¹](#), [So Shan Ng¹](#), [Terry Cheuk Fung Yip²](#), [Grace Lai Hung Wong¹](#), [Ka Pang Chan¹](#), [Tat On Chan¹](#), [David Shu Cheong Hui¹](#)

Affiliations expand

- PMID: 36065624
- PMCID: [PMC9538077](#)
- DOI: [10.1111/resp.14345](#)

Abstract

Background and objective: Decline in hospitalizations for various respiratory diseases has been reported during the COVID-19 pandemic, but what led to such an observation is uncertain.

Methods: This was a territory-wide, retrospective cohort study involving all public hospital admissions in Hong Kong from 1 January 2017 to 31 December 2020. Hospital admissions for respiratory diseases, including asthma, COPD and non-COVID pneumonia, were assessed. COVID-related admissions were excluded from this study. The time of commencement of the pandemic was taken from the fourth week of January 2020. The associations between air pollutant levels, influenza and mask-wearing rates with hospital admissions were assessed by mediation analyses.

Results: There were altogether 19,485, 78,693 and 238,781 admissions for asthma, COPD and non-COVID pneumonia from January 2017 to December 2020. There was a marked reduction in hospital admissions of asthma, COPD and non-COVID pneumonia (37%, 36% and 12% decrease in average daily admissions, respectively) during the COVID-19 pandemic compared to before. Air pollutant levels and influenza rate were decreased while mask-wearing rate was increased. Collinearity of mask-wearing rates and pandemic year was observed. For COPD, NO₂, SO₂, PM10 and influenza rates (4%, 11%, 4% and 4% of the total effect, respectively), while for non-COVID pneumonia, PM10 and influenza rates (11% and 52%, respectively) had significant mediation effect on changes in hospital admissions before and during the COVID-19 pandemic.

Conclusion: During the COVID-19 pandemic, a decrease in air pollutant levels and influenza rate had mediation effect on the reduction in hospitalizations of COPD and non-COVID pneumonia.

Keywords: COPD; COVID-19; asthma; coronavirus disease; pneumonia.

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Conflict of interest statement

None declared.

- [Cited by 2 articles](#)
- [34 references](#)
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Respirology



. 2023 Jan;28(1):29-36.

doi: 10.1111/resp.14349. Epub 2022 Aug 23.

[Global, regional and national burden of chronic obstructive pulmonary disease over a 30-year period: Estimates from the 1990 to 2019 Global Burden of Disease Study](#)

[Hao-Yang Li](#)¹, [Teng-Yu Gao](#)¹, [Wei Fang](#)¹, [Chen-Yang Xian-Yu](#)¹, [Nian-Jia Deng](#)¹, [Chao Zhang](#)¹, [Yu-Ming Niu](#)²

Affiliations expand

- PMID: 36054068
- DOI: [10.1111/resp.14349](https://doi.org/10.1111/resp.14349)

Free article

Abstract

Background and objective: Chronic obstructive pulmonary disease (COPD) is the most prevalent chronic respiratory disease. This study investigated the global, regional and country burden of COPD based on gender, age and socio-demographic indices (SDIs) in the last 30-year period from 1990 to 2019.

Methods: The COPD data, including incidence, mortality and disability-adjusted life years (DALYs), were obtained from the 2019 Global Burden of Disease Study. If age-standardized incidence rate (ASIR) or death rate (ASDR) remains almost constant or decreases, the number of cases will still increase as the global population increases substantially. Estimated annual percentage change (EAPC) was calculated to assess incidence, mortality and DALY trends.

Results: The incidence of COPD increased by 85.89% from 8,722,966 cases in 1990 to 16,214,828 cases in 2019, and the ASIR decreased from 216.48/100,000 persons in 1990 (95%UI, 204.56-227.33) to 200.49 per 100,000 persons (95%UI, 188.63-212.57) in 2019. The ASIR increased (EAPC = 0.05, 95%CI, 0.01-0.10) in the low SDI region, was stable in the high SDI region, and fell in the other three SDI regions. Men had a higher ASIR than women over the past 30 years, and there were differences in the incidence rates for different age groups. Male mortality and DALYs were higher than female mortality. ASDR decreased by 2.13% (95%CI, -2.23% to -2.02%) per year and the annual age-standardized DALY rate decreased by 1.97% (95%CI, -2.05% to -1.89%).

Conclusions: The ASIR, ASDR and age-standardized DALY rate of COPD declined overall in the last 30 years, and were highest in the low-middle SDI region.

Keywords: chronic obstructive pulmonary disease; disability adjusted life-years; global burden of disease; incidence; mortality.

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Ann Am Thorac Soc

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. 2023 Jan;20(1):38-46.

doi: 10.1513/AnnalsATS.202203-226OC.

Diffusing Capacity and Mortality in Chronic Obstructive Pulmonary Disease

[Aparna Balasubramanian](#)¹, [Nirupama Putcha](#)¹, [Neil R MacIntyre](#)², [Robert L Jensen](#)³, [Gregory Kinney](#)⁴, [William W Stringer](#)⁵, [Craig P Hersh](#)⁶, [Russell P Bowler](#)⁷, [Richard Casaburi](#)⁸, [MeiLan K Han](#)⁸, [Janos Porszasz](#)⁵, [R Graham Barr](#)⁹, [Elizabeth Regan](#)^{4,10}, [Barry J Make](#)⁴, [Nadia N Hansel](#)¹, [Robert A Wise](#)¹, [Meredith C McCormack](#)¹

Affiliations expand

- PMID: 35969416
- DOI: [10.1513/AnnalsATS.202203-226OC](https://doi.org/10.1513/AnnalsATS.202203-226OC)

Abstract

Rationale: Chronic obstructive pulmonary disease (COPD) mortality risk is often estimated using the BODE (body mass index, obstruction, dyspnea, exercise capacity) index, including body mass index, forced expiratory volume in 1 second, dyspnea score, and 6-minute walk distance. Diffusing capacity of the lung for carbon monoxide (DL_{CO}) is a potential predictor of mortality that reflects physiology distinct from that in the BODE index. **Objectives:** This study evaluated DL_{CO} as a predictor of mortality using participants from the COPDGene study. **Methods:** We performed time-to-event analyses of individuals with COPD (former or current smokers with forced expiratory volume in 1 second/forced vital capacity < 0.7) and DL_{CO} measurements from the COPDGene phase 2 visit. Cox proportional hazard methods were used to model survival, adjusting for age, sex, pack-years, smoking status, BODE index, computed tomography (CT) percent emphysema (low attenuation areas below -950 Hounsfield units), CT airway wall thickness, and history of cardiovascular or kidney diseases. C statistics for models with DL_{CO} and BODE scores were used to compare discriminative accuracy. **Results:** Of 2,329 participants, 393 (16.8%) died during the follow-up period (median = 4.9 yr). In adjusted analyses, for every 10% decrease in DL_{CO} percent predicted, mortality increased by 28% (hazard ratio = 1.28; 95% confidence interval, 1.17-1.41, *P* < 0.001). When compared with other clinical predictors, DL_{CO} percent predicted performed similarly to BODE (C statistic DL_{CO} = 0.68; BODE = 0.70), and the addition of DL_{CO} to BODE improved its discriminative accuracy (C statistic = 0.71). **Conclusions:** Diffusing capacity, a measure of gas transfer, strongly predicted all-cause mortality in individuals with COPD, independent of BODE index and CT evidence of emphysema and airway wall thickness. These findings support inclusion of DL_{CO} in prognostic models for COPD.

Keywords: COPD; mortality; pulmonary diffusing capacity; pulmonary gas exchange.

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39

Am J Respir Crit Care Med

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. 2023 Jan 1;207(1):60-68.

doi: 10.1164/rccm.202203-0550OC.

Suspected Interstitial Lung Disease in COPD Gene Study

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Affiliations expand

- PMID: 35930450
- DOI: [10.1164/rccm.202203-0550OC](https://doi.org/10.1164/rccm.202203-0550OC)

Abstract

Rationale: Although interstitial lung abnormalities (ILA), specific patterns of incidentally-detected abnormal density on computed tomography, have been associated with abnormal lung function and increased mortality, it is unclear if a subset with incidental interstitial lung disease (ILD) accounts for these adverse consequences. **Objectives:** To

define the prevalence and risk factors of suspected ILD and assess outcomes. **Methods:** Suspected ILD was evaluated in the COPDGene (Chronic Obstructive Pulmonary Disease Genetic Epidemiology) study, defined as ILA and at least one additional criterion: definite fibrosis on computed tomography, FVC less than 80% predicted, or DL_{co} less than 70% predicted. Multivariable linear, longitudinal, and Cox proportional hazards regression models were used to assess associations with St. George's Respiratory Questionnaire, 6-minute-walk test, supplemental oxygen use, respiratory exacerbations, and mortality. **Measurements and Main Results:** Of 4,361 participants with available data, 239 (5%) had evidence for suspected ILD, whereas 204 (5%) had ILA without suspected ILD. In multivariable analyses, suspected ILD was associated with increased St. George's Respiratory Questionnaire score (mean difference [MD], 3.9 points; 95% confidence interval [CI], 0.6-7.1; $P = 0.02$), reduced 6-minute-walk test (MD, -35 m; 95% CI, -56 m to -13 m; $P = 0.002$), greater supplemental oxygen use (odds ratio [OR], 2.3; 95% CI, 1.1-5.1; $P = 0.03$) and severe respiratory exacerbations (OR, 2.9; 95% CI, 1.1-7.5; $P = 0.03$), and higher mortality (hazard ratio, 2.4; 95% CI, 1.2-4.6; $P = 0.01$) compared with ILA without suspected ILD. Risk factors associated with suspected ILD included self-identified Black race (OR, 2.0; 95% CI, 1.1-3.3; $P = 0.01$) and pack-years smoking history (OR, 1.2; 95% CI, 1.1-1.3; $P = 0.0005$). **Conclusions:** Suspected ILD is present in half of those with ILA in COPDGene and is associated with exercise decrements and increased symptoms, supplemental oxygen use, severe respiratory exacerbations, and mortality.

Keywords: interstitial lung abnormalities; interstitial lung disease; pulmonary fibrosis.

Comment in

- [Risk Stratifying Interstitial Lung Abnormalities to Guide Early Diagnosis of Interstitial Lung Diseases.](#)

Wijsenbeek MS, Brusselle GG. *Am J Respir Crit Care Med*. 2023 Jan 1;207(1):9-11. doi: 10.1164/rccm.202209-1817ED. PMID: 36170647 No abstract available.

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Editorial

Arch Bronconeumol

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. 2023 Jan;59(1):3-4.

doi: 10.1016/j.arbres.2022.06.008. Epub 2022 Jul 7.

COPD in Women: Future Challenges

[Article in English, Spanish]

[Victoria Scicluna](#)¹, [MeiLan Han](#)²

Affiliations expand

- PMID: 35902294
- DOI: [10.1016/j.arbres.2022.06.008](https://doi.org/10.1016/j.arbres.2022.06.008)

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Case Reports

Arch Bronconeumol

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. 2023 Jan;59(1):57-58.

doi: 10.1016/j.arbres.2022.06.009. Epub 2022 Jul 11.

Classification of the Severity of COPD Exacerbations in Hospitalized Patients According to Rome vs GesEPOC Criteria

[Article in English, Spanish]

[Carlos Antonio Amado Diago](#)¹, [Juan Marco Figueira Gonçalves](#)², [Rafael Golpe](#)³, [Cristóbal Esteban](#)⁴, [Ignacio Garcia Talavera](#)⁵, [Sergio García-Martín](#)⁶

Affiliations expand

- PMID: 35872093
- DOI: [10.1016/j.arbres.2022.06.009](https://doi.org/10.1016/j.arbres.2022.06.009)

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. 2023 Jan;39(1):39-48.

doi: 10.1080/09593985.2021.2001883. Epub 2021 Nov 22.

Determinants of acute care discharge in adults with chronic obstructive pulmonary disease

[Shweta Gore](#)¹, [Jennifer Blackwood](#)², [Houser Emily](#)³, [Fernandez Natalia](#)³

Affiliations expand

- PMID: 34802385
- DOI: [10.1080/09593985.2021.2001883](https://doi.org/10.1080/09593985.2021.2001883)

Abstract

In adults with COPD basic mobility scores on the AM-PAC "6-clicks" measure completed at discharge had the best sensitivity and specificity for predicting discharge to home and need for rehab services.

Keywords: COPD; Hospitalization; chronic obstructive pulmonary disease; occupational therapy; patient discharge; physical therapy.

supplementary info

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Pediatr Pulmonol

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. 2023 Jan 2.

doi: 10.1002/ppul.26298. Online ahead of print.

Safety of biologics in severe asthmatic patients with SARS-CoV-2 infection: A prospective study

[Sara Manti](#)^{1,2}, [Alessandro Giallongo](#)³, [Giulia Pecora](#)¹, [Giuseppe Fabio Parisi](#)¹, [Maria Papale](#)¹, [Enza Mulè](#)¹, [Donatella Aloisio](#)¹, [Novella Rotolo](#)¹, [Salvatore Leonardi](#)¹

Affiliations expand

- PMID: 36593591
- DOI: [10.1002/ppul.26298](https://doi.org/10.1002/ppul.26298)

Abstract

Background: Asthma guidelines have recommended to continue treatment with biologics during COVID-19 pandemic. However, continuation of treatment with biologics in patients with SARS-CoV-2 has been little investigated.

Objective: To assess the safety of biologics in patients with SARS-CoV-2 infection.

Methods: A pilot, monocentre, prospective study. Patients aged 12 years old and older with severe asthma on treatment with biologics and confirmed SARS-CoV-2 infection were enrolled. Patients were followed-up with periodic calls at different time points up to 3 months to detect any adverse effect and its relationship with biologic treatment according to the Naranjo Adverse Probability Scale (NAPS). Severity of SARS-CoV-2 infection and clinical outcome were also assessed.

Results: Overall, we included 21 patients (10 on therapy with omalizumab, 9 with dupilumab and 2 with mepolizumab). Only a patient reported 2 local adverse events. No other adverse event was reported. Twenty out of 21 patients had a mild COVID-19 course and no adverse outcome was observed.

Conclusion: we showed that the scheduled dose of the biologic therapy can be administered safely on time in patients with SARS-CoV-2 infection, as the treatment did not result in adverse events or outcomes. This article is protected by copyright. All rights reserved.

Keywords: COVID-19; adverse events; asthma; biologics; dupilumab; mepolizumab; monoclonal antibodies; omalizumab; safety.

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Thorax

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. 2023 Jan 2;thorax-2022-219539.

doi: 10.1136/thorax-2022-219539. Online ahead of print.

Paediatric asthma hospitalisations continue to decrease in Finland and Sweden between 2015 and 2020

[Juho E Kivistö](#)^{1 2 3}, [Jennifer L P Protudjer](#)^{4 5 6 7 8}, [Jussi Karjalainen](#)^{9 2}, [Anna Bergström](#)¹⁰, [Heini Huhtala](#)¹¹, [Matti Korppi](#)³, [Erik Melén](#)¹²

Affiliations expand

- PMID: 36593115
- DOI: [10.1136/thorax-2022-219539](https://doi.org/10.1136/thorax-2022-219539)

Abstract

We previously reported a decreasing incidence of paediatric asthma hospitalisations in Finland, but a rather stable trend in Sweden, between 2005 and 2014. We now aimed to investigate the incidence of paediatric asthma hospitalisations in these countries between 2015 and 2020, using Finland's National Hospital Discharge Register and Sweden's National Patient Register, which cover all hospitalisations in the respective countries. From 2015 to 2019, the incidence of paediatric asthma hospitalisations decreased by 36.7% in Finland and by 39.9% in Sweden and are increasingly approaching parity. In 2020, despite differences in COVID-19-related restrictions, asthma hospitalisations decreased by over 40%, thus warranting future research on the subject.

Keywords: Asthma; Asthma Epidemiology.

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Conflict of interest statement

Competing interests: None declared.

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Allergol Int

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. 2022 Dec 29;S1323-8930(22)00139-3.

doi: 10.1016/j.alit.2022.11.012. Online ahead of print.

Blood eosinophil count variability in chronic obstructive pulmonary disease and severe asthma

[Yuki Abe](#)¹, [Masaru Suzuki](#)², [Hirokazu Kimura](#)¹, [Kaoruko Shimizu](#)¹, [Nozomu Takei](#)¹, [Akira Oguma](#)¹, [Machiko Matsumoto-Sasaki](#)¹, [Houman Goudarzi](#)¹, [Hironi Makita](#)³, [Masaharu Nishimura](#)³, [Satoshi Konno](#)¹

Affiliations expand

- PMID: 36586746
- DOI: [10.1016/j.alit.2022.11.012](https://doi.org/10.1016/j.alit.2022.11.012)

Free article

Abstract

Background: Blood eosinophils are essential biomarkers that vary substantially over time in patients with COPD and asthma. However, no study has identified the changes and effects in the changes of the blood eosinophil counts over time in both diseases. This study aimed to demonstrate blood eosinophil variability in patients with COPD and severe asthma based on these backgrounds.

Methods: A total of 172 patients with COPD from the Hokkaido COPD cohort study and 96 patients with severe asthma from the Hokkaido Severe Asthma Cohort Study, whose blood eosinophil counts were measured annually over a 3-year period, were analyzed. The factors contributing to consistently high or low blood eosinophil counts were examined in each cohort. The stability of the eosinophil classification (<150 , $150\text{--}299$, ≥ 300 cells/ μL) was compared based on the number of asthma-like features in patients with COPD and the smoking status in patients with severe asthma.

Results: Among all the patients, the most stable range of baseline blood eosinophil counts differed between the two diseases, with <150 cells/ μL in COPD and ≥ 300 cells/ μL in severe asthma. In COPD, the number of asthma-like features (bronchodilator reversibility, blood eosinophilia, and atopy) affects the blood eosinophil count variation patterns. In severe asthma, smoking status did not affect the blood eosinophil count variation patterns.

Conclusions: We identified variations in the blood eosinophil counts and their contributing factors in patients with COPD and severe asthma.

Keywords: Asthma; Chronic obstructive pulmonary disease; Cohort studies; Eosinophils.

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Review

Allergol Int

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. 2022 Dec 28;S1323-8930(22)00137-X.

doi: 10.1016/j.alit.2022.12.001. Online ahead of print.

Group 2 innate lymphoid cells in human asthma

[Arifumi Iwata](#)¹, [Yosuke Toda](#)¹, [Hiroki Furuya](#)¹, [Hiroshi Nakajima](#)²

Affiliations [expand](#)

- PMID: 36585333
- DOI: [10.1016/j.alit.2022.12.001](https://doi.org/10.1016/j.alit.2022.12.001)

Free article

Abstract

Asthma is characterized by increased airway hyperresponsiveness, reversible airflow limitation, and remodeling due to allergic airway inflammation. Asthma has been proposed to be classified into various phenotypes by cluster analyses integrating clinical information and laboratory data. Recently, asthma has been classified into two major endotypes, Type 2-high and Type 2-low asthma, and various subtypes based on the underlying molecular mechanisms. In Type 2-high asthma, Th2 cells, together with group 2 innate lymphoid cells (ILC2s), produce type 2 cytokines such as IL-4, IL-5, IL-9, and IL-13, which play crucial roles in causing airway inflammation. The roles of ILC2s in asthma pathogenesis have been analyzed primarily in murine models, demonstrating their importance not only in IL-33- or papain-induced innate asthma models but also in house dust mite (HDM)- or ovalbumin (OVA)-induced acquired asthma models evoked in an antigen-specific manner. Recently, evidence regarding the roles of ILC2s in human asthma is also accumulating. This minireview summarizes the roles of ILC2s in asthma, emphasizing human studies.

Keywords: Asthma; Epithelial cytokines; Humans; ILC2s; Type 2-high.

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Eur Respir J

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. 2022 Dec 30;2202305.

doi: 10.1183/13993003.02305-2022. Online ahead of print.

Moving towards patient-centred outcomes: the Severe Asthma Questionnaire

[D Davies](#)¹, [M E Hyland](#)², [J W Lanario](#)², [R C Jones](#)³, [M Masoli](#)⁴

Affiliations expand

- PMID: 36585255
- DOI: [10.1183/13993003.02305-2022](https://doi.org/10.1183/13993003.02305-2022)

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6

Respir Med

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. 2022 Dec 28;207:107099.

doi: 10.1016/j.rmed.2022.107099. Online ahead of print.

Evaluating the effect of antidepressants on the relationship between depression and asthma

[Edna Eurídes Theodoro](#)¹, [Daniel Gimenez da Rocha](#)², [Jessica Regina Bertolino](#)³, [Raissa Martins Guinossi](#)⁴, [Monique Olivia Burch](#)⁵, [Cintia Fernanda Bertagni Mingotti](#)⁶, [Renata Pletsch Assunção](#)⁷, [Eduardo Vieira Ponte](#)⁸

Affiliations expand

- PMID: 36584793
- DOI: [10.1016/j.rmed.2022.107099](https://doi.org/10.1016/j.rmed.2022.107099)

Abstract

Background: It is unclear if depression is associated with impaired lung function in subjects with asthma, while few studies evaluated the effect of antidepressants on the relationship between depression and asthma. We designed this study to investigate if subjects with concomitant asthma and depression not taking antidepressants have worse asthma outcomes compared to asthmatic subjects without depression, and to evaluate whether antidepressants modify this association.

Methods: This is a cross-sectional study. We included non-smokers with asthma, 18 years old or above. Study subjects attended an appointment with a chest physician, answered study questionnaires and underwent a spirometry test. We performed crude and adjusted binary logistic regression analyses.

Results: We enrolled 309 subjects with asthma, of whom 48 with depression taking antidepressants, 52 with depression not taking antidepressants, and 209 without depression (control group). Asthmatic subjects with depression who had not used antidepressants before enrollment were more likely to have uncontrolled symptoms of asthma [adjusted OR 3.10, 95CI (1.56-6.15)] and airway obstruction [adjusted OR 2.41, 95CI (1.24-4.69)] compared to the control group. Subjects who had used antidepressants had higher odds of uncontrolled symptoms of asthma [adjusted OR 3.02, 95CI (1.50-6.07)], but similar odds of airway obstruction [adjusted OR 1.24, 95CI (0.87-1.77)] compared to the control group.

Conclusions: Non-treated depression is associated with airway obstruction in subjects with asthma, but antidepressants modify this association. Thus, we recommend regular screening of depression in subjects with asthma, and prescription of antidepressants whenever depression symptoms justify pharmacological therapy.

Keywords: Airway obstruction; Comorbidity; Inhaled corticosteroids; Spirometry.

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Conflict of interest statement

Declaration of competing interest Authors declare no conflict of interest.

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J Allergy Clin Immunol Pract

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. 2022 Dec 26;S2213-2198(22)01325-3.

doi: 10.1016/j.jaip.2022.12.012. Online ahead of print.

Omalizumab in allergic bronchopulmonary aspergillosis (ABPA): A systematic review and meta-analysis

[Meiling Jin](#)¹, [Jo A Douglass](#)², [J Stuart Elborn](#)³, [Ritesh Agarwal](#)⁴, [William J Calhoun](#)⁵, [Slawomir Lazarewicz](#)⁶, [Xavier Jaumont](#)⁶, [Meng Yan](#)⁶

Affiliations expand

- PMID: 36581073
- DOI: [10.1016/j.jaip.2022.12.012](https://doi.org/10.1016/j.jaip.2022.12.012)

Abstract

Background: An unmet clinical need exists in the management of treatment-refractory allergic bronchopulmonary aspergillosis (ABPA). Omalizumab has shown promising effects in case series and cohort studies; however, evidence to support its routine clinical use is lacking.

Objective: The aim of this systematic review and meta-analysis was to evaluate the clinical effectiveness and safety of omalizumab in patients with ABPA.

Methods: A systematic search across standard databases was conducted using specific keywords until May 13, 2021. A meta-analysis was performed to compare the effectiveness (exacerbations, oral corticosteroid [OCS] use, lung function, patient-reported asthma control) and safety of pre- and post- omalizumab treatment. Subgroup analyses were performed for treatment duration and underlying disease.

Results: In total, 49 studies (n=267) were included in the qualitative synthesis and 14 case series (n=186) in the quantitative meta-analysis. Omalizumab treatment significantly reduced the annualized exacerbation rate versus pre-treatment (mean difference [MD]: -2.09 [-3.07; -1.11], $P < 0.01$). There was a reduction in the OCS use (risk difference [RD]: 0.65 [0.46;0.84], $P < 0.01$), an increase in termination of OCS use (RD: 0.53 [0.24;0.82], $P < 0.01$), and a reduction in OCS dose (mg/day) (MD: -14.62 [-19.86; -9.39]; $P < 0.01$) in ABPA patients receiving omalizumab. Omalizumab improved forced expiratory volume in 1 second (FEV1) % predicted by 11.9% (8.2; 15.6, $P < 0.01$) and asthma control, and was well tolerated.

Conclusion: Omalizumab treatment reduced exacerbations and OCS use and improved lung function and asthma control in patients with ABPA and was well tolerated. The results highlight the potential role of omalizumab in the treatment of ABPA.

Keywords: ACT score; allergic bronchopulmonary aspergillosis; asthma; cystic fibrosis; exacerbations; lung function; meta-analysis; omalizumab; oral corticosteroids.

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Association between Electronic Cigarettes Use and Asthma in the United States: Data from the National Health Interview Survey 2016-2019

[Seo Yoon Lee](#)¹, [Jaeyong Shin](#)²

Affiliations expand

- PMID: 36579380
- DOI: [10.3349/ymj.2022.0292](https://doi.org/10.3349/ymj.2022.0292)

Free article

Abstract

Purpose: This article aimed to investigate 1) whether electronic cigarette (EC) users are more likely to experience asthma attacks or emergency room (ER) visits due to asthma than non-users and 2) how age and smoking behaviors moderate the effect size of the association.

Materials and methods: We used National Health Interview Survey data from 2016-2019. Multiple logistic regression analysis was performed to identify the association between current EC use and having an asthma attack and ER visitation due to asthma. Interaction terms were included to explore the moderation effects of age and cigarette smoking status. Subgroup analysis was conducted according to age group.

Results: Of the 218911 participants, 2.0% of them experienced an asthma attack, and 0.5% visited the ER due to asthma. Current EC use was associated with higher odds of having an asthma attack. In interaction analysis, age and smoking status were identified as a moderator in the relationship between EC use and asthma attacks. Participants in their 20s or 30s showed the highest interaction effect.

Conclusion: Our analysis indicates the potential impact of EC use on public health and the moderating effects of smoking behavior.

Keywords: E-cigarette vapor; asthma; cigarette smoking; electronic nicotine delivery systems; public health.

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Conflict of interest statement

The authors have no potential conflicts of interest to disclose.

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Case Reports

Respir Med Case Rep

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. 2022 Dec 13;41:101795.

doi: 10.1016/j.rmcr.2022.101795. eCollection 2023.

Two years follow-up of relapsing eosinophilic pneumonia with concomitant severe asthma successfully treated with

benralizumab: A case report and brief review of the literature

[G Angeletti](#)¹, [M Mazzolini](#)¹, [A Rocca](#)¹

Affiliations expand

- PMID: 36579077
- PMCID: [PMC9791164](#)
- DOI: [10.1016/j.rmcr.2022.101795](#)

Free PMC article

Abstract

Relapsing eosinophilic pneumonia and severe eosinophilic asthma are rare and disabling diseases, which share common inflammatory backgrounds and often require long-term systemic steroid therapy. Benralizumab is a humanized antibody targeting IL-5 receptor that reduces corticosteroid dependence and flares up in severe eosinophilic asthma on long term. In this case report, successful treatment of eosinophilic pneumonia and severe eosinophilic asthma with benralizumab is described after a 2-year follow up, showing the promising results of this therapy for eosinophilic pneumonia management.

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Conflict of interest statement

The authors have no conflict of interest to declare.

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Sci Rep



. 2022 Dec 28;12(1):22476.

doi: 10.1038/s41598-022-26949-7.

A sputum bioassay for airway eosinophilia using an eosinophil peroxidase aptamer

[M Monsur Ali](#)^{#1}, [Michael G Wolfe](#)^{#1}, [Manali Mukherjee](#)^{#2}, [Katherine Radford](#)², [Zil Patel](#)², [Dawn White](#)¹, [Julijana Milojevic](#)¹, [Alfredo Capretta](#)¹, [Parameswaran Nair](#)³, [John D Brennan](#)⁴

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- PMID: 36577785
- PMCID: [PMC9797489](#)
- DOI: [10.1038/s41598-022-26949-7](#)

Free PMC article

Abstract

Eosinophils are granulocytes that play a significant role in the pathogenesis of asthma and other airway diseases. Directing patient treatment based on the level of eosinophilia has been shown to be extremely effective in reducing exacerbations and therefore has tremendous potential as a routine clinical test. Herein, we describe the in vitro selection and optimization of DNA aptamers that bind to eosinophil peroxidase (EPX), a protein biomarker unique to eosinophils. Fifteen rounds of magnetic bead aptamer selection were performed prior to high throughput DNA sequencing. The top 10 aptamer candidates were assessed for EPX binding using a mobility shift assay. This process identified a lead aptamer candidate termed EAP1-05 with low nanomolar affinity and high specificity for EPX over other common sputum proteins. This aptamer sequence was further optimized through truncation and used to develop an easy-to-use colourimetric pull-down assay that can detect EPX over a concentration range from 1 - 100 nM in processed sputum. Forty-six clinical samples were processed using a new sputum dispersal method, appropriate for a

rapid assessment assay, that avoids centrifugation and lengthy processing times. The assay showed 89% sensitivity and 96% specificity to detect eosinophilia (compared to gold standard sputum cytometry), with results being produced in under an hour. This assay could allow for an easy assessment of eosinophil activity in the airway to guide anti-inflammatory therapy for several airway diseases.

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Conflict of interest statement

The authors declare no competing interests.

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

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Thorax

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. 2022 Dec 27;thorax-2022-219642.

doi: 10.1136/thorax-2022-219642. Online ahead of print.

Observational UK cohort study to describe intermittent oral corticosteroid prescribing patterns and their association with adverse outcomes in asthma

[Heath Heatley](#)¹, [Trung N Tran](#)², [Arnaud Bourdin](#)³, [Andrew Menzies-Gow](#)⁴, [David J Jackson](#)⁵, [Ekaterina Maslova](#)⁶, [Jatin Chapaneri](#)⁶, [Derek Skinner](#)¹, [Victoria Carter](#)¹, [Jeffrey Shi Kai Chan](#)¹, [Con Ariti](#)¹, [John Haughney](#)⁷, [David B Price](#)^{8,9}

Affiliations expand

- PMID: 36575040
- DOI: [10.1136/thorax-2022-219642](https://doi.org/10.1136/thorax-2022-219642)

Free article

Abstract

Introduction: Oral corticosteroids (OCS) for asthma are associated with increased risks of developing adverse outcomes (adverse outcomes); no previous study has focused exclusively on intermittent OCS use.

Methods: This historical (2008-2019) UK cohort study using primary care medical records from two anonymised, real-life databases (OPCRD and CPRD) included patients aged ≥ 4 years with asthma receiving only intermittent OCS. Patients were indexed on their first recorded intermittent OCS prescription for asthma and categorised by OCS prescribing patterns: one-off (single), less frequent (≥ 90 day gap) and frequent (< 90 day gap). Non-OCS patients matched 1:1 on gender, age and index date served as controls. The association of OCS prescribing patterns with OCS-related AO risk was studied, stratified by age, Global Initiative for Asthma (GINA) 2020 treatment step, and pre index inhaled corticosteroid (ICS) and short-acting β_2 -agonist (SABA) prescriptions using a multivariable Cox-proportional hazard model.

Findings: Of 476 167 eligible patients, 41.7%, 26.8% and 31.6% had one-off, less frequent and frequent intermittent OCS prescribing patterns, respectively. Risk of any AO increased with increasingly frequent patterns of intermittent OCS versus non-OCS (HR; 95% CI: one-off 1.19 (1.18 to 1.20), less frequent 1.35 (1.34 to 1.36), frequent 1.42 (1.42 to 1.43)), and was consistent across age, GINA treatment step and ICS and SABA subgroups. The highest risks of individual OCS-related adverse outcomes with increasingly frequent OCS were for pneumonia and sleep apnoea.

Conclusion: A considerable proportion of patients with asthma receiving intermittent OCS experienced a frequent prescribing pattern. Increasingly frequent OCS prescribing patterns were associated with higher risk of OCS-related adverse outcomes. Mitigation strategies are needed to minimise intermittent OCS prescription in primary care.

Keywords: Asthma.

Conflict of interest statement

Competing interests: HH, DS, JSKC, CA and VC are employees of Observational and Pragmatic Research Institute Singapore who conducted this study, funded by AstraZeneca. JC, EM and TNT are employees of, and own stock in, AstraZeneca. AB has received consultancy fees and speakers' fees from AstraZeneca, Amgen, Boehringer Ingelheim, Novartis, GlaxoSmithKline, Sanofi Regeneron and Chiesi, and research grants from GlaxoSmithKline, Boehringer Ingelheim and AstraZeneca. AM-G has received grants, advisory board fees, lecture fees and consulting fees from AstraZeneca; advisory board fees from GlaxoSmithKline; advisory board fees and lecture fees from Novartis; advisory board fees, lecture fees and travel expenses from Teva; advisory board fees from Regeneron; advisory board fees, lecture fees and consulting fees from Sanofi. DJJ has received consultancy fees and speakers' fees from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Sanofi Regeneron and Chiesi, and research grants from AstraZeneca. JH reports personal fees from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, Circassia and Teva unrelated to the conduct of the study. DP has advisory board membership with AstraZeneca, Boehringer Ingelheim, Chiesi, Mylan, Novartis, Regeneron Pharmaceuticals, Sanofi Genzyme, Thermofisher; consultancy agreements with Airway Vista Secretariat, AstraZeneca, Boehringer Ingelheim, Chiesi, EPG Communication Holdings Ltd, FIECON Ltd, Fieldwork International, GlaxoSmithKline, Mylan, Mundipharma, Novartis, OM Pharma SA, PeerVoice, Phadia AB, Spirosure Inc, Strategic North Limited, Synapse Research Management Partners S.L., Talos Health Solutions, Theravance and WebMD Global LLC; grants and unrestricted funding for investigator-initiated studies (conducted through Observational and Pragmatic Research Institute Pte Ltd) from AstraZeneca, Boehringer Ingelheim, Chiesi, Mylan, Novartis, Regeneron Pharmaceuticals, Respiratory Effectiveness Group, Sanofi Genzyme, Theravance and UK National Health Service; payment for lectures/speaking engagements from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, GlaxoSmithKline, Kyorin, Mylan, Mundipharma, Novartis, Regeneron Pharmaceuticals and Sanofi Genzyme; payment for travel/accommodation/meeting expenses from AstraZeneca, Boehringer Ingelheim, Mundipharma, Mylan, Novartis, Thermofisher; stock/stock options from AKL Research and Development Ltd which produces phytopharmaceuticals; owns 74% of the social enterprise Optimum Patient Care Ltd (Australia and UK) and 92.61% of Observational and Pragmatic Research Institute Pte Ltd (Singapore); 5% shareholding in Timestamp which develops adherence monitoring technology; is peer reviewer for grant committees of the UK Efficacy and Mechanism Evaluation programme, and Health Technology Assessment; and was an expert witness for GlaxoSmithKline.

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Life Sci Alliance



. 2022 Dec 27;6(3):e202201609.

doi: 10.26508/lsa.202201609. Print 2023 Mar.

De novo discovery of traits co-occurring with chronic obstructive pulmonary disease

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Affiliations expand

- PMID: 36574990
- PMCID: [PMC9795035](#)
- DOI: [10.26508/lsa.202201609](#)

Free PMC article

Abstract

Chronic obstructive pulmonary disease (COPD) is a heterogeneous group of chronic lung conditions. Genome-wide association studies have identified single-nucleotide polymorphisms (SNPs) associated with COPD and the co-occurring conditions, suggesting common biological mechanisms underlying COPD and these co-occurring conditions. To identify them, we have integrated information across different biological levels (i.e., genetic variants, lung-specific 3D genome structure, gene expression and protein-protein interactions) to build lung-specific gene regulatory and protein-protein interaction networks. We have queried these networks using disease-associated SNPs for COPD, unipolar depression and coronary artery disease. COPD-associated SNPs can control genes involved in the regulation of lung or pulmonary function, asthma, brain region volumes, cortical surface area, depressed affect, neuroticism, Parkinson's disease, white matter microstructure and smoking behaviour. We describe the regulatory connections, genes and biochemical pathways that underlay these co-occurring trait-SNP-gene associations. Collectively, our findings provide new avenues for the investigation of the underlying

biology and diverse clinical presentations of COPD. In so doing, we identify a collection of genetic variants and genes that may aid COPD patient stratification and treatment.

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Conflict of interest statement

The authors declare that they have no conflict of interest.

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Pediatr Pulmonol

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. 2022 Dec 27.

doi: 10.1002/ppul.26295. Online ahead of print.

Pediatric pulmonology 2021 year in review: Asthma

[Nicole Stephenson](#)¹, [Ceila E Loughlin](#)¹

Affiliations expand

- PMID: 36573469

- DOI: [10.1002/ppul.26295](https://doi.org/10.1002/ppul.26295)

Abstract

Asthma is the most common chronic disease in children, affecting an estimated 6.1 million children in the United States. SARS-CoV2 had a significant impact on asthma exacerbations and healthcare utilization of patients with asthma in 2021. Additionally, studies in 2021 influenced the field of asthma with improvements in diagnostic testing and monitoring, treatment of severe exacerbations, social determinants of health, and evaluation of medical costs. This article is part of our 2021 "Year in Review" series, in which we summarize publications in major pulmonary topics, in the context of selected literature from other journals relevant to our discipline.

Keywords: 2021; YIR; asthma; childhood; pediatric.

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Respir Res

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. 2022 Dec 26;23(1):378.

doi: 10.1186/s12931-022-02304-2.

[Gene network analysis for identification of microRNA biomarkers for asthma](#)

Affiliations expand

- PMID: 36572876
- PMCID: [PMC9793650](#)
- DOI: [10.1186/s12931-022-02304-2](#)

Free PMC article

Abstract

Background: To date, reliable biomarkers for asthma have not been identified. MicroRNAs (miRNAs) are small, non-coding RNAs that negatively regulate post-transcriptional gene expression, and they are involved in various diseases, including asthma. MiRNAs may serve as ideal biomarkers due to their ability to regulate multiple pathways. This study aims to identify miRNA biomarker signatures for asthma.

Methods: We used the house dust mite (HDM) mouse model of allergic inflammation. Mice were phenotyped by assessing lung function, allergic response, airway inflammation, and remodeling. The miRNA signature profiles in serum and lung tissue were determined by small RNA sequencing, and data were analyzed using Qiagen CLC Genomics Workbench. To identify relevant gene targets, we performed mRNA sequencing, followed by miRNA-targets analysis. These miRNAs and targets were subject to subsequent pathway and functional analyses.

Results: Mice exposed to HDM developed phenotypic features of allergic asthma. miRNA sequencing analysis showed that 213 miRNAs were substantially dysregulated (FDR p-value < 0.05 and fold change expression > + 1.5 and < - 1.5) in the lung of HDM mice relative to the control mice. In contrast, only one miRNA (miR-146b-5p) was significantly increased in serum. Target analysis of lung dysregulated miRNAs revealed a total of 131 miRNAs targeting 211 mRNAs. Pathway analysis showed T helper 2/1 (Th2/Th1) as the top significantly activated signaling pathway associated with the dysregulated miRNAs. The top enriched diseases were inflammatory response and disease, which included asthma. Asthma network analysis indicated that 113 of 131 miRNAs were directly associated with asthma pathogenesis.

Conclusions: These findings suggest that most dysregulated miRNAs in the HDM model were associated with asthma pathogenesis via Th2 signaling. We identified a panel of 30 miRNAs as potential biomarker candidates for asthma.

Keywords: Asthma; Biomarker; HDM mouse model; microRNA.

Conflict of interest statement

The authors have no competing or financial interests to declare.

- [45 references](#)
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15

Review

Respir Care

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. 2023 Jan;68(1):114-128.

doi: 10.4187/respcare.10254.

Comparison of National and Global Asthma Management Guiding Documents

[Joyce A Baker](#)¹, [Paul R Houin](#)^{2 3}

Affiliations expand

- PMID: 36566032
- DOI: [10.4187/respcare.10254](https://doi.org/10.4187/respcare.10254)

Abstract

Asthma is a common chronic disease that affects both adults and children, and that continues to have a high economic burden. Asthma management guidelines were first developed nearly 30 years ago to standardize care, maintain asthma control, improve quality of life, maintain normal lung function, prevent exacerbations, and prevent asthma mortality. The two most common asthma guidelines used today were developed by the National Asthma Education and Prevention Program (NAEPP) Expert Panel Working Group and the Global Initiative for Asthma Science Committee. Both guiding documents use scientific methodology to standardize their approach for formulating recommendations based on pertinent literature. Before the 2020 National Asthma Education and Prevention Program (Expert Panel Report 4), nothing had been released since the 2007 guidelines, whereas the Global Initiative for Asthma publishes updates annually. Although each of these asthma strategies is similar, there are some noted differences. Over the years, the focus of asthma treatment has shifted from acute to chronic management. Frontline respiratory therapists and other health-care providers should have a good understanding of these 2 guiding references and how they can impact acute and chronic asthma management. The primary focus of this narrative is to look at the similarities and differences of these 2 guiding documents as they pertain to the 6 key questions identified by the Expert Panel of the National Asthma Education and Prevention Program.

Keywords: Acute disease; Asthma; Chronic disease; Guidelines; Medications; Patient care management.

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Conflict of interest statement

The authors have disclosed no conflicts of interest.

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Review

Respir Med

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. 2023 Jan;206:107067.

doi: 10.1016/j.rmed.2022.107067. Epub 2022 Dec 9.

The clinical features of asthma exacerbations in early-onset and eosinophilic late-onset asthma may differ significantly

[Thomas Rothe](#)¹, [Christophe von Garnier](#)², [Pierre-Olivier Bridevaux](#)³, [Florian Charbonnier](#)⁴, [Christian Clarenbach](#)⁵, [Pietro Gianella](#)⁶, [Anja Jochmann](#)⁷, [Lukas Kern](#)⁸, [Pavlov Nikolay](#)⁹, [Claudia Steurer-Stey](#)¹⁰, [Joerg D Leuppi](#)¹¹, [members of the SIG Obstructive Lung Diseases of the Swiss Society of Pneumology](#)

Affiliations expand

- PMID: 36563609
- DOI: [10.1016/j.rmed.2022.107067](https://doi.org/10.1016/j.rmed.2022.107067)

Free article

Abstract

Over 20 years ago, the concept of asthma control was created and appropriate measurement tools were developed and validated. Loss of asthma control can lead to an exacerbation. Years ago, the term "clinically significant asthma exacerbation" was introduced to define when a loss of control is severe enough to declare it an asthma exacerbation. This term is also used by health insurances to determine when an exacerbation is eligible for reimbursement of biologics in clinical practice, however, it sometimes becomes apparent that a clear separation between loss of "asthma control" and an exacerbation is not always possible. In this review, we attempt to justify why exacerbations in early allergic asthma and adult eosinophilic asthma can differ significantly and why this is important in clinical practice as well as when dealing with health insurers.

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Review

Eur Respir Rev



. 2022 Dec 21;31(166):220134.

doi: 10.1183/16000617.0134-2022. Print 2022 Dec 31.

[Role of autophagy in lung diseases and ageing](#)

[Yan Zhang](#)¹, [Jin Zhang](#)¹, [Zhiling Fu](#)²

Affiliations expand

- PMID: 36543345
- DOI: [10.1183/16000617.0134-2022](https://doi.org/10.1183/16000617.0134-2022)

Free article

Abstract

The lungs face ongoing chemical, mechanical, biological, immunological and xenobiotic stresses over a lifetime. Advancing age progressively impairs lung function. Autophagy is a "housekeeping" survival strategy involved in numerous physiological and pathological processes in all eukaryotic cells. Autophagic activity decreases with age in several species,

whereas its basic activity extends throughout the lifespan of most animals. Dysregulation of autophagy has been proven to be closely related to the pathogenesis of several ageing-related pulmonary diseases. This review summarises the role of autophagy in the pathogenesis of pulmonary diseases associated with or occurring in the context of ageing, including acute lung injury, chronic obstructive pulmonary disease, asthma and pulmonary fibrosis, and describes its potential as a therapeutic target.

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Conflict of interest statement

Conflicts of interest: The authors declare no conflict of interest.

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Respir Med



. 2023 Jan;206:107089.

doi: 10.1016/j.rmed.2022.107089. Epub 2022 Dec 12.

Association of serum CC16 levels with eosinophilic inflammation and respiratory dysfunction in severe asthma

[Houman Goudarzi](#)¹, [Hirokazu Kimura](#)², [Hiroki Kimura](#)², [Hironi Makita](#)², [Michiko Takimoto-Sato](#)², [Yuki Abe](#)², [Akira Oguma](#)², [Munehiro Matsumoto](#)², [Nozomu Takei](#)², [Machiko Matsumoto-Sasaki](#)², [Kaoruko Shimizu](#)², [Masaru Suzuki](#)², [Noriharu Shijubo](#)³, [Shau-Ku Huang](#)⁴, [Nobuyuki Hizawa](#)⁵, [Masaharu Nishimura](#)², [Satoshi Konno](#)²

Affiliations expand

- PMID: 36542961
- DOI: [10.1016/j.rmed.2022.107089](https://doi.org/10.1016/j.rmed.2022.107089)

Abstract

Background: There are knowledge gaps in the potential role of Club cell 16-kDa secretory protein (CC16) in severe asthma phenotypes and type 2 inflammation, as well as the longitudinal effect of CC16 on pulmonary function tests and exacerbation risk in epidemiological studies.

Objective and methods: To assess whether serum CC16 is associated with eosinophilic inflammation in patients with severe asthma. We also examined the effect of this protein on the annual decline in forced expiratory volume in the first second (FEV₁) and the risk of exacerbation using a longitudinal approach. We recruited 127 patients with severe asthma from 30 hospitals/pulmonary clinics in Hokkaido, Japan. The least square means and standard error were calculated for T-helper 2 (Th2) biomarkers and pulmonary function test across CC16 tertiles at baseline. We did the same for asthma exacerbation and annual decline in FEV₁ with 3 and 5 years' follow-up, respectively.

Results: We found that serum CC16 was inversely associated with sputum eosinophils and blood periostin in a dose-response manner. Baseline CC16 and FEV₁/forced vital capacity ratio were positively associated in adjusted models (p for trend = 0.008). Patients with the lowest tertile of serum CC16 levels at baseline had a -14.3 mL decline in FEV₁ than those with the highest tertile over 5 years of follow-up (p for trend = 0.031, fully adjusted model). We did not find any association of CC16 with exacerbation risk.

Conclusion: Patients with severe asthma with lower circulatory CC16 had enhanced eosinophilic inflammation with rapid FEV₁ decline over time.

Keywords: CC16; Eosinophilic inflammation; Periostin; Respiratory function; Severe asthma; Sputum eosinophils; T-helper 2 biomarkers.

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Conflict of interest statement

Declaration of competing interest None to declare.

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Case Reports

Respirol Case Rep



. 2022 Dec 15;11(1):e01074.

doi: 10.1002/rcr2.1074. eCollection 2023 Jan.

Successful treatment with dupilumab for mucus plugs in severe asthma

[Moriyasu Anai](#)¹, [Chieko Yoshida](#)¹, [Hiroki Izumi](#)¹, [Kei Muramoto](#)¹, [Koichi Saruwatari](#)¹, [Yusuke Tomita](#)¹, [Hidenori Ichiyasu](#)¹, [Takuro Sakagami](#)¹

Affiliations expand

- PMID: 36540290
- PMCID: [PMC9752256](#)
- DOI: [10.1002/rcr2.1074](#)

Free PMC article

Abstract

A 29-year-old man presented to our hospital with severe eosinophilic asthma. He needed a short OCS burst for exacerbation of asthma once every 1 or 2 months, although he used a high dose of inhaled corticosteroids and a long-acting beta-2 agonists. Chest CT showed multiple mucous plugs with bronchiectasis, but further examination found that he did not meet the diagnostic criteria for allergic bronchopulmonary aspergillosis. After starting

dupilumab for his severe eosinophilic asthma, his asthma control improved without exacerbation. Furthermore, most mucus plugs disappeared on chest CT after 16 weeks from initiating dupilumab. This case suggests that dupilumab may be an effective treatment against mucus plugs associated with severe eosinophilic asthma.

Keywords: dupilumab; mucus plugs; severe asthma.

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Conflict of interest statement

None declared.

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Case Reports

Respir Med Case Rep

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. 2022 Dec 6;41:101789.

doi: 10.1016/j.rmcr.2022.101789. eCollection 2023.

Use of point-of-care ultrasound by internists to rapidly diagnose acute decompensated heart failure

[Nancy L Hagood](#)¹, [Marc Heincelman](#)¹, [Meghan K Thomas](#)¹

Affiliations expand

- PMID: 36530864
- PMCID: [PMC9747626](#)
- DOI: [10.1016/j.rmcr.2022.101789](#)

Free PMC article

Abstract

Dyspnea is a common presenting complaint seen by hospitalists. The differential is broad, including life-threatening and less urgent etiologies. We report a 43-year-old male presenting to an inpatient medicine service with dyspnea in the setting of asthma, tobacco and occupational exposures, and no prior cardiac history. Use of point-of-care ultrasound (POCUS) immediately confirmed diagnosis of acute decompensated heart failure, allowing prompt decision making and care. Use of POCUS is widespread among emergency physicians and intensivists; however, use among medical students, internal medicine residents, and hospitalists remains variable. Increased use of POCUS by hospitalists may increase speed and accuracy of diagnosis.

Keywords: Cardiac ultrasound; Left heart dysfunction; Lung ultrasound; Pulmonary edema.

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Conflict of interest statement

Please check the following as appropriate: All authors have participated in (a) conception and design, or analysis and interpretation of the data; (b) drafting the article or revising it critically for important intellectual content; and (c) approval of the final version. This manuscript has not been submitted to, nor is under review at, another journal or other publishing venue. The authors have no affiliation with any organization with a direct or indirect financial interest in the subject matter discussed in the manuscript. The following authors have affiliations with organizations with direct or indirect financial interest in the subject matter discussed in the manuscript:

- [19 references](#)

- [4 figures](#)

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Ann Epidemiol

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. 2023 Jan;77:90-97.

doi: 10.1016/j.annepidem.2022.11.009. Epub 2022 Dec 5.

Parental occupational exposures prior to conception and offspring wheeze and eczema during first year of life

[Felix Forster](#)¹, [Christian Heumann](#)², [Bianca Schaub](#)³, [Andreas Böck](#)⁴, [Dennis Nowak](#)⁵, [Christian Vogelberg](#)⁶, [Katja Radon](#)⁵

Affiliations [expand](#)

- PMID: 36476404
- DOI: [10.1016/j.annepidem.2022.11.009](https://doi.org/10.1016/j.annepidem.2022.11.009)

Abstract

Purpose: Parental exposures prior to conception might influence asthma and allergy risk in offspring. As occupational exposures are established risk factors for asthma and allergies, we investigated if parental occupational exposures prior to conception cause wheeze and eczema in offspring during the first year of life.

Methods: We analysed data of 436 families from an offspring cohort based on a follow-up study of German participants of the International Study of Asthma and Allergies in Childhood (ISAAC). Offspring cohort data was collected between 2009 and 2019. Occupational exposures were based on participants' work histories and measured by a Job-Exposure-Matrix. We used Bayesian logistic regression models for analysis. Inference and confounder selection were based on directed acyclic graphs.

Results: In mothers, for both allergic and irritative occupational exposures prior to conception suggestive effects on offspring eczema during the first year of life were found (allergens: odds ratio (OR) 1.22, 95% compatibility interval (CI) 0.92-1.57; irritants: OR 1.36, 95% CI 0.99-1.77), while no relation with wheeze was suggested.

Conclusions: Our results suggest that reduction of asthma-related occupational exposures might not only reduce the burden of disease for occupationally induced or aggravated asthma and allergies in employees but also in their children.

Keywords: Asthma; Dermatitis, atopic; Maternal exposure; Occupational exposure; Paternal exposure.

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J Appl Physiol (1985)

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. 2023 Jan 1;134(1):142-146.

doi: 10.1152/jappphysiol.00491.2022. Epub 2022 Dec 8.

Differences in respiratory oscillometry measurements using mouthpiece, mouth, and nasal mask in healthy adults

[Malak Alshlowi](#)¹, [Ali Hakizimana](#)^{1,2}, [Afnan Alraimi](#)¹, [Pooja Devani](#)^{1,2}, [Lennart K A Lundblad](#)³, [Caroline S Beardsmore](#)^{1,2}, [Erol A Gaillard](#)^{1,2}

Affiliations expand

- PMID: 36476160
- DOI: [10.1152/japplphysiol.00491.2022](https://doi.org/10.1152/japplphysiol.00491.2022)

Abstract

Airway resistance measurements using oscillometry provide a potential alternative to spirometry in assessing airway obstruction and dynamics due to measurements taken during tidal breathing. Oscillometry typically requires participants to form a tight seal around a mouthpiece that can prove challenging for some people. To address this challenge, we conducted a prospective study to evaluate the effect of different interfaces like mouthpiece, mouth mask, and nasal mask on respiratory impedance results from oscillometry in a cohort of healthy adults. Ten healthy adults [7 females; mean age: 38.9 yr (SD \pm 15.5)] underwent oscillometry using each of the three interfaces. We measured resistance at 5 Hz (R_{rs5}), frequency dependence of resistance at 5-20 Hz (R_{rs5-20}), and reactance area (A_x). R_{rs5} was not different when using the mouthpiece compared with the mouth mask [mean 2.98 cmH₂O/L/s (SD \pm 0.68) vs. mean 3.2 cmH₂O/L/s (SD \pm 0.81); P = 0.92; 95% CI -0.82 to +0.38], respectively. Nasal mask R_{rs5} measurements were significantly higher than mouthpiece measurements (mean 7.31 cmH₂O/L/s; SD \pm 2.62; P < 0.01; 95%CI -6.91 to -1.75). With A_{x5} , we found a mean of 4.01 cmH₂O/L (SD \pm 2.04) with the mouth mask compared with a mean of 4.02 cmH₂O/L (SD \pm 1.87; P = 1.0 95% CI -1.86 to +1.87) for the mouthpiece, however, we found a significant difference between the mouthpiece and nasal mask for A_x (mean = 10.71; SD \pm 7.0 H₂O/L; P = 0.04, 95% CI -12.96 to -0.43). Our findings show that oscillometry using a mouth mask may be just as effective as using a mouthpiece in assessing airway dynamics and resistance. **NEW & NOTEWORTHY** This is the first study to compare the use of different interfaces: mouthpiece, mouth mask, and nasal mask, for oscillometry in an adult population. We report that using a mouth mask in oscillometry may provide a valid alternative to a mouthpiece in cohorts who may struggle to form the required tight seal that is typically required in oscillometry or spirometry.

Keywords: airway resistance; asthma; lung function; wheeze.

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MeSH terms, Grant supportexpand

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Review

Curr Opin Pulm Med

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. 2023 Jan 1;29(1):43-46.

doi: 10.1097/MCP.0000000000000927. Epub 2022 Nov 7.

Bronchial thermoplasty for the treatment of severe persistent asthma

[Arnaldo Abraham Rodriguez](#)¹, [Dorys Chavez](#), [Sadia Benzaquen](#)

Affiliations expand

- PMID: 36474463
- DOI: [10.1097/MCP.0000000000000927](https://doi.org/10.1097/MCP.0000000000000927)

Abstract

Purpose of review: Severe asthma is associated with frequent hospital visits and impact in quality of life as well as healthcare associated costs. Limited treatment modalities exist to assist in reduction of frequent exacerbations in patients with severe asthma who are already on maximum inhaler therapy. As supporting data becomes more robust, novel treatments have gained attention such as bronchial thermoplasty and immune-directed therapies.

Recent findings: Based on review of recent studies, bronchial thermoplasty poses itself as a potential intervention for severe asthma, demonstrating a decrease in asthma exacerbations with long term clinical effect and safety profile at the expense of temporary uncontrolled asthma symptoms for the first six weeks following the procedure.

Summary: In select patients with severe asthma, bronchial thermoplasty is a well tolerated and effective treatment to reduce asthma exacerbation.

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Publication types, MeSH termsexpand

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Case Reports

Respir Med Case Rep

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. 2022 Nov 28;41:101785.

doi: 10.1016/j.rmcr.2022.101785. eCollection 2023.

Successful and safe treatment of severe steroid depended eosinophilic asthma with mepolizumab in a woman during pregnancy

Affiliations expand

- PMID: 36466584
- PMCID: [PMC9712986](#)
- DOI: [10.1016/j.rmcr.2022.101785](#)

Free PMC article

Abstract

A 26-year-old female with steroid dependent eosinophilic asthma and nasal polyps who had successfully been treated with mepolizumab for 17 consecutive months with complete steroid withdrawal and symptoms control, stopped biologic treatment due to pregnancy efforts. Mepolizumab discontinuation resulted in frequent exacerbations and daily symptoms despite high dose ICS/LABA and re-initiation of oral steroids. Mepolizumab was initiated again, followed by improvement of asthma control and gradual withdrawal of steroids within 2 months. The patient became pregnant during the fourth month of mepolizumab re-initiation. The patient presented two asthma exacerbations during pregnancy treated with short course (3 days) oral steroids and delivery was uneventful (female, Apgar 9, weight 2750 g, length 59 cm) in week 40 by caesarean section.

Keywords: ACT, Asthma Control Score; Asthma; FEV1, Forced Expiratory Volume in 1 second; ICS, Inhaled Corticosteroids; LABA, Long-Acting Beta-Agonists; LAMA, Long-Acting Muscarinic Antagonists; Mepolizumab; OCS, Oral Corticosteroids; Pregnancy.

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Conflict of interest statement

The authors whose names are listed immediately below certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript. Author names: Stylianios K. Vittorakis, Georgia Giannakopoulou, Konstantinos Samitas, Eleftherios Zervas

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Respir Med



. 2023 Jan;206:107058.

doi: 10.1016/j.rmed.2022.107058. Epub 2022 Nov 26.

Efficacy and safety of dupilumab as add-on therapy for patients with severe asthma: A real-world Dutch cohort study

[John C Thelen](#)¹, [Cathelijne M van Zelst](#)², [Sigrid E van Brummelen](#)³, [Simone Rauh](#)⁴, [Johannes C C M In 't Veen](#)³, [Jasper H Kappen](#)³, [Gert-Jan Braunstahl](#)⁵

Affiliations expand

- PMID: 36462399
- DOI: [10.1016/j.rmed.2022.107058](https://doi.org/10.1016/j.rmed.2022.107058)

Abstract

Background: Dupilumab as add-on treatment for severe uncontrolled asthma (SA) has shown to be effective and safe by phase-III-trials. Real-world data on clinical efficacy and safety is limited.

Objective: We aim to investigate the efficacy and safety of dupilumab as add-on therapy for SA in a real-world cohort.

Material and methods: The primary endpoint was annually exacerbation-rate (AER). Secondary outcomes were maintenance oral corticosteroid (mOCS) dependency, asthma control (ACQ-5), pulmonary function (FEV₁), quality of life (AQLQ) and frequency of reported adverse events (AEs).

Results: Overall, 148 patients were included. Median AER [IQR] reduced from 4.00 [2.00-5.00] at baseline to 1.00 [0.00-2.00] at 12 months ($p < 0.001$). mOCS-dependency reduced from 39.9% of the patients at baseline, to 20.3% at 6 months and to 14.9% at 12 months ($p < 0.001$). Median ACQ improved from 3.00 [2.00-3.80] at baseline to 1.80 [0.60-2.95] after 6 months and to 1.40 [0.20-2.60] after 12 months ($p < 0.001$). Median FEV₁ (L) improved from 2.21 [1.58-2.85] to 2.50 [2.00-3.06] at 6 months and to 2.51 [1.88-3.04] after 12 months ($p < 0.001$). The outcomes improved most in subgroups with high eosinophils ($\geq 300/\mu\text{L}$) or FeNO (≥ 50 ppb) at baseline. AEs were reported by 45.3% (67/148), of which headache was most frequent.

Conclusions: This study indicates that dupilumab as add-on therapy for SA is associated with significant improvements in exacerbation-rate, mOCS-dependency, asthma control, pulmonary function, and quality of life. These results are in line with those of previous phase-III-trials.

Keywords: Asthma exacerbation; Dupilumab; Real life; Severe asthma; T2-inflammation.

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J Asthma

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. 2022 Dec 30;1-12.

doi: 10.1080/02770903.2022.2155189. Online ahead of print.

Dexamethasone versus prednisone/prednisolone in the management of pediatric patients with acute asthmatic exacerbations: a systematic review and meta-analysis

[Elise Dahan](#)^{1,2}, [Nour El Ghazal](#)^{1,2}, [Hayato Nakanishi](#)^{1,2}, [Joe El Haddad](#)^{1,2}, [Reem H Matar](#)^{1,2,3}, [Danijel Tosovic](#)⁴, [Azizullah Beran](#)⁵, [Christian A Than](#)^{1,2,4}, [David Stiasny](#)⁶

Affiliations expand

- PMID: 36461938
- DOI: [10.1080/02770903.2022.2155189](https://doi.org/10.1080/02770903.2022.2155189)

Abstract

Objective: Acute asthmatic exacerbation is a common condition for pediatric emergency visits. Recently, dexamethasone has increasingly been used as an alternative to prednisone. This study aimed to evaluate the safety and efficacy of dexamethasone (DEX) against prednisone/prednisolone (PRED) in managing pediatric patients with acute asthmatic exacerbation.

Data sources: Cochrane, Embase, PubMed, Scopus, and Web of Science were searched for articles from their inception to August 2022 by two independent reviewers using the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) system. The review was registered prospectively with PROSPERO (CRD42022353462).

Study selections: From 316 studies screened, seventeen studies met the eligibility criteria, with 5967 pediatric patients experiencing an asthma exacerbation requiring treatment with either DEX ($n = 2865$) or PRED ($n = 3102$). Baseline patient characteristics (age, sex, PRAM (pediatric respiratory assessment measure), previous corticosteroid and beta-agonist inhaler) were comparable between groups.

Results: After treatment administration, the DEX group had fewer vomiting incidents (OR = 0.24, 95% CI: 0.11, 0.51, $I^2 = 58\%$) and reduced noncompliance events (OR = 0.12, 95% CI: 0.04, 0.34, $I^2 = 0\%$) when compared to the PRED group. Regarding emergency-department (ED)-related outcomes, there were no differences in hospital admission rates (OR = 0.83, 95% CI: 0.58, 1.19, $I^2 = 15\%$), time spent in the ED (MD = -0.11 h, 95% CI: -0.52; 0.30, $I^2 = 82\%$) or relapse occurrences (OR = 0.67, 95% CI: 0.30, 1.49, $I^2 = 52\%$) between both groups.

Conclusion: Although there were no differences between the DEX and PRED groups in terms of hospital admission rates, time spent in the ED or relapse events, pediatric patients receiving DEX experienced lower noncompliance and vomiting rates.

Keywords: Meta-analysis; asthma; dexamethasone; pediatric; prednisolone; prednisone.

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J Asthma



. 2022 Dec 30;1-8.

doi: 10.1080/02770903.2022.2155187. Online ahead of print.

Role of high-sensitivity C-reactive protein (hs-CRP) in assessment of asthma control in children

[Arvind Kumar](#)¹, [Kana Ram Jat](#)¹, [Jhuma Sankar](#)¹, [R Lakshmy](#)², [Rakesh Lodha](#)¹, [S K Kabra](#)¹

Affiliations expand

- PMID: 36461906
- DOI: [10.1080/02770903.2022.2155187](https://doi.org/10.1080/02770903.2022.2155187)

Abstract

Introduction: Data are scarce on hs-CRP as a biomarker for airway inflammation in pediatric asthma. We aimed to examine correlation between hs-CRP and asthma control levels.

Methods: Children with physician-diagnosed asthma, ages 6-15 years, were enrolled. GINA-2016 criteria were used to assess the level of asthma control. The relationships between serum hs-CRP and each of asthma control measures (asthma control criteria, spirometry, impulse oscillometry, eosinophil counts and fractional exhaled nitric oxide (FeNO) were assessed.

Results: 150 asthmatic children were enrolled; 52 (35%) had well controlled asthma, 76 (51%), and 22 (14%) children had partly controlled and uncontrolled asthma, respectively. Median (IQR) values of hs-CRP were 0.47 (0.1, 1.67) mg/L in well controlled, 0.30 (0.1, 1.83) mg/L in partly controlled, and 2.74 (0.55, 3.74) mg/L in uncontrolled asthma ($p = 0.029$). Using receiver operator characteristic (ROC) curve analysis, area under the curve for hs-CRP (mg/L) to discriminate between uncontrolled and (controlled + partly controlled) asthma was 0.67 (95% CI 0.55, 0.80) and a cutoff 1.1 mg/L of serum hs-CRP level had a sensitivity of 68.1% with specificity of 67.97%. In two groups of hs-CRP (<3 mg/L) and hs-CRP (≥ 3 mg/L), high hs-CRP group had higher proportion of uncontrolled asthmatic children ($p = 0.03$).

Conclusion: We observed higher serum hs-CRP values in children with uncontrolled asthma, suggesting its potential role as a biomarker of asthma control.

Keywords: Absolute eosinophil count; FeNO; hs-CRP; level of asthma control; spirometry.

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Lancet Digit Health



. 2023 Jan;5(1):e16-e27.

doi: 10.1016/S2589-7500(22)00187-X. Epub 2022 Nov 29.

Identifying and visualising multimorbidity and comorbidity patterns in patients in

the English National Health Service: a population-based study

[Valerie Kuan](#)¹, [Spiros Denaxas](#)², [Praveetha Patalay](#)³, [Dorothea Nitsch](#)⁴, [Rohini Mathur](#)⁵, [Arturo Gonzalez-Izquierdo](#)⁶, [Reecha Sofat](#)⁷, [Linda Partridge](#)⁸, [Amanda Roberts](#)⁹, [Ian C K Wong](#)¹⁰, [Melanie Hingorani](#)¹¹, [Nishi Chaturvedi](#)¹², [Harry Hemingway](#)¹³, [Aroon D Hingorani](#)¹⁴, [Multimorbidity Mechanism and Therapeutic Research Collaborative \(MMTRC\)](#)

Collaborators, Affiliations expand

- PMID: 36460578
- DOI: [10.1016/S2589-7500\(22\)00187-X](https://doi.org/10.1016/S2589-7500(22)00187-X)

Free article

Abstract

Background: Globally, there is a paucity of multimorbidity and comorbidity data, especially for minority ethnic groups and younger people. We estimated the frequency of common disease combinations and identified non-random disease associations for all ages in a multiethnic population.

Methods: In this population-based study, we examined multimorbidity and comorbidity patterns stratified by ethnicity or race, sex, and age for 308 health conditions using electronic health records from individuals included on the Clinical Practice Research Datalink linked with the Hospital Episode Statistics admitted patient care dataset in England. We included individuals who were older than 1 year and who had been registered for at least 1 year in a participating general practice during the study period (between April 1, 2010, and March 31, 2015). We identified the most common combinations of conditions and comorbidities for index conditions. We defined comorbidity as the accumulation of additional conditions to an index condition over an individual's lifetime. We used network analysis to identify conditions that co-occurred more often than expected by chance. We developed online interactive tools to explore multimorbidity and comorbidity patterns overall and by subgroup based on ethnicity, sex, and age.

Findings: We collected data for 3 872 451 eligible patients, of whom 1 955 700 (50.5%) were women and girls, 1 916 751 (49.5%) were men and boys, 2 666 234 (68.9%) were White, 155 435 (4.0%) were south Asian, and 98 815 (2.6%) were Black. We found that a higher proportion of boys aged 1-9 years (132 506 [47.8%] of 277 158) had two or more diagnosed conditions than did girls in the same age group (106 982 [40.3%] of 265 179), but more women and girls were diagnosed with multimorbidity than were boys aged 10 years and older and men (1 361 232 [80.5%] of 1 690 521 vs 1 161 308 [70.8%] of 1 639 593). White individuals (2 097 536 [78.7%] of 2 666 234) were more likely to be diagnosed with two or more conditions than were Black (59 339 [60.1%] of 98 815) or south Asian

individuals (93 617 [60.2%] of 155 435). Depression commonly co-occurred with anxiety, migraine, obesity, atopic conditions, deafness, soft-tissue disorders, and gastrointestinal disorders across all subgroups. Heart failure often co-occurred with hypertension, atrial fibrillation, osteoarthritis, stable angina, myocardial infarction, chronic kidney disease, type 2 diabetes, and chronic obstructive pulmonary disease. Spinal fractures were most strongly non-randomly associated with malignancy in Black individuals, but with osteoporosis in White individuals. Hypertension was most strongly associated with kidney disorders in those aged 20-29 years, but with dyslipidaemia, obesity, and type 2 diabetes in individuals aged 40 years and older. Breast cancer was associated with different comorbidities in individuals from different ethnic groups. Asthma was associated with different comorbidities between males and females. Bipolar disorder was associated with different comorbidities in younger age groups compared with older age groups.

Interpretation: Our findings and interactive online tools are a resource for: patients and their clinicians, to prevent and detect comorbid conditions; research funders and policy makers, to redesign service provision, training priorities, and guideline development; and biomedical researchers and manufacturers of medicines, to provide leads for research into common or sequential pathways of disease and inform the design of clinical trials.

Funding: UK Research and Innovation, Medical Research Council, National Institute for Health and Care Research, Department of Health and Social Care, Wellcome Trust, British Heart Foundation, and The Alan Turing Institute.

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Conflict of interest statement

Declaration of interests DN is the UK Kidney Association Director of Informatics Research based at the UK Renal Registry and is on the steering committee for two GlaxoSmithKline-funded studies looking at kidney function markers in sub-Saharan Africa. ICKW was a member of the ISAC of CPRD and has received funding from Amgen, Bristol-Myers Squibb, Pfizer, Janssen, Bayer, GSK, and Novartis to conduct pharmacoepidemiological research outside the submitted work. RM has received consulting fees from Amgen. ADH is a co-investigator on a grant from Pfizer to identify potential therapeutic targets for heart failure using human genomics. NC is remunerated for her membership of a data safety and monitoring committee of a trial sponsored by AstraZeneca. All other authors declare no competing interests.

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Respir Med

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. 2023 Jan;206:107059.

doi: 10.1016/j.rmed.2022.107059. Epub 2022 Nov 26.

Computed tomographic airway morphology after targeted lung denervation treatment in COPD

[Jorine E Hartman](#)¹, [Felix J F Herth](#)², [Pallav Shah](#)³, [Christophe Pison](#)⁴, [Arschang Valipour](#)⁵, [Dirk-Jan Slebos](#)⁶; [AIRFLOW-2 Study Group](#)

Collaborators, Affiliations expand

- PMID: 36459953
- DOI: [10.1016/j.rmed.2022.107059](https://doi.org/10.1016/j.rmed.2022.107059)

Free article

Abstract

This post-hoc analysis of the AIRFLOW-2 trial investigated the changes in airway CT-parameters after targeted lung denervation (TLD) and whether these changes are associated with treatment response. In the treatment group (n = 32), an improvement in air trapping was significantly associated with an improvement in residual volume (RV). Furthermore, improvements in Pi10 and airway lumen were significantly associated with an improvement in both RV and FEV₁. Our results could suggest that when improving airway characteristics like decreasing airway wall thickness and increasing the airway lumen, this leads to less air trapping and an improvement in clinical outcomes.

Conflict of interest statement

Declaration of competing interest DJS is a PI for Nuaira, USA and reports consultancy fees from Nuaira paid to the institution. AV reports speaker fees from Nuaira in the past. PS reports clinical trial expenses reimbursed to the host institutions in the past 36 months. CP reports payments for lectures and to CHUGA to conduct phase 3 trials from Nuaira (AIRFLOW 2 and 3 trials), GSK, AZ, Boehringer Ingelheim, Novartis and Chiesi. JH and FH have nothing to disclose.

supplementary info

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Eur Clin Respir J

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. 2022 Nov 26;10(1):2149918.

doi: 10.1080/20018525.2022.2149918. eCollection 2023.

Adherence to treatment guidelines and good asthma control in Finland

[Johanna Pakkasela](#)^{1,2}, [Petri Salmela](#)¹, [Pekka Juntunen](#)², [Jussi Karjalainen](#)^{2,3}, [Lauri Lehtimäki](#)^{2,3}

Affiliations expand

- PMID: 36457457
- PMCID: [PMC9707375](#)

- DOI: [10.1080/20018525.2022.2149918](https://doi.org/10.1080/20018525.2022.2149918)

Free PMC article

Abstract

Background: Asthma program in Finland decreased asthma-related mortality and expenses of care on national level, but there is lack of data on adherence to treatment guidelines and disease control on individual level. We aimed to assess adherence to guidelines and disease control among Finnish adult asthmatics.

Methods: Questionnaires were sent in Finland to 2000 randomly selected recipients aged 18-80 years, who had bought medication for obstructive airways disease during the previous 12 months. The questionnaire included questions on asthma medication, exacerbations, self-management and follow-up. Asthma symptom control was assessed by the Asthma Control Test (ACT).

Results: A high proportion (82.4%) of the 541 responders with physician-diagnosed asthma reported regular use of asthma medication and 97.1% of them used inhaled corticosteroids. Almost all (97.0%) of the asthmatics were taught how to use their inhaler and 78.4% had an asthma self-management plan, but only 35.7% reported regular annual follow-up visits. According to symptoms, 60.0% had their asthma well-controlled (ACT score ≥ 20). On the other hand, 29.2% had a course of oral corticosteroid and 21.8% had an asthma-related unscheduled health care visit during the previous year, but only 2.6% reported a hospitalization. Asthma control was better in those not using regular asthma medication.

Conclusions: The guidelines are well adopted in Finnish adult asthma care except for regular follow-up visits. Majority of patients had good symptom control and hospitalizations were rare. Better asthma control among those not using regular asthma medication implies they are not undertreated but have a mild disease.

Keywords: Asthma; adult; control; exacerbation; follow-up; guideline; management; medication; symptom.

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Conflict of interest statement

The authors report no conflicts of interest related to this study.

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Eur Clin Respir J



. 2022 Nov 24;10(1):2149920.

doi: 10.1080/20018525.2022.2149920. eCollection 2023.

[Adherence to inhaled corticosteroids in relation to quality of life and symptoms of anxiety and depression in asthma](#)

[Martino Renzi-Lomholt](#)¹, [Kjell Erik Julius Håkansson](#)¹, [Charlotte Suppli Ulrik](#)^{1,2}

Affiliations expand

- PMID: 36452910
- PMCID: [PMC9704108](#)
- DOI: [10.1080/20018525.2022.2149920](#)

Free PMC article

Abstract

Background: Poor asthma control, often caused by non-adherence with controller medication, is a well-known risk factor for impaired quality of life (QoL) and major mood disorders (MMD). Previous studies have shown a relationship between non-adherence,

lower QoL, and MMD across chronic diseases, but the relationship remains uncertain in asthma.

Methods: All asthma patients followed at the respiratory outpatient clinic at Copenhagen University Hospital - Hvidovre were invited to fill-in the Hospital Anxiety and Depression Scale (HADS) and the Mini Asthma Quality of Life Questionnaire (miniAQLQ). Medication Possession Ratio (MPR) was calculated using pharmacy redemption data. Relationships between questionnaire scores, inhaled corticosteroid MPR and use of rescue medication were investigated using Pearson correlation and multivariable linear regression adjusted for age, sex, FEV₁, and GINA Step. Data from scheduled visits were collected from patients' medical records.

Results: A total of 308 patients (73% females, median age 51 years (interquartile range (IQR) 37, 62)) completed the questionnaires and had 1-year medication data available. Median adherence to inhaled corticosteroids (ICS) was 57% (35%, 75%) with 18% of patients having adherence above 80%. Of the participating patients, 14% and 27% reported depressive and anxiety-related symptoms, respectively, and 72% reported impaired QoL. In correlation analyses, ICS adherence was not significantly associated with either prevalence of MMD symptoms or impaired QoL in asthma patients. However, a strong correlation was found between ACQ-6 and both MMD symptoms and impaired QoL, as well as between rescue medication use and impaired QoL. In adjusted analysis, however, the latter correlation was no longer statistically significant.

Conclusion: Our results suggest that ICS adherence is not directly correlated with either impaired quality of life or major mood disorder symptoms in asthma patients. Self-reported asthma control, on the other hand, is strongly correlated with both QoL and MMD.

Keywords: Asthma; anxiety; depression; inhaled corticosteroids; major mood disorder.

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Conflict of interest statement

MRL has nothing to declare. KEJH has received personal fees from AstraZeneca, Chiesi, GSK, Sanofi Genzyme, and TEVA. CSU has received personal fees from AstraZeneca, GSK, TEVA, Sanofi Genzyme, Boehringer-Ingelheim, Chiesi, Orion Pharma, Novartis, ALK-Abello, Mundipharma, and Actelion.

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

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32 Review

Eur Respir Rev



. 2022 Nov 29;31(166):220099.

doi: 10.1183/16000617.0099-2022. Print 2022 Dec 31.

Inhaled corticosteroids for the treatment of COVID-19

[Mona Bafadhel](#)¹, [Rosa Faner](#)², [Camille Taillé](#)³, [Richard E K Russell](#)⁴, [Tobias Welte](#)⁵, [Peter J Barnes](#)⁶, [Alvar Agustí](#)⁷

Affiliations expand

- PMID: 36450371
- PMCID: [PMC9724831](#)
- DOI: [10.1183/16000617.0099-2022](#)

Free PMC article

Abstract

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has caused severe illness and mortality for millions worldwide. Despite the development, approval and rollout of vaccination programmes globally to prevent infection by SARS-CoV-2 and the development of coronavirus disease 2019 (COVID-19), treatments are still urgently needed to improve outcomes. Early in the pandemic it was observed that patients with pre-existing

asthma or COPD were underrepresented among those with COVID-19. Evidence from clinical studies indicates that the inhaled corticosteroids (ICS) routinely taken for asthma and COPD could have had a protective role in preventing severe COVID-19 and, therefore, may be a promising treatment for COVID-19. This review summarises the evidence supporting the beneficial effects of ICS on outcomes in patients with COVID-19 and explores the potential protective mechanisms.

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Conflict of interest statement

Conflict of interest: M. Bafadhel has unrestricted research grants from AstraZeneca and Roche, and has received honoraria to her institution for speaker's fees from AstraZeneca, Chiesi, Cipla and GlaxoSmithKline. She is a scientific adviser to Albus Health and ProAxis. Conflict of interest: R. Faner has received research funding, advisory board fees and lecture fees from AstraZeneca, Chiesi, GlaxoSmithKline and Menarini. Conflict of interest: C. Taillé has received grants to her institution, advisory board fees and lecture fees from AstraZeneca, Chiesi, GlaxoSmithKline, Novartis and Sanofi. Conflict of interest: R.E.K. Russell has received advisory board fees and lecture fees from AstraZeneca, Chiesi, Cipla and GlaxoSmithKline. Conflict of interest: T. Welte has received lecture fees from AstraZeneca, Basilea, Bayer, Berlin Chemie, Biotest, Boehringer Ingelheim, GlaxoSmithKline, MSD, Novartis, Pfizer, Roche and Sanofi-Aventis, and advisory board fees from AstraZeneca, Basilea, Bayer, Biotest, Boehringer Ingelheim, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer and Roche. Conflict of interest: P.J. Barnes has received research funding from AstraZeneca and Boehringer Ingelheim, and funding for consultancy, scientific advisory boards and talks from AstraZeneca, Boehringer Ingelheim, Covis, Epi-Endo, Novartis, Pieris and Teva. Conflict of interest: A. Agustí has unrestricted research grants from AstraZeneca and GlaxoSmithKline, and has received honoraria for speaker's fees from AstraZeneca, Chiesi, GlaxoSmithKline, Menarini, Orion Pharma and Zambon.

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

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Environ Res

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. 2023 Jan 1;216(Pt 3):114713.

doi: 10.1016/j.envres.2022.114713. Epub 2022 Nov 5.

Early-life exposure to air pollution associated with food allergy in children: Implications for 'one allergy' concept

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Affiliations expand

- PMID: 36347392
- DOI: [10.1016/j.envres.2022.114713](https://doi.org/10.1016/j.envres.2022.114713)

Abstract

Background: The rapid increase of food allergy (FA) has become the "second wave" of allergy epidemic and is now a major global public health concern. Mounting evidence indicates that early life exposure to air pollution is associated with the "first wave" of allergy epidemic (including asthma, allergic rhinitis and eczema) in children, but little is known about its association with FA.

Objectives: We hypothesize FA has triple exposure pathways, gut-skin-airway, and investigate the effects of airway exposure to outdoor and indoor air pollution on childhood FA.

Methods: A cohort study of 2598 preschool children aged 3-6 years old was conducted in Changsha, China. The prevalence of FA was surveyed using a standard questionnaire by International Study of Asthma and Allergies in Childhood (ISAAC). Exposure to indoor air pollution was assessed by four indicators: new furniture, redecoration, mold or dampness, and window condensation. Exposure to outdoor air pollution was evaluated by the concentrations of PM10, SO2 and NO2, which were obtained from the monitored stations. Both prenatal and postnatal exposure windows were considered. The association between exposure to outdoor/indoor air pollution and childhood FA was estimated by multiple logistic regression models using odds ratio (OR) and a 95% confidence interval (CI).

Results: A total of 14.9% children reported FA. The prevalence was significantly associated with exposure to indoor air pollution, OR (95% CI) = 1.93 (1.35-2.75) for prenatal exposure to mold/dampness and 1.49 (1.07-2.10) and 1.41 (1.04-1.89) respectively for postnatal exposure to new furniture and window condensation. The prevalence of FA was also associated with prenatal and postnatal exposure to outdoor air pollution, particularly the traffic-related air pollutant NO₂, with adjusted ORs (95% CIs) respectively 1.24 (1.00-1.54) and 1.38 (1.03-1.85) per interquartile range (IQR) increase. Sensitivity analysis showed that the association between outdoor/indoor air pollution and childhood FA was significant only in young children aged 3-4 years.

Conclusion: Early-life exposure to high levels of outdoor and indoor air pollution in China due to the rapid economic growth and fast urbanization in the past decades may contribute to the rapid increase of food allergy (FA) in children. Our study indicates that, in addition to gut and skin, airway may be a new route of food sensitization. Air pollution leads to the first and second waves of allergy epidemics, suggesting a concept of 'one allergy' disease.

Keywords: Allergic diseases; One allergy; Traffic-related air pollution; Triple exposure hypothesis; Urbanization.

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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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Review

Prevalence, risk factors and treatments for post-COVID-19 breathlessness: a systematic review and meta-analysis

[Bang Zheng](#)¹, [Luke Daines](#)¹, [Qing Han](#)², [John R Hurst](#)³, [Paul Pfeffer](#)^{4,5}, [Manu Shankar-Hari](#)⁶, [Omer Elneima](#)⁷, [Samantha Walker](#)⁸, [Jeremy S Brown](#)³, [Salman Siddiqui](#)^{7,9}, [Jennifer K Quint](#)¹⁰, [Christopher E Brightling](#)⁷, [Rachael A Evans](#)⁷, [Louise V Wain](#)^{7,11}, [Liam G Heaney](#)¹², [Aziz Sheikh](#)¹³

Affiliations expand

- PMID: 36323418
- PMCID: [PMC9724798](#)
- DOI: [10.1183/16000617.0071-2022](#)

Free PMC article

Abstract

Persistent breathlessness >28 days after acute COVID-19 infection has been identified as a highly debilitating post-COVID symptom. However, the prevalence, risk factors, mechanisms and treatments for post-COVID breathlessness remain poorly understood. We systematically searched PubMed and Embase for relevant studies published from 1 January 2020 to 1 November 2021 (PROSPERO registration number: CRD42021285733) and included 119 eligible papers. Random-effects meta-analysis of 42 872 patients with COVID-19 reported in 102 papers found an overall prevalence of post-COVID breathlessness of 26% (95% CI 23-29) when measuring the presence/absence of the symptom, and 41% (95% CI 34-48) when using Medical Research Council (MRC)/modified MRC dyspnoea scale. The pooled prevalence decreased significantly from 1-6 months to 7-12 months post-infection. Post-COVID breathlessness was more common in those with severe/critical acute infection, those who were hospitalised and females, and was less likely to be reported by patients in Asia than those in Europe or North America. Multiple pathophysiological mechanisms have been proposed (including deconditioning, restrictive/obstructive airflow limitation, systemic inflammation, impaired mental health),

but the body of evidence remains inconclusive. Seven cohort studies and one randomised controlled trial suggested rehabilitation exercises may reduce post-COVID breathlessness. There is an urgent need for mechanistic research and development of interventions for the prevention and treatment of post-COVID breathlessness.

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Conflict of interest statement

Conflict of interest: A. Sheikh is a member of the Scottish Government Chief Medical Officer's COVID-19 Advisory Group and its Standing Committee on Pandemics, and a member of the UK Government's Risk Stratification Subgroup and AstraZeneca's Thrombotic Thrombocytopenic Taskforce; all roles are unremunerated. P. Pfeffer reports grants from NIHR, outside the submitted work. M. Shankar-Hari reports grants from National Institute for Health Research, outside the submitted work. C.E. Brightling reports grants from UKRI-MRC/DHSC-NIHR. R.A. Evans reports a grant from NIHR Clinician Scientist Fellowship, outside the submitted work. L.V. Wain reports grants from GSK, grants from Orion, outside the submitted work. L.G. Heaney reports personal fees from Novartis, Hoffman la Roche/Genentech Inc, Sanofi, Evelo Biosciences, GlaxoSmithKline, AstraZeneca, Teva, Theravance and Circassia; grants from Medimmune, Novartis UK, Roche/Genentech Inc, GlaxoSmithKline, Amgen, Genentech/Hoffman la Roche, AstraZeneca, Medimmune, Aerocrine and Vitalograph; and other support from Boehringer Ingelheim, Chiesi and Napp Pharmaceuticals, outside the submitted work. All other authors declare no competing interests.

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Review

Risk of serious COVID-19 outcomes among adults and children with moderate-to-severe asthma: a systematic review and meta-analysis

[Bohee Lee](#)^{1,2}, [Grace Lewis](#)^{2,3}, [Eldad Agyei-Manu](#)¹, [Nadege Atkins](#)¹, [Urmila Bhattacharyya](#)¹, [Marshall Dozier](#)¹, [Jasmin Rostron](#)¹, [Aziz Sheikh](#)^{1,2}, [Ruth McQuillan](#)^{4,5}, [Evropi Theodoratou](#)^{6,7,8}; [Usher Network for COVID-19 Evidence Reviews \(UNCOVER\) group](#)

Affiliations expand

- PMID: 36323417
- PMCID: [PMC9724896](#)
- DOI: [10.1183/16000617.0066-2022](#)

Free PMC article

Abstract

Background: The Joint Committee on Vaccination and Immunisation in the United Kingdom requested an evidence synthesis to investigate the relationship between asthma and coronavirus disease 2019 (COVID-19) outcomes.

Objective: We conducted a systematic review and meta-analysis to summarise evidence on the risk of severe COVID-19 outcomes in people with uncontrolled asthma or markers of asthma severity.

Methods: High-dose inhaled corticosteroids (ICS) or oral corticosteroids (OCS) were used as markers of asthma severity, following international or national asthma guidelines. Risk of bias was assessed using Joanna Briggs Institute tools. Adjusted point estimates were extracted for random-effects meta-analyses and subgroup analyses.

Results: After screening, 12 studies (11 in adults and one in children) met the eligibility criteria. Adults using high-dose ICS or OCS had a pooled adjusted hazard ratio (aHR) of 1.33 (95% CI 1.06-1.67, $I^2=0\%$) for hospitalisation and an aHR of 1.22 (95% CI 0.90-1.65, $I^2=70\%$) for mortality for COVID-19. We found insufficient evidence for associations between markers on COVID-19 mortality in the subgroup analyses.

Conclusions: Adults with severe asthma are at increased risk of COVID-19 hospitalisation compared to nonusers. Our analysis highlighted the dearth of studies in children with asthma investigating serious COVID-19 outcomes.

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Conflict of interest statement

Conflict of interest: B. Lee has nothing to disclose. Conflict of interest: G. Lewis has nothing to disclose. Conflict of interest: E. Agyei-Manu has nothing to disclose. Conflict of interest: N. Atkins has nothing to disclose. Conflict of interest: U. Bhattacharyya has nothing to disclose. Conflict of interest: M. Dozier has nothing to disclose. Conflict of interest: J. Rostron has nothing to disclose. Conflict of interest: A. Sheikh is a member of GINA and was a co-author of two of the studies included in this review; he was not involved in their assessment. A. Sheikh is a member of the UK Government's NERVTAG Risk Stratification Subgroup and the Scottish Government's Standing Committee on Pandemics. He was a member of AstraZeneca's Thrombotic Thrombocytopenic Task Force. All A. Sheikh's roles are unremunerated. Conflict of interest: R. McQuillan has nothing to disclose. Conflict of interest: E. Theodoratou has nothing to disclose.

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PM_{2.5} elemental composition in indoor residential environments and co-exposure effects on respiratory health in an industrial area

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- DOI: [10.1016/j.envres.2022.114630](https://doi.org/10.1016/j.envres.2022.114630)

Free article

Abstract

This study aimed to identify and characterise indoor sources of particulate matter (PM) in domestic environments. 74 inhabited apartments located in the urban area of Gela (Sicily, Italy), close to a refinery, and in three villages of the hinterland were evaluated, in real-world conditions, for the elemental composition of PM_{2.5}. The samples were collected simultaneously inside and outside each apartment for 48 h. In addition, two of the apartments were simultaneously studied for four weeks. The elemental composition of PM_{2.5} was determined by applying a chemical fractionation procedure followed by inductively-coupled plasma spectrometry analysis, with both optical emission and mass detection. The extractable, more bio-accessible fraction (_{ext}), and the mineralised residual fraction (_{res}) of each element were determined, thus increasing the selectivity of elements as source tracers. Indoor air in the considered apartments was affected by both outdoor pollution and specific indoor emission sources. The behaviour of each source was studied in detail, identifying a reliable tracer: Ti_{res} for soil, As_{ext} for industrial sources, V_{ext} for heavy oil combustion, Ce for cigarette smoking and Mo for the use of vacuum dust cleaners. As_{ext} and V_{ext} showed an excellent infiltration capacity, while the concentration of Ti_{res} was affected by a low infiltration capacity and by the contribution of particles re-suspension caused by the residents' movements. In the case of Ce and Mo, indoor concentrations were much higher than outdoor with a high variability among the apartments, due to the inhabitants' habits concerning cigarette smoke and use of electric appliances. To test the

overall effect of the concomitant exposure to the identified sources on Wh12 M and on DDA, a WQS analysis was conducted. Cigarette smoking and heavily oil combustion driven the Wh12 M odds increase, while the DDA odds increase was mainly driven by heavily oil combustion and the use of vacuum dust cleaners.

Keywords: Asthma; Chemical fractionation; Indoor air quality; Infiltration; Source tracers; Weighted quantile sum regression.

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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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. 2023 Jan 1;216(Pt 2):114538.

doi: 10.1016/j.envres.2022.114538. Epub 2022 Oct 15.

Early life exposure to outdoor air pollution and indoor environmental factors on the development of childhood allergy from early symptoms to diseases

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Affiliations expand

- PMID: 36252839
- DOI: [10.1016/j.envres.2022.114538](https://doi.org/10.1016/j.envres.2022.114538)

Abstract

Background: The prevalence of childhood allergies has increased during past decades leading to serious hospitalization and heavy burden worldwide, yet the key factors responsible for the onset of early symptoms and development of diagnosed diseases are unclear.

Objective: To explore the role of early life exposure to ambient air pollution and indoor environmental factors on early allergic symptoms and doctor diagnosed allergic diseases.

Methods: A retrospective cohort study of 2598 preschool children was conducted at 36 kindergartens in Changsha, China from September of 2011 to February of 2012. A questionnaire was developed to survey each child's early onset of allergic symptoms (wheeze and rhinitis-like symptoms) and doctor diagnosis of allergic diseases (asthma and rhinitis) as well as home environments. Each mother's and child's exposures to ambient air pollutants (PM₁₀, SO₂, and NO₂) and temperature were estimated for in utero and postnatal periods. The associations of early symptoms and diagnosed diseases with outdoor air pollution and indoor environmental variables were examined by logistic regression models.

Results: Childhood early allergic symptoms (33.9%) including wheeze (14.7%) and rhinitis-like symptoms (25.4%) before 2 years old were not associated with outdoor air pollution exposure but was significantly associated with maternal exposure of window condensation at home in pregnancy with ORs (95% CI) of 1.33 (1.11-1.59), 1.30 (1.01-1.67) and 1.27 (1.04-1.55) respectively, and was associated with new furniture during first year after birth with OR (95% CI) of 1.43 (1.02-2.02) for early wheeze. Childhood diagnosed allergic diseases (28.4%) containing asthma (6.7%) and allergic rhinitis (AR) (7.2%) were significantly associated with both outdoor air pollutants (mainly for SO₂ and NO₂) during first 3 years and indoor new furniture, redecoration, and window condensation. We found that sex, age, parental atopy, maternal productive age, environmental tobacco smoke (ETS), antibiotics use, economic stress, early and late introduction of complementary foods, and outdoor air pollution modified the effects of home environmental exposure in early life on early allergic symptoms and diagnosed allergic diseases.

Conclusion: Our study indicates that early life exposure to indoor environmental factors plays a key role in early onset of allergic symptoms in children, and further exposure to ambient air pollution and indoor environmental factors contribute to the later development of asthma and allergic rhinitis.

Keywords: Ambient air pollution; Antibiotics use; Childhood asthma and allergies; Complementary feeding; Early life exposure; Home environments.

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Review

Environ Res

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. 2023 Jan 1;216(Pt 2):114489.

doi: 10.1016/j.envres.2022.114489. Epub 2022 Oct 5.

Asthma triggered by extreme temperatures: From epidemiological evidence to biological plausibility

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- PMID: 36208788
- DOI: [10.1016/j.envres.2022.114489](https://doi.org/10.1016/j.envres.2022.114489)

Free article

Abstract

Background: There is rapidly growing evidence indicating that extreme temperature is a crucial trigger and potential activator of asthma; however, the effects of extreme temperature on asthma are inconsistently reported and the its potential mechanisms remain undefined.

Objectives: This review aims to estimate the impacts of extreme heat, extreme cold, and temperature variations on asthma by systematically summarizing the existing studies from epidemiological evidence to biological plausibility.

Methods: We conducted a systematic search in PubMed, Embase, and Web of Science from inception to June 30, 2022, and we retrieved articles of epidemiology and biological studies which assessed associations between extreme temperatures and asthma. This protocol was registered with PROSPERO (CRD42021273613).

Results: From 12,435 identified records, 111 eligible studies were included in the qualitative synthesis, and 37 articles were included in the meta-analysis (20 for extreme heat, 16 for extreme cold, and 15 for temperature variations). For epidemiological evidence, we found that the synergistic effects of extreme temperatures, indoor/outdoor environments, and individual vulnerabilities are important triggers for asthma attacks, especially when there is extreme heat or cold. Meta-analysis further confirmed the associations, and the pooled relative risks for asthma attacks in extreme heat and extreme cold were 1.07 (95%CI: 1.03-1.12) and 1.20 (95%CI: 1.12-1.29), respectively. Additionally, this review discussed the potential inflammatory mechanisms behind the associations between extreme temperatures and asthma exacerbation, and highlighted the regulatory role of immunological pathways and transient receptor potential ion channels in asthma triggered by extreme temperatures.

Conclusions: We concluded that both extreme heat and cold could significantly increase the risk of asthma. Additionally, we proposed a potential mechanistic framework, which is important for understanding the disease pathogenesis that uncovers the complex mechanisms of asthma triggered by extreme temperatures and protects the sensitive individuals from impacts of extreme weather events and climate change.

Keywords: Asthma; Epidemiology; Extreme temperature; Mechanism; Review.

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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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Review

J Thorac Imaging



. 2023 Jan 1;38(1):W1-W18.

doi: 10.1097/RTI.0000000000000683. Epub 2022 Oct 10.

[A Computer-based Analysis for Identification and Quantification of Small Airway Disease in Lung Computed Tomography Images: A Comprehensive Review for Radiologists](#)

[Mohammad Mehdi Baradaran Mahdavi](#)¹, [Masoud Arabfard](#)¹, [Mehravat Rafati](#)², [Mostafa Ghanei](#)¹

Affiliations expand

- PMID: 36206107

- DOI: [10.1097/RTI.0000000000000683](https://doi.org/10.1097/RTI.0000000000000683)

Abstract

Computed tomography (CT) imaging is being increasingly used in clinical practice for detailed characterization of lung diseases. Respiratory diseases involve various components of the lung, including the small airways. Evaluation of small airway disease on CT images is challenging as the airways cannot be visualized directly by a CT scanner. Small airway disease can manifest as pulmonary air trapping (AT). Although AT may be sometimes seen as mosaic attenuation on expiratory CT images, it is difficult to identify diffuse AT visually. Computer technology advances over the past decades have provided methods for objective quantification of small airway disease on CT images. Quantitative CT (QCT) methods are being rapidly developed to quantify underlying lung diseases with greater precision than subjective visual assessment of CT images. A growing body of evidence suggests that QCT methods can be practical tools in the clinical setting to identify and quantify abnormal regions of the lung accurately and reproducibly. This review aimed to describe the available methods for the identification and quantification of small airway disease on CT images and to discuss the challenges of implementing QCT metrics in clinical care for patients with small airway disease.

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Conflict of interest statement

The authors declare no conflicts of interest.

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Allergy

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. 2023 Jan;78(1):20-46.

doi: 10.1111/all.15533. Epub 2022 Oct 18.

A practical toolbox for the effective transition of adolescents and young adults with asthma and allergies: An EAACI position paper

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Affiliations expand

- PMID: 36176045
- DOI: [10.1111/all.15533](https://doi.org/10.1111/all.15533)

Abstract

Introduction: Adolescence is a critical stage of rapid biological, emotional and social change and development. Adolescents and young adults (AYA) with asthma and allergies need to develop the knowledge and skills to self-manage their health independently. Healthcare professionals (HCP), parents and their wider network play an essential role in supporting AYA in this process. Previous work showed significant limitations in transition care across Europe. In 2020, the first evidence-based guideline on effective transition for AYA with asthma and allergies was published by EAACI.

Aim: We herein summarize practical resources to support this guideline's implementation in clinical practice.

Methods: For this purpose, multi-stakeholder Task Force members searched for resources in peer review journals and grey literature. These resources were included if relevant and of good quality and were pragmatically rated for their evidence-basis and user friendliness.

Results: Resources identified covered a range of topics and targeted healthcare professionals, AYA, parents/carers, schools, workplace and wider community. Most resources were in English, web-based and had limited evidence-basis.

Conclusions: This position paper provides a valuable selection of practical resources for all stakeholders to support effective transitional care for AYA with asthma and allergies. Future research should focus on developing validated, patient-centred tools to further assist evidence-based transition care.

Keywords: adolescent; allergy; asthma; transition; young adult.

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Am J Respir Crit Care Med

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. 2023 Jan 1;207(1):109-110.

doi: 10.1164/rccm.202207-1419LE.

Mechanisms of Obesity-related Asthma: Is Insulin Getting on Your Nerves?

[Zhenying Nie](#)¹, [Allison D Fryer](#)¹, [David B Jacoby](#)¹, [Matthew G Drake](#)¹

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- PMID: 36029301
- DOI: [10.1164/rccm.202207-1419LE](https://doi.org/10.1164/rccm.202207-1419LE)

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Acta Paediatr

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. 2023 Jan;112(1):122-123.

doi: 10.1111/apa.16524. Epub 2022 Aug 29.

Role of FEF₂₅₋₇₅ in children sent by primary care paediatricians for asthma diagnosis

[Maria Angela Tosca¹](#), [Irene Schiavetti²](#), [Emanuele Medone¹](#), [Michele Miraglia Del Giudice³](#), [Giorgio Ciprandi⁴](#)

Affiliations expand

- PMID: 36001059
- DOI: [10.1111/apa.16524](https://doi.org/10.1111/apa.16524)

No abstract available

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. 2023 Jan;78(1):156-167.

doi: 10.1111/all.15487. Epub 2022 Aug 28.

IL1RAP expression and the enrichment of IL-33 activation signatures in severe neutrophilic asthma

[Yusef Eamon Badi](#)^{1,2,3}, [Barbora Salcman](#)⁴, [Adam Taylor](#)⁵, [Batika Rana](#)⁶, [Nazanin Zounemat Kermani](#)², [John H Riley](#)⁴, [Sally Worsley](#)⁷, [Sharon Mumby](#)¹, [Sven-Eric Dahlen](#)⁸, [David Cousins](#)⁹, [Silvia Bulfone-Paus](#)⁴, [Karen Affleck](#)¹⁰, [Kian Fan Chung](#)¹, [Stewart Bates](#)^{#4}, [Ian M Adcock](#)^{#1}

Affiliations expand

- PMID: 35986608
- DOI: [10.1111/all.15487](https://doi.org/10.1111/all.15487)

Abstract

Background: Interleukin (IL)-33 is an upstream regulator of type 2 (T2) eosinophilic inflammation and has been proposed as a key driver of some asthma phenotypes.

Objective: To derive gene signatures from in vitro studies of IL-33-stimulated cells and use these to determine IL-33-associated enrichment patterns in asthma.

Methods: Signatures downstream of IL-33 stimulation were derived from our in vitro study of human mast cells and from public datasets of in vitro stimulated human basophils, type 2 innate lymphoid cells (ILC2), regulatory T cells (Treg) and endothelial cells. Gene Set Variation Analysis (GSVA) was used to probe U-BIOPRED and ADEPT sputum transcriptomics to determine enrichment scores (ES) for each signature according to asthma severity, sputum granulocyte status and previously defined molecular phenotypes.

Results: IL-33-activated gene signatures were cell-specific with little gene overlap. Individual signatures, however, were associated with similar signalling pathways (TNF, NF- κ B, IL-17 and JAK/STAT signalling) and immune cell differentiation pathways (Th17, Th1 and Th2 differentiation). ES for IL-33-activated gene signatures were significantly enriched in asthmatic sputum, particularly in patients with neutrophilic and mixed granulocytic phenotypes. IL-33 mRNA expression was not elevated in asthma whereas the expression of mRNA for IL1RL1, the IL-33 receptor, was up-regulated in the sputum of severe eosinophilic asthma. The mRNA expression for IL1RAP, the IL1RL1 co-receptor, was greatest in severe neutrophilic and mixed granulocytic asthma.

Conclusions: IL-33-activated gene signatures are elevated in neutrophilic and mixed granulocytic asthma corresponding with IL1RAP co-receptor expression. This suggests incorporating T2-low asthma in anti-IL-33 trials.

Keywords: IL-33; gene set variation analysis; severe asthma.

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. 2023 Jan;78(1):258-269.

doi: 10.1111/all.15481. Epub 2022 Sep 1.

Urine eosinophil-derived neurotoxin: A potential marker of activity in select eosinophilic disorders

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Affiliations expand

- PMID: 35971862
- DOI: [10.1111/all.15481](https://doi.org/10.1111/all.15481)

Abstract

Background: Biomarkers of eosinophilic disease activity, especially in the context of novel therapies that reduce blood eosinophil counts, are an unmet need. Absolute eosinophil count (AEC) does not accurately reflect tissue eosinophilia or eosinophil activation. Therefore, the aims of this study were to compare the reliability of plasma and urine eosinophil major basic protein 1, eosinophil cationic protein, eosinophil-derived neurotoxin (EDN), and eosinophil peroxidase measurement and to evaluate the usefulness of eosinophil granule protein (EGP) measurement for the assessment of disease activity in patients with eosinophil-associated diseases treated with mepolizumab, benralizumab, or dexamipexole.

Methods: Eosinophil granule protein concentrations were measured in serum, plasma, and urine from healthy volunteers and patients with hypereosinophilic syndrome (HES), eosinophilic granulomatosis with polyangiitis (EGPA), and eosinophilic asthma using a multiplex assay.

Results: Urine EGP concentrations remained stable, whereas serum and plasma EGP concentrations increased significantly with delayed processing. Plasma (p) EDN, but not urine (u) EDN, concentration correlated with AEC and negatively correlated with prednisone dose. Both pEDN and uEDN decreased significantly following treatment of HES patients with benralizumab and EGPA patients with mepolizumab. uEDN appeared to increase with clinical relapse in both patient groups.

Conclusions: Measurement of EGP in urine is noninvasive and unaffected by cellular lysis. Although plasma and urine EDN concentrations showed a similar pattern following benralizumab and mepolizumab treatment, the lack of correlation between AEC or prednisone dose and uEDN concentrations suggests that measurement of uEDN may provide a potential biomarker of disease activity in patients with HES and EGPA.

Keywords: benralizumab; eosinophil granule protein; eosinophilia; hypereosinophilic syndrome; mepolizumab.

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Review

Am J Med Sci

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. 2023 Jan;365(1):93-98.

Severe eosinophilic granulomatosis with polyangiitis responding to a combination of rituximab and mepolizumab

[Georgios Tsioulos](#)¹, [Dimitris Kounatidis](#)², [Natalia G Vallianou](#)³, [Nektarios Koufopoulos](#)¹, [Pelagia Katsimiri](#)¹, [Anastasia Antoniadou](#)¹

Affiliations [expand](#)

- PMID: 35970248
- DOI: [10.1016/j.amjms.2022.07.007](https://doi.org/10.1016/j.amjms.2022.07.007)

Abstract

Eosinophilic granulomatosis with polyangiitis (EGPA), formerly known as Churg-Strauss Syndrome, is a multisystem antineutrophil cytoplasmic antibody (ANCA) positive vasculitis, characterized by the presence of chronic rhinosinusitis, asthma and prominent peripheral blood eosinophilia. Although the most commonly involved organ is the lung, followed by the skin, EGPA can affect any organ system. Herein, we present the complicated case of an 18-year-old male patient with severe life-threatening EGPA, with central nervous system, cardiac and gastrointestinal involvement, which was resistant to initial treatment with glucocorticoids and cyclophosphamide. The patient responded well, achieving complete remission after the addition of rituximab and mepolizumab to glucocorticoids and cyclophosphamide.

Keywords: Cyclophosphamide; Eosinophilic granulomatosis with polyangiitis; Glucocorticoids; Mepolizumab; Rituximab.

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Conflict of interest statement

Declaration of Competing Interest There are no conflict of interest regarding this manuscript.

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Allergy



. 2023 Jan;78(1):131-140.

doi: 10.1111/all.15466. Epub 2022 Aug 10.

Different aspects of severe asthma in real life: Role of Staphylococcus aureus enterotoxins and correlation to comorbidities and disease severity

[Cristiano Caruso](#)¹, [Stefania Colantuono](#)², [Gabriele Ciasca](#)^{3,4}, [Umberto Basile](#)⁵, [Riccardo Di Santo](#)⁴, [Diego Bagnasco](#)⁶, [Giovanni Passalacqua](#)⁶, [Marco Caminati](#)⁷, [Schiappoli Michele](#)⁸, [Gianenrico Senna](#)⁸, [Enrico Heffler](#)^{9,10}, [G Walter Canonica](#)^{9,10}, [Nunzio Crimi](#)^{11,12}, [Rossella Intravaia](#)¹³, [Eugenio De Corso](#)¹⁴, [Davide Firinu](#)¹⁵, [Antonio Gasbarrini](#)¹, [Stefano R Del Giacco](#)¹⁵

Affiliations expand

- PMID: 35922152
- DOI: [10.1111/all.15466](https://doi.org/10.1111/all.15466)

Abstract

Background: Asthma, with several phenotypes and endotypes, is considered particularly suited for precision medicine. The identification of different non-invasive biomarkers may facilitate diagnosis and treatment. Recently, *Staphylococcus aureus* and its enterotoxins (SE) have been found to have a role in inducing persistent type 2 airway inflammation in severe asthma, but also in such comorbidities as chronic rhinosinusitis with nasal polyposis (CRSwNP).

Methods: The aim of this retrospective study was to evaluate the prevalence of SE-IgE sensitization in a multicentric Italian cohort of severe asthmatic patients and correlate it with demographic and clinical characteristics.

Results: A total of 249 patients were included in the analysis, out of which 25.3% were staphylococcal enterotoxin B (SEB)-IgE positive. We found a meaningful association between SEB-IgE and female gender, a positive association was also measured between CRS and CRSwNP. No significant association was found between SEB-IgE sensitization and atopy, the occurrence of exacerbations and corticosteroid dosages. In the SEB-IgE-positive patient, blood eosinophil count does not appear to be correlated with the severity of the disease. Patients with SEB-IgE sensitization are, on average, younger and with an earlier disease onset, thus confirming the possibility to consider SEB-IgE sensitization as an independent risk factor for developing asthma.

Conclusions: Our data confirm that the search for SE in the initial screening phase of these patients is helpful to better phenotype them, may predict the evolution of comorbidities and lead to a targeted therapeutic choice; in this point of view this represents a goal of precision medicine.

Keywords: Staphylococcus aureus enterotoxins; biologicals; nasal polyposis; severe eosinophilic asthma; type 2 inflammation.

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Lancet Respir Med

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. 2023 Jan;11(1):55-64.

doi: 10.1016/S2213-2600(22)00185-0. Epub 2022 Jul 27.

Predictors and associations of the persistent airflow limitation phenotype in asthma: a post-hoc analysis of the ATLANTIS study

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Collaborators, Affiliations expand

- PMID: 35907424
- DOI: [10.1016/S2213-2600\(22\)00185-0](https://doi.org/10.1016/S2213-2600(22)00185-0)

Erratum in

- [Correction to Lancet Respir Med 2022; published online July 27.
https://doi.org/10.1016/S2213-2600\(22\)00185-0.](#)

[No authors listed] Lancet Respir Med. 2022 Dec;10(12):e116. doi: 10.1016/S2213-2600(22)00415-5. Epub 2022 Oct 22. PMID: 36279882 No abstract available.

Abstract

Background: Persistent airflow limitation (PAL) occurs in a subset of patients with asthma. Previous studies on PAL in asthma have included relatively small populations, mostly restricted to severe asthma, or have not included longitudinal data. The aim of this post-hoc analysis was to investigate the determinants, clinical implications, and outcome of PAL in patients with asthma who were included in the ATLANTIS study.

Methods: In this post-hoc analysis of the ATLANTIS study, we assessed the prevalence, clinical characteristics, and implications of PAL across the full range of asthma severity. The study population included patients aged 18-65 years who had been diagnosed with asthma at least 6 months before inclusion. We defined PAL as a post-bronchodilator FEV₁/forced vital capacity (FVC) of less than the lower limit of normal at recruitment.

Asthma severity was defined according to the Global Initiative for Asthma. We used Mann-Whitney U test, t test, or χ^2 test to analyse differences in baseline characteristics between patients with and without PAL. Logistic regression was used for multivariable analysis of the associations between PAL and baseline data. Cox regression was used to analyse risk of exacerbation in relation to PAL, and a linear mixed-effects model was used to analyse change in FEV₁ over time in patients with versus patients without PAL. Results were validated in the U-BIOPRED cohort.

Findings: Between June 30, 2014 and March 3, 2017, 773 patients were enrolled in the ATLANTIS study of whom 760 (98%) had post-bronchodilator FEV₁/FVC data available. Of the included patients with available data, mean age was 44 years (SD 13), 441 (58%) of 760 were women, 578 (76%) were never-smokers, and 248 (33%) had PAL. PAL was not only present in patients with severe asthma, but also in 21 (16%) of 133 patients with GINA step 1 and 24 (29%) of 83 patients with GINA step 2. PAL was independently associated with older age at baseline (46 years in PAL group vs 43 years in non-PAL group), longer duration of asthma (24 years vs 12 years), male sex (51% vs 38%), higher blood eosinophil counts (median 0.27×10^9 cells per L vs 0.20×10^9 cells per L), more small airway dysfunction, and more exacerbations during 1 year of follow-up. Associations between PAL, age, and eosinophilic inflammation were validated in the U-BIOPRED cohort, whereas associations with sex, duration of asthma, and risk of exacerbations were not validated.

Interpretation: PAL is not only present in severe disease, but also in a considerable proportion of patients with milder disease. In patients with mild asthma, PAL is associated with eosinophilic inflammation and a higher risk of exacerbations. Our findings are important because they suggest that increasing treatment intensity should be considered in patients with milder asthma and PAL.

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Conflict of interest statement

Declaration of interests MK reports grants paid personally from Chiesi Farmaceutici for support of this study; grants paid to institution from the National Institute of Health, American Lung Association, Astra-Zeneca, Sanofi-Regeneron; personal fees for consultancies from Chiesi Farmaceutici, AstraZeneca, Genetech, Sanofi-Regeneron; speaker fees from Chiesi Farmaceutici; personal fees from participation in a data safety and monitoring board for AstraZeneca and ALung; and previous leadership in the American Thoracic Society (ATS) and Association for Professors of Medicine. MCN reports research grants paid to their institution from the European Commission and Netherlands Lung Foundation. SS reports personal fees for consulting from AstraZeneca, GSK, CSL Behring, Owlstone Medical, Boehringer Ingelheim, and ERT Medical; speaker fees from Chiesi Farmaceutici; and reports board membership of both the Medical Research Council (MRC)

and the National Institute for Health and Care Research (NIHR) Artificial Intelligence, and leadership in the European Respiratory Society (ERS) Clinical Research Collaboration and UK National Asthma Strategy Group. LMF reports personal grants paid by Chiesi Farmaceutici for consultation for this study; consulting fees from Chiesi Farmaceutici; speaker fees or fees for membership of advisory boards for Chiesi Farmaceutici, AstraZeneca, GlaxoSmithKline, Alfasigma, Novartis, Verona Pharma, Lusofarmaco; travel expenses reimbursements from Chiesi Farmaceutici, Novartis, and Menarini; and participation of a data safety and monitoring board or advisory board of Novartis. KFR reports personal speaker fees from AstraZeneca, Boehringer Ingelheim, Chiesi Farmaceutici, Novartis, Sanofi-Regeneron, GlaxoSmithKline, Berlin Chemie, and Roche Pharma; participation on data safety and monitoring board or advisory boards for AstraZeneca, Boehringer Ingelheim and Sanofi-Regeneron; and KFR is a current board member of German Center for Lung Research, past president of the German Chest Society, and past member of ATS committees. KFC reports grants paid to institution from GlaxoSmithKline, UK MRC, Engineering and Physical Sciences Research Council (EPSRC); personal speaker fees from Novartis and AstraZeneca; and membership of advisory boards for AstraZeneca, GlaxoSmithKline, Roche, and Novartis. GN is an employee of Chiesi Farmaceutici. AP reports grants paid to institution from Chiesi Farmaceutici, AstraZeneca, GlaxoSmithKline, Boehringer Ingelheim, Pfizer, Teva, and Sanofi; personal consulting fees from Chiesi Farmaceutici, AstraZeneca, GlaxoSmithKline, Novartis, Sanofi, IQVIA, Avillion, and Elpen pharmaceuticals; and personal speaker fees from Chiesi Farmaceutici, AstraZeneca, GlaxoSmithKline, Boehringer Ingelheim, Menarini, Novartis, Zambon, Mundipharma, TEVA, Sanofi, Edmond pharma, IQVIA, Merck Sharp & Dohme (MSD), Avillion, Elpen pharmaceuticals. CB reports personal grants paid by Chiesi Farmaceutici for support of this study; grants paid to institution from AstraZeneca, GlaxoSmithKline, Boehringer Ingelheim, MSD, Teva Pharmaceuticals, Novartis, Sanofi, Genentech, Roche, 4DPharma, Mologic; consulting fees from AstraZeneca, GlaxoSmithKline, Boehringer Ingelheim, Novartis, MSD, Teva Pharmaceuticals, Sanofi, Genentech, Roche, 4DPharma, Mologic; and chair of the ERS Science Council. DS reports consulting fees from Aerogen, AstraZeneca, Boehringer Ingelheim, Chiesi Farmaceutici, Cipla, CSL Behring, Epiendo, Genentech, GlaxoSmithKline, Glenmark, Gossamerbio, Kinaset, Menarini, Novartis, Pulmatrix, Sanofi, Synairgen, TEVA, Theravanca, and Verona. TvdM reports consulting fees from Chiesi Farmaceutici. SED reports a grant paid to institution from Chiesi Farmaceutici for execution of the study; grants paid to institution by the Swedish MRC, Heart-Lung foundation, Country council funds for clinical research; personal consulting fees from AstraZeneca, GlaxoSmithKline, Merck, Novartis, Regeneron, Sanofi, TEVA; and personal speaker fees from AstraZeneca, GlaxoSmithKline, and Sanofi. AA reports grants from AstraZeneca, Chiesi Farmaceutici, GlaxoSmithKline, Menarini; consulting fees from AstraZeneca, GlaxoSmithKline, Chiesi Farmaceutici, and Menarini; speaker fees from AstraZeneca, GlaxoSmithKline, Chiesi Farmaceutici, Menarini; travel reimbursements from AstraZeneca, GlaxoSmithKline, Chiesi Farmaceutici, Menarini; and participation of a data safety and monitoring or advisory board of AstraZeneca, GlaxoSmithKline, Chiesi Farmaceutici, and Menarini. RF reports grants paid to the CADSET collaboration for this study; grants from Instituto de Salud Carlos III, Menarini, GlaxoSmithKline, and AstraZeneca

outside of submitted work; and speaker fees from Chiesi Farmaceutici. JAW reports grants paid to institution from Genentech, GlaxoSmithKline, AstraZeneca, Boehringer Ingelheim, Novartis, Chiesi Farmaceutici; and meeting expenses from Novartis, Boehringer Ingelheim, and Astra Zeneca. GCD reports grants from Novartis, AstraZeneca, Chiesi Farmaceutici, GlaxoSmithKline, Boehringer-Ingelheim; royalties or licenses from a book chapter on Respiratory Physiology; honoraria from ATS as statistical editor; and participation of a data safety and monitoring or advisory board for the Mister Study. IMA reports grant paid to institution for the execution of the study from the EU Innovative Medicines Initiative; grants paid to institution from GlaxoSmithKline, MRC, and EPSRC; consulting fees from GlaxoSmithKline, Sanofi, Chiesi Farmaceutici, Kinaset; presenter fees from AstraZeneca, Sanofi, Eurodrug, Sunovion; payment for expert testimony from Chiesi Farmaceutici; and travel grants from AstraZeneca. LL reports speaker fees paid to institution from the Instituut voor Permanente Studie voor Apothekers (non-profit organisation). HAMK reports grants from Chiesi Farmaceutici, GlaxoSmithKline, Novartis; and consulting fees paid to institution by GlaxoSmithKline and Novartis. MvdB report research grants paid to institution by GlaxoSmithKline, Chiesi Farmaceutici, AstraZeneca, Novartis, Genentech, and Roche. All other authors declare no competing interests.

Comment in

- [Bronchodilator reversibility in patients with asthma and persistent airflow limitation.](#)

Crisafulli E, Sartori G, Patruno V, Fantin A. *Lancet Respir Med.* 2022 Nov;10(11):e94-e95. doi: 10.1016/S2213-2600(22)00363-0. PMID: 36332640 No abstract available.

- [Bronchodilator reversibility in patients with asthma and persistent airflow limitation - Authors' reply.](#)

Kole TM, Kerstjens HAM, van den Berge M; ATLANTIS, UBIOPRED, CADSET contributors. *Lancet Respir Med.* 2022 Nov;10(11):e96. doi: 10.1016/S2213-2600(22)00366-6. PMID: 36332641 No abstract available.

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. 2023 Jan;78(1):233-243.

doi: 10.1111/all.15456. Epub 2022 Aug 9.

Dupilumab reduced impact of severe exacerbations on lung function in patients with moderate-to-severe type 2 asthma

[Alberto Papi](#)¹, [Jonathan Corren](#)², [Mario Castro](#)³, [Christian Domingo](#)⁴, [Linda Rogers](#)⁵, [Kenneth R Chapman](#)⁶, [Daniel J Jackson](#)⁷, [Nadia Daizadeh](#)⁸, [Nami Pandit-Abid](#)⁹, [Rebecca Gall](#)¹⁰, [Juby A Jacob-Nara](#)⁹, [Paul J Rowe](#)⁹, [Yamo Deniz](#)¹⁰, [Benjamin Ortiz](#)¹⁰

Affiliations expand

- PMID: 35899469
- DOI: [10.1111/all.15456](https://doi.org/10.1111/all.15456)

Abstract

Background: Severe asthma exacerbations increase the risk of accelerated lung function decline. This analysis examined the effect of dupilumab on forced expiratory volume in 1 s (FEV₁) in patients with moderate-to-severe asthma and elevated type 2 biomarkers from phase 3 LIBERTY ASTHMA QUEST ([NCT02414854](#)).

Methods: Changes from baseline in pre- and post-bronchodilator (BD) FEV₁ and 5-item Asthma Control Questionnaire (ACQ-5) scores were assessed in patients with elevated type 2 biomarkers at baseline (type 2-150/25: eosinophils ≥ 150 cells/ μ l and/or fractional exhaled nitric oxide [FeNO] ≥ 25 ppb; type 2-300/25: eosinophils ≥ 300 cells/ μ l and/or FeNO ≥ 25 ppb), stratified as exacerbators (≥ 1 severe exacerbation during the study) or non-exacerbators.

Results: In exacerbators and non-exacerbators, dupilumab increased pre-BD FEV₁ by Week 2 vs placebo; differences were maintained to Week 52 (type 2-150/25: LS mean difference (LSMD) vs placebo: 0.17 L (95% CI: 0.10-0.24) and 0.17 L (0.12-0.23); type 2-300/25: 0.22 L (0.13-0.30) and 0.21 L (0.15-0.28)), in exacerbators and non-exacerbators, respectively ($p < .0001$). Similar trends were seen for post-BD FEV₁. Dupilumab vs placebo also showed

significantly greater improvements in post-BD FEV₁ 0-42 days after first severe exacerbation in type 2-150/25 (LSMD vs placebo: 0.13 L [0.06-0.20]; p = .006) and type 2-300/25 (0.14 L [0.06-0.22]; p = .001) patients. ACQ-5 improvements were greater with dupilumab vs placebo in both groups.

Conclusion: Dupilumab treatment led to improvements in lung function independent of exacerbations and appeared to reduce the impact of exacerbations on lung function in patients who experienced a severe exacerbation during the study.

Keywords: FEV₁; dupilumab; severe exacerbations; type 2 biomarkers.

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Allergy

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. 2023 Jan;78(1):192-201.

doi: 10.1111/all.15457. Epub 2022 Aug 8.

Detergent exposure induces epithelial barrier dysfunction and eosinophilic inflammation in the esophagus

[Alfred D Doyle](#)¹, [Mia Y Masuda](#)¹, [Grace C Pyon](#)¹, [Huijun Luo](#)¹, [Arina Putikova](#)¹, [William E LeSuer](#)¹, [Samuel Flashner](#)², [Matthew A Rank](#)^{1,3}, [Hiroshi Nakagawa](#)², [Hirohito Kita](#)¹, [Benjamin L Wright](#)^{1,3}

Affiliations expand

- PMID: 35899466
- PMCID: PMC9797443 (available on 2024-01-01)
- DOI: [10.1111/all.15457](https://doi.org/10.1111/all.15457)

Abstract

Background: Eosinophilic esophagitis (EoE) is a chronic allergic disease associated with type 2 inflammation and epithelial barrier dysfunction. The etiology is unknown, however, genetic heritability studies suggest environmental factors play a key role in pathogenesis. Detergents, such as sodium dodecyl sulfate (SDS), are common ingredients in household products such as dish soap and toothpaste. We hypothesized detergent exposure decreases epithelial barrier function and induces esophageal inflammation.

Methods: Immortalized esophageal epithelial cells (EPC2) were cultured in air-liquid interface (ALI) and exposed to SDS. Barrier function/activity was assessed by transepithelial electrical resistance (TEER), FITC-dextran flux, and RT-PCR. Additionally, SDS-treated mouse esophageal organoids were evaluated for morphology. To investigate the effects of SDS in vivo, mice were treated with 0.5% SDS in drinking water for 14 days. Esophagi were assessed by gross morphology, histopathology, protein expression, and bulk RNA sequencing.

Results: When EPC2 cells were exposed to SDS (5 µg/ml) for 96 h, TEER decreased ($p = 0.03$), and FITC-dextran flux increased ($p = 0.0002$). mRNA expression of IL-33 increased 4.5-fold ($p = 0.02$) at 6 h and DSG1 decreased ($p < 0.0001$) by 72 h. Disrupted epithelial integrity was noted in SDS-treated esophageal organoids. When mice were exposed to SDS, they showed increased esophageal width, chemokine, and metalloprotease levels. Mice treated with SDS also showed increased IL-33 protein expression, basal zone hyperplasia, CD4⁺ cell infiltration, and esophageal eosinophilia. RNA sequencing revealed upregulation of immune response pathway genes.

Conclusion: Exposure to SDS decreases esophageal barrier integrity, stimulates IL-33 production, and promotes epithelial hyperplasia and tissue eosinophilia. Detergents may be a key environmental trigger in EoE pathogenesis.

Keywords: IL-33; detergent; eosinophilic esophagitis; epithelium.

Conflict of interest statement

Conflicts of Interest: The author have no conflicts of interest to report.

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Allergy

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. 2023 Jan;78(1):287-290.

doi: 10.1111/all.15452. Epub 2022 Aug 5.

SARS-CoV-2 infection in severe asthma is associated with worsening of COVID-19 through respiratory NLRP3 inflammasome activation

[Jae Seok Jeong](#)^{1,2}, [Jin Young Choi](#)³, [Jong Seung Kim](#)^{4,5}, [Seong Ok Park](#)³, [Wankyu Kim](#)^{6,7}, [Yeo-Gha Yoon](#)⁶, [Hae Jin Park](#)¹, [Kyung Hwa Park](#)¹, [Doo Hwan Kim](#)^{8,9}, [Jung Mo Kim](#)¹⁰, [Gou Young Koh](#)^{10,11}, [Seong Kug Eo](#)³, [Yong Chul Lee](#)^{1,2}

Affiliations expand

- PMID: 35871401

- PMID: [PMC9349818](#)
- DOI: [10.1111/all.15452](#)

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Review

Curr Probl Diagn Radiol

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. 2023 Jan-Feb;52(1):56-65.

doi: 10.1067/j.cpradiol.2022.04.009. Epub 2022 Apr 22.

Hypersensitivity Reactions and the Respiratory System: Imaging Based Review

[Surabhi Vyas](#)¹, [Abhinav Bansal](#)¹, [Narasiman Murugan](#)¹, [Ashu Seith Bhalla](#)², [Priyanka Naranje](#)¹, [Smita Manchanda](#)¹

Affiliations expand

- PMID: 35610069
- DOI: [10.1067/j.cpradiol.2022.04.009](https://doi.org/10.1067/j.cpradiol.2022.04.009)

Abstract

Hypersensitivity reactions are characterized by inappropriate response of the immune system to an inciting antigen, which results in damage to various body tissues. Respiratory system can be involved as a part of hypersensitivity reaction by a myriad of conditions ranging from infective pathologies like tuberculosis to non-infective processes such as asthma, graft- versus host disease, sarcoidosis and vasculitic disorders. Recognition of specific imaging features in appropriate clinical setting helps in diagnosing these conditions. We present a review of mechanism of different types of hypersensitivity reactions; and imaging features of various such pathological conditions affecting the respiratory system.

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Review

Ann Pharmacother

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. 2023 Jan;57(1):62-70.

doi: 10.1177/10600280221095540. Epub 2022 May 10.

Tezepelumab in the Treatment of Uncontrolled Severe Asthma

[Jacqueline Feist](#)¹, [Melissa Lipari](#)², [Pramodini Kale-Pradhan](#)³

Affiliations expand

- PMID: 35535458
- DOI: [10.1177/10600280221095540](https://doi.org/10.1177/10600280221095540)

Abstract

Objective: To review the pharmacology, efficacy, and safety of subcutaneous tezepelumab in the treatment of severe uncontrolled asthma.

Data sources: The PubMed database and ClinicalTrials.gov were searched using the following terms: *tezepelumab*, *Tezspire*, *AMG157*, and *MEDI9929*.

Study selection and data extraction: Articles published in English between January 2000 and March 2022 related to pharmacology, safety, and clinical trials were assessed.

Data synthesis: In a phase 2 trial, tezepelumab at low, medium, and high doses reduced the annualized asthma exacerbation rate by 62%, 71%, and 66%, respectively, when compared with placebo ($P < 0.001$). In addition to significant reduction of asthma exacerbation rate in the overall treatment population, a phase 3 trial showed significant reduction of asthma exacerbation across all subgroups analyzed regardless of serum eosinophil count (EOS), fractionated exhaled nitric oxide (FeNO) level, or allergic status as determined by IgE sensitivity.

Relevance to patient care and clinical practice: Tezepelumab is indicated to treat nonallergic and noneosinophilic severe uncontrolled asthma phenotypes in addition to type 2 inflammatory asthma. When selecting the most appropriate biologic agent, consider the risks, benefits, and costs. There is a paucity of data on the efficacy of tezepelumab in patients with comorbid conditions. In the case of a patient presenting with uncontrolled severe asthma with such comorbid conditions, it may be prudent to consider a biologic therapy that can target both.

Conclusion: Tezepelumab has shown clinical utility in severe uncontrolled asthma regardless of phenotype, fulfilling the need for treatment options in individuals with severe, uncontrolled, noneosinophilic, and nonallergic asthma.

Keywords: Tezspire; asthma; biologic; monoclonal antibody; tezepelumab.

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Am J Perinatol

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. 2023 Jan;40(2):172-180.

doi: 10.1055/s-0041-1727233. Epub 2021 Apr 21.

[Asthma Medication Regimens in Pregnancy: Longitudinal Changes in Asthma Status](#)

[Matthew C H Rohn](#)¹, [Danielle R Stevens](#)¹, [Jenna Kanner](#)¹, [Carrie Nobles](#)¹, [Zhen Chen](#)¹, [Katherine L Grantz](#)¹, [Seth Sherman](#)², [William A Grobman](#)³, [Rajesh Kumar](#)^{3,4}, [Joseph Biggio](#)^{5,6}, [Pauline Mendola](#)^{1,7}

Affiliations expand

- PMID: 33882589
- PMCID: PMC8865050 (available on 2024-01-01)
- DOI: [10.1055/s-0041-1727233](https://doi.org/10.1055/s-0041-1727233)

Abstract

Objective: This study aimed to assess the impact of common asthma medication regimens on asthma symptoms, exacerbations, lung function, and inflammation during pregnancy.

Study design: A total of 311 women with asthma were enrolled in a prospective pregnancy cohort. Asthma medication regimen was categorized into short-acting β agonist (SABA) alone, SABA + inhaled corticosteroid (ICS), SABA + ICS + long-acting β agonist (LABA), and no asthma medications (reference). We evaluated asthma control at enrollment (< 15 weeks' gestation) and its change into trimesters 2 and 3, including per cent predicted forced expiratory volume in 1 second (%FEV1) and peak expiratory flow (%PEF), pulse oximetry, fractional exhaled nitric oxide (FeNO), asthma symptoms (asthma attacks/month, night symptoms/week), and severe exacerbations. Linear mixed models adjusted for site, age, race, annual income, gestational age, body mass index, and smoking, and propensity scores accounted for asthma control status at baseline.

Results: Women taking SABA + ICS and SABA + ICS + LABA had better first trimester %PEF (83.5% [75.7-91.3] and 84.6% [76.9-92.3], respectively) compared with women taking no asthma medications (72.7% [66.0-79.3]). Women taking SABA + ICS + LABA also experienced improvements in %FEV1 (+11.1%, $p < 0.01$) in the third trimester and FeNO in the second (-12.3 parts per billion [ppb], $p < 0.01$) and third (-11.0 ppb, $p < 0.01$) trimesters as compared with the trajectory of women taking no medications. SABA + ICS use was associated with increased odds of severe exacerbations in the first (odds ratio [OR]: 2.22 [1.10-4.46]) and second (OR: 3.15 [1.11-8.96]) trimesters, and SABA + ICS + LABA use in the second trimester (OR: 7.89 [2.75-21.47]). Women taking SABA alone were similar to those taking no medication.

Conclusion: Pregnant women taking SABA + ICS and SABA + ICS + LABA had better lung function in the first trimester. SABA + ICS + LABA was associated with improvements in lung function and inflammation across gestation. However, both the SABA + ICS and SABA + ICS + LABA groups had a higher risk of severe exacerbation during early to mid-pregnancy.

Key points: · Medication regimens may affect perinatal asthma control.. · Intensive regimens improved lung function/inflammation.. · Women on intensive regimens had more acute asthma events..

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Conflict of interest statement

None declared.

- [Cited by 1 article](#)

supplementary info

MeSH terms, Substances, Grant supportexpand

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CHRONIC COUGH

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BMC Pulm Med

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. 2022 Dec 29;22(1):492.

doi: 10.1186/s12890-022-02219-0.

Change in health outcomes for First Nations children with chronic wet cough: rationale and study protocol for a multi-centre implementation science study

[Pamela J Laird](#)^{1 2 3}, [Roz Walker](#)^{4 5 6}, [Gabrielle McCallum](#)⁷, [Maree Toombs](#)⁸, [Melanie Barwick](#)^{9 10}, [Peter Morris](#)⁷, [Robyn Aitken](#)^{7 11 12}, [Matthew Cooper](#)¹, [Richard Norman](#)¹³, [Bhavini Patel](#)¹⁴, [Gloria Lau](#)^{1 2}, [Anne B Chang](#)^{7 15 16}, [André Schultz](#)^{17 18 19}

Affiliations expand

- PMID: 36581812
- PMCID: [PMC9798941](#)
- DOI: [10.1186/s12890-022-02219-0](#)

Free PMC article

Abstract

Background: In children, chronic wet cough may be a sign of underlying lung disease, including protracted bacterial bronchitis (PBB) and bronchiectasis. Chronic (> 4 weeks in duration) wet cough (without indicators pointing to alternative causes) that responds to antibiotic treatment is diagnostic of PBB. Timely recognition and management of PBB can prevent disease progression to irreversible bronchiectasis with lifelong consequences. However, detection and management require timely health-seeking by carers and effective management by clinicians. We aim to improve (a) carer health-seeking for chronic wet cough in their child and (b) management of chronic wet cough in children by clinicians. We hypothesise that implementing a culturally integrated program, which is informed by

barriers and facilitators identified by carers and health practitioners, will result in improved lung health of First Nations children, and in the future, a reduced the burden of bronchiectasis through the prevention of the progression of protracted bacterial bronchitis to bronchiectasis.

Methods: This study is a multi-centre, pseudorandomised, stepped wedge design. The intervention is the implementation of a program. The program has two components: a knowledge dissemination component and an implementation component. The implementation is adapted to each study site using a combined Aboriginal Participatory Action Research and an Implementation Science approach, guided by the Consolidated Framework of Implementation Research. There are three categories of outcome measures related to (i) health (ii) cost, and (iii) implementation. We will measure health-seeking as the proportion of parents seeking help for their child in a 6-month period before the intervention and the same 6-month period (i.e., the same six calendar months) thereafter. The parent-proxy, Cough-specific Quality of Life (PC-QoL) will be the primary health-related outcome measure.

Discussion: We hypothesise that a tailored intervention at each site will result in improved health-seeking for carers of children with a chronic wet cough and improved clinician management of chronic wet cough. In addition, we expect this will result in improved lung health outcomes for children with a chronic wet cough.

Trial registration: Australian New Zealand Clinical Trials Registry; ACTRN12622000430730 , registered 16 March 2022, Retrospectively registered.

Keywords: Chronic wet cough; First Nations children; Knowledge Translation; Protracted bacterial bronchitis.

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Conflict of interest statement

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

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2

Review

Neurosci Lett



. 2023 Jan 1;792:136934.

doi: 10.1016/j.neulet.2022.136934. Epub 2022 Oct 26.

Mini-review: Hypertussivity and allotussivity in chronic cough endotypes

[Jaclyn A Smith](#)¹, [Imran Satia](#)², [Huda Badri](#)³, [Paul Marsden](#)³

Affiliations expand

- PMID: 36309151
- DOI: [10.1016/j.neulet.2022.136934](https://doi.org/10.1016/j.neulet.2022.136934)

Abstract

In recent years our understanding of the neurophysiological basis of cough has increased substantially. In conjunction, concepts around the drivers of chronic coughing in patients have also significantly evolved. Increasingly it is recognised that dysregulation of the neuronal pathways mediating cough play an important role in certain phenotypes of chronic cough and therefore pathological processes affecting the nervous system are likely to represent key endotypes in patients. Taking inspiration from the study of neuropathic pain, the term hypertussia has been employed to describe the phenomenon of abnormal

excessive coughing in response to airway irritation and allotussia to describe coughing in response to stimuli not normally provoking cough. This review aims to summarise current clinical evidence supporting a role for the hyperexcitability of neuronal pathways contributing to chronic coughing and suggest how these might align with the clinical features observed in patients.

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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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J Clin Nurs

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. 2023 Jan;32(1-2):298-310.

doi: 10.1111/jocn.16234. Epub 2022 Jan 30.

Symptom clusters, associated factors and health-related quality of life in patients with chronic obstructive pulmonary disease: A structural equation modelling analysis

Affiliations expand

- PMID: 35098602
- DOI: [10.1111/jocn.16234](https://doi.org/10.1111/jocn.16234)

Abstract

Aims and objectives: To identify symptom clusters and develop a symptom cluster model among people living with chronic obstructive pulmonary disease (COPD).

Background: The examination of symptom clusters in COPD patients is an emerging field of scientific inquiry directed towards symptom management. However, no studies have modelled the relationships among symptom clusters, associated factors and health-related quality of life.

Design: A cross-sectional design with convenience sampling following STROBE guidelines.

Methods: Data were collected from 450 COPD participants in three university teaching hospitals. Participants were invited to complete a structured questionnaire comprised of a socio-demographic/clinical questionnaire, Integrated Palliative Care Outcome Scale and Clinical Respiratory Questionnaire. Exploratory factor analysis and confirmatory factor analysis were used to identify symptom clusters. Structural equation modelling was used to examine the proposed model.

Results: The respiratory related symptom cluster, psychological symptom cluster and cough-insomnia related symptom cluster were identified. The final model demonstrated a good fit with the data. Gender, stage of disease and monthly income were significant factors associated with symptom clusters. Respiratory related and cough-insomnia related symptom clusters had a direct negative impact on health-related quality of life, while the psychological symptom cluster was found to have a direct and indirect negative effect on health-related quality of life.

Conclusions: Final COPD symptom cluster model should serve as a framework to guide intervention research targeting symptom clusters to improve health-related quality of life of people living with COPD.

Relevance to clinical practice: Nurses should be especially attuned to identify those at most risk of facing a higher symptom burden in this case those who are female, have advanced stage COPD and/or lower income. During the clinical symptom assessment, nurses should pay attention to the close relationships among symptoms within a cluster to identify any 'trigger' symptom that could cause the development or exacerbation of other symptoms.

Keywords: chronic obstructive pulmonary disease; health-related quality of life; structural equation modelling; symptom assessment; symptom cluster.

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RHINITIS

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Eur Arch Otorhinolaryngol

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. 2022 Dec 31.

doi: 10.1007/s00405-022-07798-6. Online ahead of print.

Causal relationships between potential risk factors and chronic rhinosinusitis: a bidirectional two-sample Mendelian randomization study

[Zengxiao Zhang](#)^{1,2}, [Gongfei Li](#)³, [Longgang Yu](#)¹, [Jiaxin Jiang](#)⁴, [Ruixia Li](#)⁵, [Shizhe Zhou](#)², [Yan Jiang](#)^{6,7}

[Affiliations expand](#)

- PMID: 36585990
- DOI: [10.1007/s00405-022-07798-6](https://doi.org/10.1007/s00405-022-07798-6)

Abstract

Purpose: Smoking, alcohol consumption, allergic rhinitis (AR), asthma, and obesity are associated with chronic rhinosinusitis (CRS), albeit the causal relationships between them remain elusive. Therefore, we conducted a bidirectional two-sample Mendelian randomization (MR) study to investigate the bidirectional causal effects between these potential risk factors and CRS.

Methods: The data for daily cigarette consumption, age of smoking initiation, weekly alcohol consumption, AR, asthma, body mass index (BMI), and CRS were drawn from large sample size genome-wide association studies. Single-nucleotide polymorphisms associated with each exposure were considered instrumental variables in this study. We investigated causal effects by using the inverse-variance weighted (IVW) method with random effects, and weighted median and MR-Egger methods were used for sensitivity analyses. Pleiotropic effects were detected and corrected by the MR pleiotropy residual sum and outlier test and MR-Egger model.

Results: We found the causal effects of daily cigarette consumption (IVW, OR = 1.15, 95% CI 1.00-1.32, $p = 0.046$), AR (IVW, OR = 4.77, 95% CI 1.61-14.13, $p = 0.005$), asthma (IVW, OR = 1.45, 95% CI 1.31 - 1.60, $p < 0.001$), and BMI (IVW, OR = 1.05, 95% CI 1.00-1.09, $p = 0.028$) on CRS. Furthermore, we found a causal effect of CRS on asthma (IVW OR = 1.08, 95% CI 1.05-1.12, $p < 0.001$).

Conclusions: We confirmed the causal effects of daily cigarette consumption, AR, asthma, and BMI on CRS, and the causal effect of CRS on asthma, while no causal relationship between age of smoking initiation, weekly alcohol consumption, and CRS was found. These findings are expected to provide high-quality causal evidence for clinical practice and the pathogenesis of CRS and asthma.

Keywords: Causal relationship; Chronic rhinosinusitis; Mendelian randomization; Risk factors.

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J Allergy Clin Immunol

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. 2022 Dec 27;S0091-6749(22)02555-6.

doi: 10.1016/j.jaci.2022.11.025. Online ahead of print.

Environmental Justice and Allergic Disease: A Work Group Report of the AAAAI Environmental Exposure and Respiratory Health Committee and the Diversity, Equity and Inclusion Committee

[Allison J Burbank](#)¹, [Michelle L Hernandez](#)², [Akilah Jefferson](#)³, [Tamara T Perry](#)³, [Wanda Phipatanakul](#)⁴, [Jill Poole](#)⁵, [Elizabeth C Matsui](#)⁶

Affiliations expand

- PMID: 36584926
- DOI: [10.1016/j.jaci.2022.11.025](https://doi.org/10.1016/j.jaci.2022.11.025)

Abstract

Environmental justice is the concept that all people have the right to live in a healthy environment, to be protected against environmental hazards, and to participate in decisions affecting their communities. Communities of color and low-income populations live, work and play in environments with disproportionate exposure to hazards associated with allergic disease. This unequal distribution of hazards has contributed to health disparities and is largely the result of systemic racism that promotes segregation of neighborhoods, disinvestment in predominantly racial/ethnic minority neighborhoods, and discriminatory housing, employment and lending practices. The AAAAI Environmental Exposure and Respiratory Health (EERH) Committee and Diversity, Equity and Inclusion (DEI) Committee jointly developed this report to improve allergy/immunology specialists' awareness of environmental injustice, its roots in systemic racism, and its impact on health disparities in allergic disease. We present evidence supporting the relationship between exposure to environmental hazards, particularly at the neighborhood level, and the

disproportionately high incidence and poor outcomes from allergic diseases in marginalized populations. Achieving environmental justice requires investment in at-risk communities to increase access to safe housing, clean air and water, employment opportunities, education, nutrition, and healthcare. Through policies that promote environmental justice, we can achieve greater health equity in allergic disease.

Keywords: Environmental justice; allergen; allergic rhinitis; asthma; atopic dermatitis; ethnicity; health disparities; nutrition; obesity; pollution; psychosocial stress; race; segregation; systemic racism.

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3
Health Sci Rep



. 2022 Dec 24;6(1):e1015.

doi: 10.1002/hsr2.1015. eCollection 2023 Jan.

Associative factors for atopic dermatitis and other atopic diseases in middle-aged adults: A population-based birth cohort study among 5373 subjects

[Anna K Haarala](#)^{1,2}, [Suvi-Päivikki Sinikumpu](#)^{1,2}, [Jari Jokelainen](#)³, [Juha Pekkanen](#)^{4,5,6}, [Laura Huilaja](#)^{1,2}

Affiliations expand

- PMID: 36582624
- PMCID: [PMC9789389](#)

- DOI: [10.1002/hsr2.1015](https://doi.org/10.1002/hsr2.1015)

Free PMC article

Abstract

Background and aims: The study aimed to examine parental, longitudinal and current associative factors for atopic dermatitis (AD) and to compare those to other atopic diseases in 46-year-old adults.

Methods: Questionnaire data from the Northern Finland Birth Cohort 1966 study were used. To analyze allergic sensitization, skin prick tests ($n = 5373$) were performed for birch, timothy, cat, and house dust mite at age 46.

Results: Maternal (odds ratio [OR] 1.81; 95% confidence interval [CI] 1.25-2.59) and paternal allergy (OR 2.54; CI 1.76-3.64), sensitization to any of the four tested aeroallergens (OR 1.56; CI 1.04-2.30) as well as polysensitization (OR 3.04; CI 2.10-4.37) were associated with current AD. Living on a farm in infancy was negatively associated with allergic rhinitis, allergic conjunctivitis, and atopic multimorbidity. Current AD (OR 2.65; CI 1.44-4.60) and all atopic diseases associated with indoor air related symptoms. Current AD associated with other atopic diseases, most strongly with allergic rhinitis (OR 4.92; CI 3.92-6.22).

Conclusion: Current AD in a 46-year-old general population occurred frequently with allergic rhinitis, allergic conjunctivitis, and asthma in the Northern Finland Birth Cohort study 1966. Parental allergy and sensitization to common aeroallergens were found as shared associative factors for AD, allergic rhinitis, allergic conjunctivitis, and asthma. AD and other atopic diseases associated with symptoms related to poor indoor air quality. In daily practice, it is important to take these comorbidities into consideration when treating patients with AD.

Keywords: adult; allergic conjunctivitis; allergic rhinitis; asthma; atopic dermatitis; sensitization.

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Conflict of interest statement

The authors declare no conflict of interest.

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- [2 figures](#)

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Published Erratum

Allergy Asthma Clin Immunol

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. 2022 Dec 27;18(1):112.

doi: 10.1186/s13223-022-00754-3.

Correction: Fexofenadine: review of safety, efficacy and unmet needs in children with allergic rhinitis

[Eli O Meltzer](#)¹, [Nelson Augusto Rosario](#)², [Hugo Van Bever](#)³, [Luiz Lucio](#)⁴

Affiliations expand

- PMID: 36575521
- PMCID: [PMC9793548](#)
- DOI: [10.1186/s13223-022-00754-3](#)

Free PMC article

No abstract available

Erratum for

- [Fexofenadine: review of safety, efficacy and unmet needs in children with allergic rhinitis.](#)
Meltzer EO, Rosario NA, Van Bever H, Lucio L. Allergy Asthma Clin Immunol. 2021 Nov 2;17(1):113. doi: 10.1186/s13223-021-00614-6. PMID: 34727966 **Free PMC article.** Review.

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ORL J Otorhinolaryngol Relat Spec

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. 2022 Dec 27;1-9.

doi: 10.1159/000527885. Online ahead of print.

Progression of Rhinitis to Rhinosinusitis: A Cohort Study

[Bram van Schie](#)¹, [Joel J Vavrina](#)², [Michael B Soyka](#)³

Affiliations [expand](#)

- PMID: 36574765
- DOI: [10.1159/000527885](https://doi.org/10.1159/000527885)

Free article

Abstract

Introduction: Chronic rhinitis (CR) and rhinosinusitis are prevalent conditions affecting people all over the world. Their exact relationship is still not fully understood. We sought to find out, whether CR is a risk factor for chronic rhinosinusitis (CRS) and which main subgroup or other factors could be predisposing.

Methods: Patients with diagnosed CR between 2005 and 2010 were selected from the electronic medical record and were contacted by phone call. They were interviewed and screened for possible CRS using internationally approved questionnaires, e.g. NOSE-D and SNOT-20-GAV. Those with elevated scores were invited for a clinical examination.

Results: Of 113 patients available for statistical analysis (48/65 = f/m), mean age of 52 ± 15 years, 13 patients were diagnosed with CRS. Extrapolated for the total cohort of 334, calculated prevalence was 9.5%. No statistical significantly higher probability of developing CRS for either main subgroup of CR was found. Age of onset, prior surgery of the nose, and use of topical nasal treatments were associated with the development of CRS in multivariate analyses (OR = 0.1, 3.2, and 3.2, respectively).

Discussion/conclusions: Only a small number of rhinitis patients developed CRS, questioning the paradigm of CR being a clear risk factor for CRS.

Keywords: Age of onset; Chronic rhinitis; Chronic rhinosinusitis with/without polyps; Disease burden; Risk factor.

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6 Meta-Analysis

J Environ Sci (China)

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. 2023 Jan;123:306-316.

doi: 10.1016/j.jes.2022.04.026. Epub 2022 May 2.

Fine particulate matter and cardiorespiratory health in China: A

systematic review and meta-analysis of epidemiological studies

[Huihuan Luo](#)¹, [Qingli Zhang](#)¹, [Yue Niu](#)¹, [Haidong Kan](#)¹, [Renjie Chen](#)²

Affiliations expand

- PMID: 36521994
- DOI: [10.1016/j.jes.2022.04.026](https://doi.org/10.1016/j.jes.2022.04.026)

Abstract

This review aimed to systematically summarize the epidemiological literature on the cardiorespiratory effects of PM_{2.5} published during the 13th Five-Year Plan period (2016–2020) in China. Original articles published between January 1, 2016 and June 30, 2021 were searched in PubMed, Web of Science, the China National Knowledge Internet Database and Wanfang Database. Random- or fixed-effects models were used to pool effect estimates where appropriate. Of 8558 records identified, 145 met the full eligibility criteria. A 10 µg/m³ increase in short-term PM_{2.5} exposure was significantly associated with increases of 0.70%, 0.86%, 0.38% and 0.96% in cardiovascular mortality, respiratory mortality, cardiovascular morbidity, and respiratory morbidity, respectively. The specific diseases with significant associations included stroke, ischemic heart disease, heart failure, arrhythmia, chronic obstructive pulmonary disease, pneumonia and allergic rhinitis. The pooled estimates per 10 µg/m³ increase in long-term PM_{2.5} exposure were 15.1%, 11.9% and 21.0% increases in cardiovascular, stroke and lung cancer mortality, and 17.4%, 11.0% and 4.88% increases in cardiovascular, hypertension and lung cancer incidence respectively. Adverse changes in blood pressure, heart rate variability, systemic inflammation, blood lipids, lung function and airway inflammation were observed for either short-term or long-term PM_{2.5} exposure, or both. Collectively, we summarized representative exposure-response relationships between short- and long-term PM_{2.5} exposure and a wide range of cardiorespiratory outcomes applicable to China. The magnitudes of estimates were generally smaller in short-term associations and comparable in long-term associations compared with those in developed countries. Our findings are helpful for future standard revisions and policy formulation. There are still some notable gaps that merit further investigation in China.

Keywords: Air pollution; Cardiovascular system; Epidemiological studies; Fine particulate matter; Mortality Morbidity; Respiratory system.

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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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7

Review

Allergy

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. 2023 Jan;78(1):84-120.

doi: 10.1111/all.15578. Epub 2022 Dec 8.

Biomarkers associated with the development of comorbidities in patients with atopic dermatitis: A systematic review

[Conor Broderick](#)¹, [Stefanie Ziehfrend](#)², [Karin van Bart](#)³, [Bernd Arents](#)⁴, [Kilian Eyerich](#)^{2,5}, [Stephan Weidinger](#)⁶, [Joseph Rastrick](#)⁷, [Alexander Zink](#)^{2,5}, [Carsten Flohr](#)¹, [BIOMAP Consortium](#)

Affiliations expand

- PMID: 36366871
- DOI: [10.1111/all.15578](https://doi.org/10.1111/all.15578)

Abstract

Biomarkers associated with the development of comorbidities in atopic dermatitis (AD) patients have been reported, but have not yet been systematically reviewed. Seven electronic databases were searched, from database inception to September 2021. English language randomized controlled trials, prospective and retrospective cohort, and case-control studies that investigated the association between a biomarker and the development of comorbidities in AD patients were included. Two authors independently screened the records for eligibility, one extracted all data, and critically appraised the quality of studies and risk of bias. Fifty six articles met the inclusion criteria, evaluating 146 candidate biomarkers. The most frequently reported biomarkers were filaggrin mutations and allergen specific-IgE. Promising biomarkers include specific-IgE and/or skin prick tests predicting the development of asthma, and genetic polymorphisms predicting the occurrence of eczema herpeticum. The identified studies and biomarkers were highly heterogeneous, and associated with predominately moderate-to-high risk of bias across multiple domains. Overall, findings were inconsistent. High-quality studies assessing biomarkers associated with the development of comorbidities in people with AD are lacking. Harmonized datasets and independent validation studies are urgently needed.

Keywords: allergic rhinitis; asthma; atopic dermatitis; biomarker; comorbidities.

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Environ Res

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. 2023 Jan 1;216(Pt 3):114713.

Early-life exposure to air pollution associated with food allergy in children: Implications for 'one allergy' concept

[Xin Zhang](#)¹, [Chan Lu](#)², [Yuguo Li](#)³, [Dan Norbäck](#)⁴, [Padmini Murthy](#)⁵, [Radim J Sram](#)⁶, [Qihong Deng](#)⁷

Affiliations expand

- PMID: 36347392
- DOI: [10.1016/j.envres.2022.114713](https://doi.org/10.1016/j.envres.2022.114713)

Abstract

Background: The rapid increase of food allergy (FA) has become the "second wave" of allergy epidemic and is now a major global public health concern. Mounting evidence indicates that early life exposure to air pollution is associated with the "first wave" of allergy epidemic (including asthma, allergic rhinitis and eczema) in children, but little is known about its association with FA.

Objectives: We hypothesize FA has triple exposure pathways, gut-skin-airway, and investigate the effects of airway exposure to outdoor and indoor air pollution on childhood FA.

Methods: A cohort study of 2598 preschool children aged 3-6 years old was conducted in Changsha, China. The prevalence of FA was surveyed using a standard questionnaire by International Study of Asthma and Allergies in Childhood (ISAAC). Exposure to indoor air pollution was assessed by four indicators: new furniture, redecoration, mold or dampness, and window condensation. Exposure to outdoor air pollution was evaluated by the concentrations of PM10, SO2 and NO2, which were obtained from the monitored stations. Both prenatal and postnatal exposure windows were considered. The association between exposure to outdoor/indoor air pollution and childhood FA was estimated by multiple logistic regression models using odds ratio (OR) and a 95% confidence interval (CI).

Results: A total of 14.9% children reported FA. The prevalence was significantly associated with exposure to indoor air pollution, OR (95% CI) = 1.93 (1.35-2.75) for prenatal exposure to mold/dampness and 1.49 (1.07-2.10) and 1.41 (1.04-1.89) respectively for postnatal exposure to new furniture and window condensation. The prevalence of FA was also associated with prenatal and postnatal exposure to outdoor air pollution, particularly the traffic-related air pollutant NO2, with adjusted ORs (95% CIs) respectively 1.24 (1.00-1.54) and 1.38 (1.03-1.85) per interquartile range (IQR) increase. Sensitivity analysis showed that

the association between outdoor/indoor air pollution and childhood FA was significant only in young children aged 3-4 years.

Conclusion: Early-life exposure to high levels of outdoor and indoor air pollution in China due to the rapid economic growth and fast urbanization in the past decades may contribute to the rapid increase of food allergy (FA) in children. Our study indicates that, in addition to gut and skin, airway may be a new route of food sensitization. Air pollution leads to the first and second waves of allergy epidemics, suggesting a concept of 'one allergy' disease.

Keywords: Allergic diseases; One allergy; Traffic-related air pollution; Triple exposure hypothesis; Urbanization.

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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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Am J Rhinol Allergy

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. 2023 Jan;37(1):83-88.

doi: 10.1177/19458924221134835. Epub 2022 Nov 4.

The Objective Assessment of dry Nose

[Yifan Meng](#)^{1,2}, [Ying Jie](#)³, [Chengshuo Wang](#)^{1,2}, [Luo Zhang](#)^{1,2,4,5}

Affiliations expand

- PMID: 36330650
- DOI: [10.1177/19458924221134835](https://doi.org/10.1177/19458924221134835)

Abstract

Background: Dry nose (DN) is a common symptom in both patients with rhinitis and healthy individuals; however, it is often overlooked.

Objective: This study aimed to investigate the characteristics of and propose objective diagnostic criteria for DN.

Methods: This study was conducted from December, 2018 to October, 2021. Patients with complaints of a dry nasal cavity and normal controls were recruited consecutively from the allergy-rhinology outpatient clinic of Beijing TongRen Hospital. Questionnaires were completed by each participant during recruitment to record demographic data. DN test strips were used to evaluate the severity of DN. The length of the strip was recorded at 30 s, 1 min, 2 min, 3 min, 4 min, and 5 min, respectively. Nasal secretions were collected on sponges and allergic status was assessed based on serum sage levels.

Results: Twenty (13 men and 7 women) patients with DN and 100 (47 men and 53 women) controls were recruited for the study. The participants' ages ranged from 23 to 73 years (mean = 47.7 years). Nine of the 20 DN patients were diagnosed with vasomotor rhinitis. The weight of the sponges of DN patients was significantly lower than that of controls. At the last time point (5 min), the strips in the control group were significantly longer than those in the DN group. The reference range of 30 s, 1 min, 2 min, 3 min, 4 min, and 5 min of controls was 3.0 mm, 6.0 mm, 10.9 mm, 13.2 mm, 16.8 mm, and 17.0 mm, respectively.

Conclusions: Our study indicated that the strip length less than 17.0 mm at 5 min is a valuable reference for the diagnostic of DN in Beijing.

Keywords: age; characteristics; clinical; diagnosis; dry nose; nasal secretion; objective assessment; reference range; rhinitis; test strip.

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10

Am J Rhinol Allergy

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. 2023 Jan;37(1):65-73.

doi: 10.1177/19458924221133898. Epub 2022 Oct 20.

Effects of Combined Visible and Infrared Light Rhinophototherapy in Patients With Allergic Rhinitis

[Alper Koycu](#)¹, [Ceren Bas](#)¹, [Ugur H Musabak](#)², [Selim Sermed Erbek](#)¹, [Huseyin Samet Koca](#)³, [Seda Turkoglu Babakurban](#)¹, [Melike Bahcecitapar](#)⁴

Affiliations expand

- PMID: 36266929
- DOI: [10.1177/19458924221133898](https://doi.org/10.1177/19458924221133898)

Abstract

Background: Intranasal phototherapy offers an alternative treatment method for patients with allergic rhinitis who cannot benefit from intranasal corticosteroids and oral antihistamines. Different wavelengths have been tried with promising results.

Objective: In this present study, we aimed to investigate the effects of visible light-infrared light phototherapy on clinical improvements together with its cytologic effects in patients with allergic rhinitis.

Methods: Patients with confirmed allergic rhinitis were given a 4-week course of intranasal phototherapy treatment. Weekly symptom questionnaires were applied to monitor clinical effects. Nasal lavage specimens were obtained before the start and at the completion of the 4-week therapy. Fluorescence-activated cell sorting analyses of CD16⁺, CD24⁺, and CD 45⁺ cells were performed. Statistical analyses are performed of weekly changes in symptoms and cell counts.

Results: CD45⁺CD16^{high}CD24⁺ neutrophil count in nasal lavages decreased significantly whereas CD45⁺CD16^{dim/-}CD24⁺ eosinophil counts significantly increased and CD45⁺ granulocyte counts remained unchanged. Symptom scores including nasal itching, nasal discharge, nasal obstruction, sneezing, eye itching, throat itching, and ear itching all statistically decreased compared to baseline at the end of 4 weeks.

Conclusion: Four-week course of intranasal phototherapy with visible and infrared light leads to clinical improvement in allergic rhinitis patients.

Keywords: allergic rhinitis; allergy; device; flowcytometry; infrared; intranasal; light; phototherapy; red; reliever; visible.

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11

Am J Otolaryngol

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. 2023 Jan-Feb;44(1):103649.

doi: 10.1016/j.amjoto.2022.103649. Epub 2022 Oct 5.

Structured histopathology and laboratory evidence in nasal polyposis with different pathogenesis

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Affiliations expand

- PMID: 36257231

- DOI: [10.1016/j.amjoto.2022.103649](https://doi.org/10.1016/j.amjoto.2022.103649)

Abstract

Purpose: Non-steroidal anti-inflammatory drugs-exacerbated respiratory disease (NERD), intrinsic asthma, eosinophilic granulomatosis with polyangiitis (EGPA) and odontogenic sinusitis may be associated with nasal polyps. The aim of the study was to compare circulating inflammatory cells and structural histopathology of these groups of nasal polyposis.

Methods: We retrospectively evaluated 71 patients with nasal polyps stratified according to the above-mentioned pathogenesis. All patients underwent preoperative laboratory investigations and primary endoscopic sinus surgery. Surgical specimens were submitted to structured histopathological evaluation.

Results: The median tissue eosinophil count (cells/HPF) was significantly different between the considered groups of nasal polyposis ($p=0.0004$). The median of NERD sub-cohort was significantly higher than intrinsic asthma ($p=0.0030$), odontogenic CRS ($p=0.0001$) and EGPA ones ($p=0.0094$). Eosinophilic aggregates positive rate was significantly higher in NERD sub-cohort than in odontogenic CRS ($p=0.0072$), EGPA ($p=0.0497$) and asthma ($p=0.0188$) ones. EGPA sub-cohort had a higher neutrophil infiltrate positive rate than NERD ($p=0.0105$) and intrinsic asthma ones ($p=0.0040$). Odontogenic CRS sub-cohort had a higher neutrophil infiltrate positive rate than NERD ($p=0.0140$) and asthma ones ($p=0.0096$). EGPA sub-cohort had a higher presence of fibrosis than NERD ($p=0.0237$) and odontogenic CRS sub-cohort ($p=0.0107$). Odontogenic sub-cohort had a lower sub-epithelial edema positive rate than NERD ($p=0.0028$) and asthma ($p=0.0149$) ones.

Conclusions: Structural histopathology may identify nasal polyps histotypes with different morphological patterns. The identified histopathological features can facilitate the recognition of rational therapeutic and follow-up approaches that consider the tissue modifications associated with the response to drugs and surgery.

Keywords: Asthma; EGPA; NERD; Nasal polyps; Odontogenic chronic rhinosinusitis; Structured histopathology.

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Conflict of interest statement

Declaration of competing interest The authors have no conflicts of interest.

- [Cited by 1 article](#)

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12

Environ Res



. 2023 Jan 1;216(Pt 2):114538.

doi: 10.1016/j.envres.2022.114538. Epub 2022 Oct 15.

Early life exposure to outdoor air pollution and indoor environmental factors on the development of childhood allergy from early symptoms to diseases

[Chan Lu](#)¹, [Zijing Liu](#)², [Wenhui Yang](#)³, [Hongsen Liao](#)⁴, [Qin Liu](#)⁵, [Qin Li](#)⁶, [Qihong Deng](#)⁷

Affiliations expand

- PMID: 36252839
- DOI: [10.1016/j.envres.2022.114538](https://doi.org/10.1016/j.envres.2022.114538)

Abstract

Background: The prevalence of childhood allergies has increased during past decades leading to serious hospitalization and heavy burden worldwide, yet the key factors responsible for the onset of early symptoms and development of diagnosed diseases are unclear.

Objective: To explore the role of early life exposure to ambient air pollution and indoor environmental factors on early allergic symptoms and doctor diagnosed allergic diseases.

Methods: A retrospective cohort study of 2598 preschool children was conducted at 36 kindergartens in Changsha, China from September of 2011 to February of 2012. A questionnaire was developed to survey each child's early onset of allergic symptoms (wheeze and rhinitis-like symptoms) and doctor diagnosis of allergic diseases (asthma and rhinitis) as well as home environments. Each mother's and child's exposures to ambient air pollutants (PM₁₀, SO₂, and NO₂) and temperature were estimated for in utero and postnatal periods. The associations of early symptoms and diagnosed diseases with outdoor air pollution and indoor environmental variables were examined by logistic regression models.

Results: Childhood early allergic symptoms (33.9%) including wheeze (14.7%) and rhinitis-like symptoms (25.4%) before 2 years old were not associated with outdoor air pollution exposure but was significantly associated with maternal exposure of window condensation at home in pregnancy with ORs (95% CI) of 1.33 (1.11-1.59), 1.30 (1.01-1.67) and 1.27 (1.04-1.55) respectively, and was associated with new furniture during first year after birth with OR (95% CI) of 1.43 (1.02-2.02) for early wheeze. Childhood diagnosed allergic diseases (28.4%) containing asthma (6.7%) and allergic rhinitis (AR) (7.2%) were significantly associated with both outdoor air pollutants (mainly for SO₂ and NO₂) during first 3 years and indoor new furniture, redecoration, and window condensation. We found that sex, age, parental atopy, maternal productive age, environmental tobacco smoke (ETS), antibiotics use, economic stress, early and late introduction of complementary foods, and outdoor air pollution modified the effects of home environmental exposure in early life on early allergic symptoms and diagnosed allergic diseases.

Conclusion: Our study indicates that early life exposure to indoor environmental factors plays a key role in early onset of allergic symptoms in children, and further exposure to ambient air pollution and indoor environmental factors contribute to the later development of asthma and allergic rhinitis.

Keywords: Ambient air pollution; Antibiotics use; Childhood asthma and allergies; Complementary feeding; Early life exposure; Home environments.

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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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13

Review

Asian J Surg



. 2023 Jan;46(1):58-65.

doi: 10.1016/j.asjsur.2022.05.006. Epub 2022 May 17.

Diagnostic and therapeutic strategies of acute invasive fungal rhinosinusitis

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Affiliations expand

- PMID: 35589479
- DOI: [10.1016/j.asjsur.2022.05.006](https://doi.org/10.1016/j.asjsur.2022.05.006)

Free article

Abstract

Acute invasive fungal rhinosinusitis (AIFR) is a rare disease, but the prognosis is by no means ideal. Pathologically, fungal infection is not only located in the sinus cavity, but also invades the sinus mucosa and bone wall, the surrounding structures and tissues such as the orbit and anterior skull base are often compromised and are accompanied with intracranial and extracranial complications. Despite decades of efforts, acute invasive fungal rhinosinusitis remains a devastating disease, the mortality of the disease continues to hover around 50%. The main impediments to improving the prognosis of acute invasive fungal rhinosinusitis are the difficulties of early diagnosis and the rapid reversal of immune insufficiency. Moreover, aggressive surgery combined with systemic antifungal therapy are significant positive prognostic factors as well. Progress and standardization of AIFR

treatment protocols have been limited by the scarcity of the disease and the absence of published randomized studies. Therewith, how to improve the therapeutic outcome and reduce the mortality rate has always been a challenging clinical discussion. We have summarized the relevant case series and literature from the recent years, management with optimal diagnostic and curative strategies are reviewed.

Keywords: Antifungal therapy; Diabetes; Endoscopic sinus surgery; Invasive fungal rhinosinusitis; Neutropenia.

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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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BRONCHIECTASIS

1

Editorial

Ann Am Thorac Soc

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. 2023 Jan;20(1):26-27.

doi: 10.1513/AnnalsATS.202209-782ED.

Preventing Continuous Damage in Primary Ciliary Dyskinesia: Is Airway Inflammation a Potential Target?

[Dvir Gatt](#)¹, [Felix Ratjen](#)^{1,2,3}

Affiliations expand

- PMID: 36584988
- DOI: [10.1513/AnnalsATS.202209-782ED](#)

No abstract available

Comment on

- [Airway Inflammation in Children with Primary Ciliary Dyskinesia.](#)
Sagel SD, Kupfer O, Wagner BD, Davis SD, Dell SD, Ferkol TW, Hoppe JE, Rosenfeld M, Sullivan KM, Tiddens HAWM, Knowles MR, Leigh MW. *Ann Am Thorac Soc.* 2023 Jan;20(1):67-74. doi: 10.1513/AnnalsATS.202204-314OC.PMID: 35984413

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Publication types, MeSH termsexpand

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2
BMC Pulm Med

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. 2022 Dec 29;22(1):492.

doi: 10.1186/s12890-022-02219-0.

Change in health outcomes for First Nations children with chronic wet cough:

rationale and study protocol for a multi-centre implementation science study

[Pamela J Laird](#)^{1,2,3}, [Roz Walker](#)^{4,5,6}, [Gabrielle McCallum](#)⁷, [Maree Toombs](#)⁸, [Melanie Barwick](#)^{9,10}, [Peter Morris](#)⁷, [Robyn Aitken](#)^{7,11,12}, [Matthew Cooper](#)¹, [Richard Norman](#)¹³, [Bhavini Patel](#)¹⁴, [Gloria Lau](#)^{1,2}, [Anne B Chang](#)^{7,15,16}, [André Schultz](#)^{17,18,19}

Affiliations expand

- PMID: 36581812
- PMCID: [PMC9798941](#)
- DOI: [10.1186/s12890-022-02219-0](#)

Free PMC article

Abstract

Background: In children, chronic wet cough may be a sign of underlying lung disease, including protracted bacterial bronchitis (PBB) and bronchiectasis. Chronic (> 4 weeks in duration) wet cough (without indicators pointing to alternative causes) that responds to antibiotic treatment is diagnostic of PBB. Timely recognition and management of PBB can prevent disease progression to irreversible bronchiectasis with lifelong consequences. However, detection and management require timely health-seeking by carers and effective management by clinicians. We aim to improve (a) carer health-seeking for chronic wet cough in their child and (b) management of chronic wet cough in children by clinicians. We hypothesise that implementing a culturally integrated program, which is informed by barriers and facilitators identified by carers and health practitioners, will result in improved lung health of First Nations children, and in the future, a reduced the burden of bronchiectasis through the prevention of the progression of protracted bacterial bronchitis to bronchiectasis.

Methods: This study is a multi-centre, pseudorandomised, stepped wedge design. The intervention is the implementation of a program. The program has two components: a knowledge dissemination component and an implementation component. The implementation is adapted to each study site using a combined Aboriginal Participatory Action Research and an Implementation Science approach, guided by the Consolidated Framework of Implementation Research. There are three categories of outcome measures related to (i) health (ii) cost, and (iii) implementation. We will measure health-seeking as the proportion of parents seeking help for their child in a 6-month period before the intervention and the same 6-month period (i.e., the same six calendar months) thereafter. The parent-proxy, Cough-specific Quality of Life (PC-QoL) will be the primary health-related outcome measure.

Discussion: We hypothesise that a tailored intervention at each site will result in improved health-seeking for carers of children with a chronic wet cough and improved clinician management of chronic wet cough. In addition, we expect this will result in improved lung health outcomes for children with a chronic wet cough.

Trial registration: Australian New Zealand Clinical Trials Registry; ACTRN12622000430730 , registered 16 March 2022, Retrospectively registered.

Keywords: Chronic wet cough; First Nations children; Knowledge Translation; Protracted bacterial bronchitis.

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Conflict of interest statement

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

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Case Reports

Respirol Case Rep

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. 2022 Dec 12;11(1):e01072.

doi: 10.1002/rcr2.1072. eCollection 2023 Jan.

A left pulmonary artery sling with left bronchiectasis in an adult patient: A case report and review of literature

[Lin Lv](#)¹, [Xue Cheng](#)¹, [Xiaohui Yu](#)¹, [Chen Cui](#)¹, [Wenwen Ji](#)¹, [Na Wang](#)¹, [Tingting Li](#)¹, [Jia Liu](#)¹, [Zhihong Shi](#)¹

Affiliations expand

- PMID: 36523544
- PMCID: [PMC9744713](#)
- DOI: [10.1002/rcr2.1072](#)

Free PMC article

Abstract

Pulmonary artery sling (PAS) is a rare congenital vascular anomaly, and is usually diagnosed during the infantile or fetal period. Adult presentation of PAS is rare. We report a 55-year-old woman with left pulmonary artery sling and left lung bronchiectasis, performing as persistent shortness of breath, coronary computed tomography angiography (CTA) showed the aberrant left pulmonary artery emerging from the right pulmonary artery and crossing to the left between the trachea and oesophagus. We experienced a rare adult case with LPAS and left bronchiectasis, stressing the importance of the anatomic abnormalities in such cases.

Keywords: anomalous pulmonary artery; bronchiectasis; case report; pulmonary artery sling.

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Conflict of interest statement

None declared.

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

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4 Case Reports

Radiol Case Rep

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. 2022 Nov 19;18(1):416-420.

doi: 10.1016/j.radcr.2022.10.089. eCollection 2023 Jan.

Mucoid impaction of the bronchi (MIB) in a young man with no previous history of hypersensitivity

[Elham Askari](#)¹, [Kiarash Soltani](#)², [Sara Haseli](#)¹, [Shekoofeh Yaghmaei](#)³

Affiliations [expand](#)

- PMID: 36425388
- PMCID: [PMC9678965](#)
- DOI: [10.1016/j.radcr.2022.10.089](#)

Abstract

Mucoid impaction of the bronchi (MIB) is a specific form of proximal bronchiectasis characterized by obstruction and dilation of bronchi usually presented with thick mucoid plug. MIB mostly occurs as the manifestation of a hypersensitivity state in patients with bronchial asthma or in association with allergic bronchopulmonary aspergillosis (ABPA) and clinical overlap between MIB and ABPA can occur. MIB with no history of allergic background is not common and is less reported in the literature. In the following report we discuss a 39-year-old man with no previous history of allergy and atopy who initially presented with fever and shortness of breath. Further assessments demonstrated that the patient had a chronic endobronchial lesion and consolidation of the left lower lobe of the lung. A tissue biopsy reveals no malignant cells. Despite antibiotic therapy, the patient's symptoms persisted, and lobectomy was performed due to no clinical improvement. Even though gross pathology suggested endoluminal impaction, the patient didn't meet the ABPA diagnostic criteria.

Keywords: ABPA, Allergic bronchopulmonary aspergillosis; CT, Computed tomography; Chronic consolidation; Ig, Immunoglobulin; MIB; MIB, Mucoid impaction of the bronchi.

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

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Observational Study

Ann Am Thorac Soc

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. 2023 Jan;20(1):67-74.

doi: 10.1513/AnnalsATS.202204-314OC.

Airway Inflammation in Children with Primary Ciliary Dyskinesia

[Scott D Sagel](#)¹, [Oren Kupfer](#)¹, [Brandie D Wagner](#)², [Stephanie D Davis](#)³, [Sharon D Dell](#)⁴, [Thomas W Ferkol](#)⁵, [Jordana E Hoppe](#)¹, [Margaret Rosenfeld](#)⁶, [Kelli M Sullivan](#)⁷, [Harm A W M Tiddens](#)⁸, [Michael R Knowles](#)⁷, [Margaret W Leigh](#)³

Affiliations expand

- PMID: 35984413
- DOI: [10.1513/AnnalsATS.202204-314OC](https://doi.org/10.1513/AnnalsATS.202204-314OC)

Abstract

Rationale: The role of airway inflammation in disease pathogenesis in children with primary ciliary dyskinesia (PCD) is poorly understood. **Objectives:** We investigated relationships between sputum inflammation measurements, age, lung function, bronchiectasis, airway infection, and ultrastructural defects in children with PCD. **Methods:** Spontaneously expectorated sputum was collected from clinically stable children and adolescents with PCD ages 6 years and older participating in a multicenter, observational study. Sputum protease and inflammatory cytokine concentrations were correlated with age, lung function, and chest computed tomography measures of structural lung disease, whereas differences in concentrations were compared between ultrastructural defect categories and between those with and without detectable bacterial infection. **Results:** Sputum from 77 children with PCD (39 females [51%]; mean [standard deviation] age, 13.9 [4.9] yr; mean [standard deviation] forced expiratory volume in 1 second [FEV₁] % predicted, 80.8 [20.5]) was analyzed. Sputum inflammatory marker measurements, including neutrophil elastase activity, IL-1 β (interleukin-1 β), IL-8, and TNF- α (tumor necrosis factor α) concentrations, correlated positively with age, percentage of bronchiectasis, and percentage of total structural lung disease on computed tomography, and negatively with lung function. Correlations between neutrophil elastase concentrations and FEV₁ % predicted and percentage of bronchiectasis were -0.32 (95% confidence interval, -0.51 to -0.10) and 0.46 (0.14 to 0.69), respectively. Sputum neutrophil elastase, IL-1 β , and TNF- α concentrations were higher in those with detectable bacterial pathogens. Participants with absent inner dynein arm and microtubular disorganization had similar inflammatory profiles compared with participants with outer dynein arm

defects. **Conclusions:** In this multicenter pediatric PCD cohort, elevated concentrations of sputum proteases and cytokines were associated with impaired lung function and structural damage as determined by chest computed tomography, suggesting that sputum inflammatory measurements could serve as biomarkers in PCD.

Keywords: biomarkers; bronchiectasis; inflammation; lung function; sputum.

Comment in

- [Preventing Continuous Damage in Primary Ciliary Dyskinesia: Is Airway Inflammation a Potential Target?](#)

Gatt D, Ratjen F. *Ann Am Thorac Soc*. 2023 Jan;20(1):26-27. doi: 10.1513/AnnalsATS.202209-782ED.PMID: 36584988 No abstract available.

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Clin Imaging

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. 2023 Jan;93:106-112.

doi: 10.1016/j.clinimag.2022.03.006. Epub 2022 Mar 9.

[Radiographic features of pneumonitis in patients treated with immunotherapy compared to traditional chemotherapy for non-small cell lung cancer](#)

[Kathleen M Capaccione](#)¹, [Sophia Huang](#)², [Belinda D'souza](#)², [Jay Leb](#)², [Lyndon Luk](#)², [Jonathan Goldstein](#)², [Benjamin May](#)², [Aileen Deng](#)³, [Mary M Salvatore](#)²

Affiliations expand

- PMID: 35307225
- DOI: [10.1016/j.clinimag.2022.03.006](https://doi.org/10.1016/j.clinimag.2022.03.006)

Abstract

Background: Pneumonitis has been described as a side effect of immunotherapy as well as traditional chemotherapy. Although immune-related adverse event (IRAE) pneumonitis has been extensively characterized, the relationship between IRAE pneumonitis and pneumonitis secondary to chemotherapy is less clear. Here, we present the first analysis of radiographic features of pneumonitis secondary to immunotherapy compared to chemotherapy.

Methods: Using our radiology records system, we searched chest computed tomography (CT) reports for the term "pneumonitis". We evaluated medical records to establish chronicity of pneumonitis occurring after medication administration and excluded cases where radiation therapy appeared to be the cause of pneumonitis. We also obtained information regarding demographic, clinical, and treatment characteristics for comparison.

Results: Patients treated with immunotherapy demonstrated more specific features of pneumonitis including consolidation, ground glass opacities, septal thickening, traction bronchiectasis, and pulmonary nodules compared to those treated with chemotherapy. Immunotherapy treatment correlated with the development of pulmonary nodules ($p = 0.048$), and administration of more than one immunotherapy agent correlated with a greater incidence of development of nodules ($p = 0.050$). Radiographic features in patients treated with immunotherapy all decreased over time. Conversely, in patients treated with chemotherapy the incidence of ground glass opacities, traction bronchiectasis, pulmonary nodules, and mediastinal/hilar adenopathy increased over time.

Conclusions: IRAE-pneumonitis has distinct features and a distinct clinical course compared to pneumonitis secondary to chemotherapy. Importantly, IRAE-pneumonitis features decreased over time, suggesting that careful consideration of the benefit-risk ratio may allow for continuation of immunotherapy in some patients who develop pneumonitis.

Keywords: Chemotherapy; Immune-related adverse events (IRAEs); Immunotherapy; Lung cancer; Pneumonitis.

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Conflict of interest statement

Declaration of competing interest Mary M. Salvatore-Speaker and Consultant: Genentech, Boehringer Ingelheim.

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