

LIBRA JOURNAL CLUB

24 SEPTEMBER – 1 OCTOBER 2022

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COPD

1

Review

Curr Heart Fail Rep

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. 2022 Sep 30.

doi: 10.1007/s11897-022-00582-x. Online ahead of print.

[Defining the Phenotypes for Heart Failure With Preserved Ejection Fraction](#)

[Dane Rucker](#)¹, [Jacob Joseph](#)^{2,3}

Affiliations expand

- PMID: 36178663
- DOI: [10.1007/s11897-022-00582-x](https://doi.org/10.1007/s11897-022-00582-x)

Abstract

Purpose of review: Heart failure with preserved ejection fraction (HFpEF) imposes a significant burden on society and healthcare. The lack in efficacious therapies is likely due to the significant heterogeneity of HFpEF. In this review, we define various phenotypes based on underlying comorbidities or etiologies, discuss phenotypes arrived at by novel methods, and explore therapeutic targets.

Recent findings: A few studies have used machine learning methods to uncover sub-phenotypes within HFpEF in an unbiased manner based on clinical features, echocardiographic findings, and biomarker levels.

We synthesized the literature and propose three broad phenotypes: (1) young, with few comorbidities, usually obese and with low natriuretic peptide levels, (2) obese with substantive cardiometabolic burden and comorbidities and impaired ventricular relaxation, (3) old, multimorbid, with high rates of atrial fibrillation, renal and coronary artery disease, chronic obstructive pulmonary disease, and left ventricular hypertrophy. We also propose potential therapeutic strategies for these phenotypes.

Keywords: Biomarkers; Heart failure with preserved ejection fraction; Imaging; Machine learning; Phenotypes; Precision medicine.

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- [122 references](#)

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[Editorial](#)

Ann Am Thorac Soc

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. 2022 Oct;19(10):1638-1639.

doi: 10.1513/AnnalsATS.202206-525ED.

[The Paradox of Obesity in Patients with Chronic Obstructive Pulmonary Disease](#)

[Abebaw Mengistu Yohannes](#)¹

Affiliations [expand](#)

- PMID: 36178401
- DOI: [10.1513/AnnalsATS.202206-525ED](#)

No abstract available

Comment on

- [Physical Activity, Exercise Capacity, and Body Composition in U.S. Veterans with Chronic Obstructive Pulmonary Disease.](#)

Wan ES, Polak M, Goldstein RL, Lazzari AA, Kantorowski A, Garshick E, Moy ML. *Ann Am Thorac Soc.* 2022 Oct;19(10):1669-1676. doi: 10.1513/AnnalsATS.202111-1221OC.PMID: 35536690

SUPPLEMENTARY INFO

Publication typesexpand

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Editorial

Ann Am Thorac Soc

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. 2022 Oct;19(10):1636-1637.

doi: 10.1513/AnnalsATS.202207-609ED.

[To \$\beta\$ -Block or Not to \$\beta\$ -Block: That Is Still the Question in Chronic Obstructive Pulmonary Disease](#)

[Robert J Hancox](#)¹

Affiliations expand

- PMID: 36178400
- DOI: [10.1513/AnnalsATS.202207-609ED](#)

No abstract available

Comment on

- [Lung Function and the Risk of Exacerbation in the \$\beta\$ -Blockers for the Prevention of Acute Exacerbations of Chronic Obstructive Pulmonary Disease Trial.](#)

Parekh TM, Helgeson ES, Connett J, Voelker H, Ling SX, Lazarus SC, Bhatt SP, MacDonald DM, Mkorombindo T, Kunisaki KM, Fortis S, Kaminsky D, Dransfield MT. *Ann Am Thorac Soc.* 2022 Oct;19(10):1642-1649. doi: 10.1513/AnnalsATS.202109-1042OC.PMID: 35363600

SUPPLEMENTARY INFO

Publication types [expand](#)

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Am J Respir Cell Mol Biol

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. 2022 Sep 29.

doi: [10.1165/rcmb.2022-0131OC](https://doi.org/10.1165/rcmb.2022-0131OC). Online ahead of print.

[Chronic Obstructive Pulmonary Disease and Cigarette Smoke Lead to Dysregulated MAIT Cell Activation](#)

[Megan E Huber](#)¹, [Emily Larson](#)², [Taylor N Lust](#)¹, [Chelsea M Heisler](#)¹, [Melanie J Harrieff](#)^{3,4}

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 (CS) is the leading risk factor for COPD, the mechanisms driving development of COPD in only a subset of smokers are incompletely understood. Lung-resident mucosal-associated invariant T (MAIT) cells play a role in both microbial infections and inflammatory diseases. The role of MAIT cells in COPD pathology is unknown. Here, we examined MAIT cell activation in response to CS-exposed primary human bronchial epithelial cells (BEC) from healthy, COPD, or smoker donors. We observed significantly higher baseline MAIT cell responses to COPD BEC than healthy BEC. However, infected COPD BEC stimulated a smaller fold-increase in MAIT cell response despite increased microbial infection. For all donor groups, CS-exposed BEC elicited reduced MAIT cell responses; conversely, CS exposure increased ligand-mediated MR1 surface translocation in healthy and COPD BEC. Our data demonstrate MAIT cell activation is dysregulated in the context of CS and COPD. MAIT cells could contribute to CS- and COPD-associated inflammation through both inappropriate activation and reduced early recognition of bacterial infection, contributing to microbial persistence and COPD exacerbations.

FULL TEXT LINKS



[Proceed to details](#)

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Respirology

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. 2022 Sep 29.

doi: 10.1111/resp.14381. Online ahead of print.

[What have we learnt from real-life research in asthma and COPD? Standards and novel designs for the future](#)

[David Price](#)^{1,2,3}, [Thendral Uthaman](#)¹

Affiliations [expand](#)

- PMID: 36172950
- DOI: [10.1111/resp.14381](https://doi.org/10.1111/resp.14381)

No abstract available

Keywords: chronic obstructive pulmonary disease; clinical guidelines; real-life research; severe asthma.

- [13 references](#)

FULL TEXT LINKS



[Proceed to details](#)

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. 2022 Sep 28;22(1):1209.

doi: 10.1186/s12913-022-08586-y.

Burden of influenza hospitalization among high-risk groups in the United States

[Aimee M Near¹](#), [Jenny Tse²](#), [Yinong Young-Xu³](#), [David K Hong⁴](#), [Carolina M Reyes⁴](#)

Affiliations expand

- PMID: 36171601
- DOI: [10.1186/s12913-022-08586-y](https://doi.org/10.1186/s12913-022-08586-y)

Free article

Abstract

Background: Seasonal influenza poses a substantial clinical and economic burden in the United States and vulnerable populations, including the elderly and those with comorbidities, are at elevated risk for influenza-related medical complications.

Methods: We conducted a retrospective cohort study using the IQVIA PharMetrics® Plus claims database in two stages. In Stage 1, we identified patients with evidence of medically-attended influenza during influenza seasons from October 1, 2014 to May 31, 2018 (latest available data for Stage 1) and used a multivariable logistic regression model to identify patient characteristics that predicted 30-day influenza-related hospitalization. The findings from Stage 1 informed high-risk subgroups of interest for Stage 2, where we selected cohorts of influenza patients during influenza seasons from October 1, 2014 to March 1, 2019 and used 1:1 propensity score matching to patients without influenza with similar high-risk characteristics to compare influenza-attributable rates of all-cause hospital and emergency department (ED) visits during follow-up (30-day and in the index influenza season).

Results: In Stage 1, more than 1.6 million influenza cases were identified, of which 18,509 (1.2%) had a hospitalization. Elderly age was associated with 9 times the odds of hospitalization (≥ 65 years vs. 5-17 years; OR = 9.4, 95% CI 8.8-10.1) and select comorbidities were associated with 2-3 times the odds of hospitalization. In Stage 2, elderly influenza patients with comorbidities had 3 to 7 times higher 30-day hospitalization rates compared to matched patients without influenza, including patients with congestive heart failure (41.0% vs. 7.9%), chronic obstructive pulmonary disease (34.6% vs. 6.1%), coronary artery disease (22.8% vs. 3.8%), and late-stage chronic kidney disease (44.1% vs. 13.1%; all $p < 0.05$).

Conclusions: The risk of influenza-related complications is elevated in the elderly, especially those with certain underlying comorbidities, leading to excess healthcare resource utilization. Continued efforts, beyond currently available vaccines, are needed to reduce influenza burden in high-risk populations.

Keywords: Comorbidities; Health resource utilization; Hospitalization; Influenza; Real-world.

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- [39 references](#)

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS



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Rev Med Suisse



. 2022 Sep 28;18(797):1792-1797.

doi: 10.53738/REVMED.2022.18.797.1792.

[\[COPD: Guidelines for primary care physicians\]](#)

[Article in French]

[Mohammad Razban](#)^{#1}, [Manuel Diego Sztajzel](#)^{#1}, [Frédéric Lador](#)², [Johanna Sommer](#)³, [Dagmar M Haller](#)^{1,3}, [Thierry Favrod-Coune](#)¹

Affiliations expand

- PMID: 36170131
- DOI: [10.53738/REVMED.2022.18.797.1792](https://doi.org/10.53738/REVMED.2022.18.797.1792)

Abstract

in [English](#), [French](#)

Chronic obstructive pulmonary disease (COPD) is common and should be suspected in any patient with chronic dyspnea, cough, or sputum with a history of exposure to tobacco or harmful particles. Spirometry is used for diagnosis. Full evaluation includes the severity of obstruction and clinical data, following the Global

Initiative for Chronic Obstructive Lung Disease guidelines. Although the only treatments that have an impact on mortality are tobacco cessation, pulmonary rehabilitation and, for advanced disease, oxygen therapy, new symptomatic treatment have recently been made available. The duration of antibiotic and corticosteroid treatment for exacerbations has been shortened. The new diagnostic and management recommendations are summarized in this article.

Conflict of interest statement

Les auteurs n'ont déclaré aucun conflit d'intérêts en relation avec cet article.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

[Proceed to details](#)

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Thorax

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. 2022 Sep 27;thorax-2022-219451.

doi: 10.1136/thorax-2022-219451. Online ahead of print.

[Changing practice by changing pressures: a role for oscillating positive expiratory pressure in chronic obstructive pulmonary disease](#)

[Adam Lewis](#)¹, [Christian Robert Osadnik](#)²

Affiliations expand

- PMID: 36167723
- DOI: [10.1136/thorax-2022-219451](https://doi.org/10.1136/thorax-2022-219451)

No abstract available

Keywords: COPD Exacerbations; Cough/Mechanisms/Pharmacology.

Conflict of interest statement

Competing interests: AL declares working on lung volume reduction, remote vital sign monitoring, and singing for lung health clinical studies with Professor Nicholas Hopkinson, Dr Keir Philip, Dr Winston Banya, Mrs Sara Buttery and Professor Michael Polkey. CRO declares no conflict of interest.

FULL TEXT LINKS



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Respir Res

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. 2022 Sep 27;23(1):267.

doi: 10.1186/s12931-022-02191-7.

[Comorbidities and mortality risk in adults younger than 50 years of age with chronic obstructive pulmonary disease](#)

[Miguel J Divo¹](#), [José M Marin²](#), [Ciro Casanova³](#), [Carlos Cabrera Lopez⁴](#), [Victor M Pinto-Plata⁵](#), [Marta Marin-Oto⁶](#), [Francesca Polverino⁷](#), [Juan P de-Torres⁸](#), [Dean Billheimer⁹](#), [Bartolome R Celli¹⁰](#), [BODE Collaborative Group](#)

Collaborators, Affiliations expand

- PMID: 36167533
- PMCID: [PMC9516817](#)
- DOI: [10.1186/s12931-022-02191-7](#)

Free PMC article

Abstract

Rationale and objective: Patients with chronic obstructive pulmonary disease (COPD), usually diagnosed after the 6th decade, frequently suffer from comorbidities. Whether COPD patients 50 years or younger

(Young COPD) have similar comorbidities with the same frequency and mortality impact as aged-matched controls or older COPD patients is unknown.

Methods: We compared comorbidity number, prevalence and type in 3 groups of individuals with ≥ 10 pack-years of smoking: A Young (≤ 50 years) COPD group ($n = 160$), an age-balanced control group without airflow obstruction ($n = 125$), and Old (> 50 years) COPD group ($n = 1860$). We also compared survival between the young COPD and control subjects. Using Cox proportional model, we determined the comorbidities associated with mortality risk and generated Comorbidomes for the "Young" and "Old" COPD groups.

Results: The severity distribution by GOLD spirometric stages and BODE quartiles were similar between Young and Old COPD groups. After adjusting for age, sex, and pack-years, the prevalence of subjects with at least one comorbidity was 31% for controls, 77% for the Young, and 86% for older COPD patients. Compared to controls, "Young" COPDs' had a nine-fold increased mortality risk ($p < 0.0001$). "Comorbidomes" differed between Young and Old COPD groups, with tuberculosis, substance use, and bipolar disorders being distinct comorbidities associated with increased mortality risk in the Young COPD group.

Conclusions: Young COPD patients carry a higher comorbidity prevalence and mortality risk compared to non-obstructed control subjects. Young COPD differed from older COPD patients by the behavioral-related comorbidities that increase their risk of premature death.

Keywords: COPD in the young; Comorbidities.

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Conflict of interest statement

Drs Miguel J. Divo, José M. Marin, Ciro Casanova Macario, Carlos Cabrera Lopez, Victor M. Pinto-Plata, Marta Marin-Oto, Francesca Polverino, Juan P. de-Torres, Dean Billheimer, and Bartolome R. Celli declare that they have no conflict of interest.

Financial/nonfinancial disclosures: The authors have no relevant financial interest in this article.

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

SUPPLEMENTARY INFO

MeSH termsexpand

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Review

Am J Physiol Lung Cell Mol Physiol

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. 2022 Sep 27.

doi: 10.1152/ajplung.00549.2020. Online ahead of print.

Exercise adaptations in COPD: the pulmonary perspective

[Stine B Nymand](#)^{1,2}, [Jacob P Hartmann](#)^{1,2,3}, [Camilla K Rysø](#)¹, [Ninna Struck Rossen](#)², [Regitse Højgaard Christensen](#)^{1,4}, [Ulrik Winning Iepsen](#)^{1,5}, [Ronan M G Berg](#)^{1,2,3}

Affiliations expand

- PMID: 36165500
- DOI: [10.1152/ajplung.00549.2020](https://doi.org/10.1152/ajplung.00549.2020)

Abstract

In chronic obstructive pulmonary disease (COPD), the progressive loss of lung tissue is widely considered non-reversible. Thus, various treatment and rehabilitation schemes, including exercise-based pulmonary rehabilitation (PR) are thought to slow down but not reverse or halt the disease. Nonetheless, the adult lung conceals the intrinsic capacity for de novo lung tissue formation in the form of abundant progenitor/stem cell populations. In COPD, these maintain their differentiation potential but appear to be halted by a state of cellular senescence in the mesenchyme, which normally functions to support and coordinate their function. We propose that notably high-intensity interval training may improve the pulmonary gas exchange during exercise in patients with COPD by interrupting mesenchymal senescence, thus reestablishing adaptive angiogenesis. By means of this, the downward spiral of dyspnea, poor quality of life, physical inactivity, and early death often observed in COPD may be halted. If this is the case, the perception of the regenerative capacity of the lungs will be fundamentally changed, which will warrant future clinical trials on various exercise schemes and other treatments targeting the formation of new lung tissue in COPD.

Keywords: alveologenesis; diffusing capacity; exercise capacity; rehabilitation; stem cells.

SUPPLEMENTARY INFO

Publication types, Grant support expand

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Review

J Med Internet Res

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. 2022 Sep 26;24(9):e38030.

doi: 10.2196/38030.

[Digital Health Interventions for Depression and Anxiety Among People With Chronic Conditions: Scoping Review](#)

[Amika Shah](#)^{1,2}, [Neesha Hussain-Shamsy](#)^{1,2}, [Gillian Strudwick](#)^{1,3}, [Sanjeev Sockalingam](#)^{3,4,5}, [Robert P Nolan](#)^{5,6,7}, [Emily Seto](#)^{1,2}

Affiliations expand

- PMID: 36155409
- DOI: [10.2196/38030](https://doi.org/10.2196/38030)

Free article

Abstract

Background: Chronic conditions are characterized by their long duration (≥ 1 year), need for ongoing medical attention, and limitations in activities of daily living. These can often co-occur with depression and anxiety as common and detrimental comorbidities among the growing population living with chronic conditions. Digital health interventions (DHIs) hold promise in overcoming barriers to accessing mental health support for these individuals; however, the design and implementation of DHIs for depression and anxiety in people with chronic conditions are yet to be explored.

Objective: This study aimed to explore what is known in the literature regarding DHIs for the prevention, detection, or treatment of depression and anxiety among people with chronic conditions.

Methods: A scoping review of the literature was conducted using the Arksey and O'Malley framework. Searches of the literature published in 5 databases between 1990 and 2019 were conducted in April 2019 and updated in March 2021. To be included, studies must have described a DHI tested with, or designed

for, the prevention, detection, or treatment of depression or anxiety in people with common chronic conditions (arthritis, asthma, diabetes mellitus, heart disease, chronic obstructive pulmonary disease, cancer, stroke, and Alzheimer disease or dementia). Studies were independently screened by 2 reviewers against the inclusion and exclusion criteria. Both quantitative and qualitative data were extracted, charted, and synthesized to provide a descriptive summary of the trends and considerations for future research.

Results: Database searches yielded 11,422 articles across the initial and updated searches, 53 (0.46%) of which were included in this review. DHIs predominantly sought to provide treatment (44/53, 83%), followed by detection (5/53, 9%) and prevention (4/53, 8%). Most DHIs were focused on depression (36/53, 68%), guided (32/53, 60%), tailored to chronic physical conditions (19/53, 36%), and delivered through web-based platforms (20/53, 38%). Only 2 studies described the implementation of a DHI.

Conclusions: As a growing research area, DHIs offer the potential to address the gap in care for depression and anxiety among people with chronic conditions; however, their implementation in standard care is scarce. Although stepped care has been identified as a promising model to implement efficacious DHIs, few studies have investigated the use of DHIs for depression and anxiety among chronic conditions using such models. In developing stepped care, we outlined DHI tailoring, guidance, and intensity as key considerations that require further research.

Keywords: anxiety; chronic disease; depression; digital health; eHealth; mHealth; mental health; mobile health; multiple chronic conditions; psychiatry; telehealth; telemedicine.

©Amika Shah, Neesha Hussain-Shamsy, Gillian Strudwick, Sanjeev Sockalingam, Robert P Nolan, Emily Seto. Originally published in the Journal of Medical Internet Research (<https://www.jmir.org>), 26.09.2022.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS



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Curr Med Res Opin

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. 2022 Sep 26;1-9.

doi: 10.1080/03007995.2022.2129229. Online ahead of print.

[Variation in costs due to virtual switching from free- to fixed-triple LABA/LAMA/ICS combinations among COPD patients: an analysis using a primary care database](#)

[Francesco Lapi](#)¹, [Ettore Marconi](#)¹, [Francesco Lombardo](#)², [Claudio Micheletto](#)³, [Claudio Cricelli](#)²

Affiliations expand

- PMID: 36154352
- DOI: [10.1080/03007995.2022.2129229](https://doi.org/10.1080/03007995.2022.2129229)

Abstract

Chronic obstructive pulmonary disease (COPD) is a condition with a relevant clinical and economic burden. Only 10% to 40% of COPD patients reporting a regular use of respiratory medications, including those who suffered from severe disease being prescribed with triple combination therapy, nominally long-acting beta agonist (LABA), long-acting muscarinic antagonist (LAMA) and inhaled corticosteroid (ICS). The recent market launch of fixed-triple LABA/LAMA/ICS therapy might contribute to improve medications adherence and costs containment, given the use of a single instead of two or three inhalers. Few data are available on costs due to triple therapy prescribed for COPD. In specific, there are no studies providing data on the potential costs saving whether COPD patients exposed to free-triple combination therapy were switched to fixed-triple combination. In this respect, we simulated some scenarios of virtual switching and calculated the related cost savings.

Keywords: COPD; LABA/LAMA/ICS; costs; triple therapy.

FULL TEXT LINKS



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Ann Intensive Care

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. 2022 Sep 24;12(1):86.

doi: 10.1186/s13613-022-01060-2.

[Early antibiotic therapy is associated with a lower probability of successful liberation from mechanical ventilation in patients with severe acute exacerbation of chronic obstructive pulmonary disease](#)

Affiliations expand

- PMID: 36153438
- PMCID: [PMC9509513](#)
- DOI: [10.1186/s13613-022-01060-2](#)

Free PMC article

Abstract

Background: While antibiotic therapy is advocated to improve outcomes in acute exacerbation of chronic obstructive pulmonary disease (AECOPD) whenever mechanical ventilation is required, the evidence relies on small studies carried out before the era of widespread antibiotic resistance. Furthermore, the impact of systematic antibiotic therapy on successful weaning from mechanical ventilation was never investigated accounting for the competitive risk of death. The aim of the study was to assess whether early antibiotic therapy (eABT) increases successful mechanical ventilation weaning probability as compared to no eABT, in patients with AECOPD without pneumoniae, using multivariate competitive risk regression.

Methods: Retrospective analysis of patients admitted in 2 intensive care units (ICU) from 2012 to 2020 for AECOPD without pneumonia and requiring mechanical ventilation. eABT was defined as any anti-bacterial chemotherapy introduced during the first 24 h after ICU admission. The primary outcomes were the adjusted subdistribution hazard ratio (SHR) of the probability of being successfully weaned from mechanical ventilation (i.e. non-invasive and invasive ventilation) according to eABT status and accounting for the competitive risk of death.

Results: Three hundred and ninety-one patients were included, of whom 66% received eABT. eABT was associated with a lower probability of successful liberation from mechanical ventilation when accounting for the competing risk of death in multivariate analyses (SHR 0.71 [95% confidence interval, 0.57-0.89], $p < 0.01$), after adjustment with covariates of disease severity. This association was present in all subgroups except in patients under invasive mechanical ventilation on ICU day-1, in patients with ICU day-1 worst $\text{PaCO}_2 > 74$ torr (median value) and in patients with a documented bacterial bronchitis at ICU admission. Ventilator-free days at day 28, ICU-free days at day 28 and invasive mechanical ventilation-free days at day 28, were significantly lower in the eABT group, while there was no significant difference in mortality at day 28 between patients who received eABT and those who did not.

Conclusions: eABT was independently associated with a lower probability of being successfully weaned from mechanical ventilation, suggesting that the clinician decision to overrule systematic administration of eABT was not associated with a detectable harm in AECOPD ICU patients without pneumonia.

Keywords: Acute exacerbation; COPD; Chronic obstructive pulmonary disease; Mechanical ventilation; Ventilation weaning.

Conflict of interest statement

All authors, except one, have declared no conflicts of interest, financial or otherwise. JCR reported study funding by Hamilton Medical (Suisse) and a lecture compensated by Gilead Sciences (France), unrelated to the present work.

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

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Review

Eur Respir Rev

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. 2022 Sep 20;31(165):220076.

doi: 10.1183/16000617.0076-2022. Print 2022 Sep 30.

[Effectiveness of home-based pulmonary rehabilitation: systematic review and meta-analysis](#)

[Md Nazim Uzzaman](#)¹, [Dhiraj Agarwal](#)², [Soo Chin Chan](#)³, [Julia Patrick Engkasan](#)³, [G M Monsur Habib](#)⁴, [Nik Sherina Hanafi](#)³, [Tracy Jackson](#)¹, [Paul Jebaraj](#)⁵, [Ee Ming Khoo](#)³, [Fatim Tahirah Mirza](#)⁶, [Hilary Pinnock](#)¹, [Ranita Hisham Shunmugam](#)⁷, [Roberto A Rabinovich](#)⁸

Affiliations expand

- PMID: 36130789
- DOI: [10.1183/16000617.0076-2022](https://doi.org/10.1183/16000617.0076-2022)

Free article

Abstract

Introduction: Despite proven effectiveness for people with chronic respiratory diseases, practical barriers to attending centre-based pulmonary rehabilitation (centre-PR) limit accessibility. We aimed to review the clinical effectiveness, components and completion rates of home-based pulmonary rehabilitation (home-PR) compared to centre-PR or usual care.

Methods and analysis: Using Cochrane methodology, we searched (January 1990 to August 2021) six electronic databases using a PICOS (population, intervention, comparison, outcome, study type) search strategy, assessed Cochrane risk of bias, performed meta-analysis and narrative synthesis to answer our objectives and used the Grading of Recommendations, Assessment, Development and Evaluations framework to rate certainty of evidence.

Results: We identified 16 studies (1800 COPD patients; 11 countries). The effects of home-PR on exercise capacity and/or health-related quality of life (HRQoL) were compared to either centre-PR (n=7) or usual care (n=8); one study used both comparators. Compared to usual care, home-PR significantly improved exercise capacity (standardised mean difference (SMD) 0.88, 95% CI 0.32-1.44; p=0.002) and HRQoL (SMD -0.62, 95% CI -0.88--0.36; p<0.001). Compared to centre-PR, home-PR showed no significant difference in exercise capacity (SMD -0.10, 95% CI -0.25-0.05; p=0.21) or HRQoL (SMD 0.01, 95% CI -0.15-0.17; p=0.87).

Conclusion: Home-PR is as effective as centre-PR in improving functional exercise capacity and quality of life compared to usual care, and is an option to enable access to pulmonary rehabilitation.

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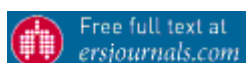
Conflict of interest statement

Conflict of interest: M.N. Uzzaman has nothing to disclose. Conflict of interest: D. Agarwal has nothing to disclose. Conflict of interest: S.C. Chan has nothing to disclose. Conflict of interest: J. Patrick Engkasan has nothing to disclose. Conflict of interest: G.M.M. Habib owns a Pulmonary Rehabilitation clinic in Bangladesh. Conflict of interest: N.S. Hanafi has nothing to disclose. Conflict of interest: T. Jackson has nothing to disclose. Conflict of interest: P. Jebaraj has nothing to disclose. Conflict of interest: E.M. Khoo reports grants from UK National Institute for Health Research (NIHR) Global Health Research Unit, during the conduct of the study; personal fees from AstraZeneca, personal fees and non-financial support from GlaxoSmithKline plc, and grants from Seqirus UK Ltd, and is President of the International Primary Care Respiratory Group, UK, outside the submitted work. Conflict of interest: F.T. Mirza has nothing to disclose. Conflict of interest: H. Pinnock reports grants from National Institute of Health Research (16/136/109 (2017-2021), during the conduct of the study. Conflict of interest: R.H. Shunmugam has nothing to disclose. Conflict of interest: R.A. Rabinovich has nothing to disclose.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS



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Observational Study

Respir Med

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. 2022 Oct;202:106982.

doi: 10.1016/j.rmed.2022.106982. Epub 2022 Sep 9.

Luminal mucus plugs are spatially associated with airway wall thickening in severe COPD and asthma: A single-centered, retrospective, observational study

[Cecilia Tran](#)¹, [Gaurav Veer Singh](#)², [Ehsan Haider](#)³, [Colm Boylan](#)³, [Carmen Venegas](#)⁴, [Shaista Riaz](#)⁵, [Suad Al Duwaiki](#)⁵, [Moustafa Yehia](#)⁵, [Terence Ho](#)⁶, [Parameswaran Nair](#)⁶, [Sarah Svenningsen](#)⁶, [Miranda Kirby](#)⁷

Affiliations expand

- PMID: 36116144
- DOI: [10.1016/j.rmed.2022.106982](https://doi.org/10.1016/j.rmed.2022.106982)

Abstract

Background: Airway wall thickening and excess airway mucus occur in asthma and chronic obstructive pulmonary disease (COPD), but few studies have investigated the relationship between them. Our objective was to determine the association between computed tomography (CT) airway wall thickening in segmental airways proximal to airways with or without mucus plugging in patients with asthma and COPD.

Methods: Mucus plugging was scored using a CT bronchopulmonary segment-based scoring system in asthma and COPD patients. For each of the 19 segmental airways, a mucus plug was defined as complete occlusion of one or more of the daughter branches (sub-segmental airways) by mucus. CT airway measurements were generated for each of the 19 segmental airways: wall-area-percentage (WA%), lumen area (LA), and total airway count (TAC) (VIDA Diagnostics Inc.). Multivariable logistic regression models were constructed for the presence of mucus plugs with corresponding CT measurement and adjusted by covariates; each of the 19 segments was treated as a nested variable.

Results: A total of 33 participants were evaluated. Participants had a mean age of 60 ± 15 yrs and there were $n = 14$ (42%) males. There were 16 (48%) participants with a diagnosis of asthma and 17 (52%) with a COPD diagnosis. The mean FEV_1 was $53 \pm 21\%$ pred and FEV_1/FVC was $54 \pm 15\%$. The mean mucus score in all participants was 15 ± 4 (min = 0, max = 19). Multivariable logistic regression analysis showed the presence of airway mucus was significantly associated with increased CT WA% ($\beta = 7.30$, $p = 0.004$) and reduced TAC ($\beta = -0.06$, $p = 0.045$).

Conclusions: There was increased airway wall thickness and reduced airway counts on CT in segments where there was a distal mucus plug compared to segments without mucus plugs in asthma and COPD.

Keywords: Airway wall thickening; Asthma; COPD; Computed tomography (CT); Imaging; Mucus plugs.

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Conflict of interest statement

Declaration of competing interest TH reports grants from Fisher and Paykel and personal fees from Sanofi, outside the submitted work. PN reports grants from AstraZeneca, Teva, Roche, Novartis, Sanofi and Foresee, and personal fees from AstraZeneca, Teva, Roche, Novartis, Merck and Equillium, outside the submitted work. SS reports grants from Cyclomedica and personal fees from AstraZeneca, Novartis, Polarean, and Arrowhead Pharmaceuticals, all outside the submitted work. All other authors do not have any potential conflicts of interest to declare.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Respir Med

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. 2022 Oct;202:106971.

doi: 10.1016/j.rmed.2022.106971. Epub 2022 Aug 30.

[Pulmonary arterial pruning is associated with CT-derived bronchiectasis progression in smokers](#)

[Wojciech R Dolliver](#)¹, [Wei Wang](#)², [Pietro Nardelli](#)³, [Farbod N Rahaghi](#)¹, [Jose L Orejas](#)¹, [Diego J Maselli](#)⁴, [Andrew Yen](#)⁵, [Kendra Young](#)⁶, [Gregory Kinney](#)⁶, [Raul San José Estépar](#)³, [Alejandro A Diaz](#)⁷

Affiliations expand

- PMID: 36116143
- DOI: [10.1016/j.rmed.2022.106971](https://doi.org/10.1016/j.rmed.2022.106971)

Abstract

Loss of small pulmonary arteries measured as the ratio of blood vessel volume in arteries $<5 \text{ mm}^2$ in cross-section to total arterial blood vessel volume (BV5a/TBVa), with lower values indicating more pruning, was associated with 5-yr progressing CT-derived bronchiectasis in smokers (Odds Ratio (OR) [95% Confidence interval], 1.28 [1.07-1.53] per 5% lower BV5a/TBVa, $P = 0.007$). Corresponding results in smokers with COPD were: OR 1.45 [1.11-1.89] per 5% lower BV5a/TBVa, $P = 0.007$. The results support a vascular factor for structural progression of bronchiectasis.

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Conflict of interest statement

Declaration of competing interest Drs. Dolliver, Wang, Nardelli, Rahaghi, Orejas, Maselli, Yen, Young, and Kinney have no disclosures to declare. Dr. San Jose, cofounder and stockholder of Quantitative Imaging Solutions; speaker fees from Chiesa; consulting fees from Leuko Labs; royalties from Imbio; Dr. Diaz, speaker fees from Boehringer Ingelheim.

SUPPLEMENTARY INFO

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Respir Med

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. 2022 Oct;202:106967.

doi: 10.1016/j.rmed.2022.106967. Epub 2022 Aug 27.

[Effectiveness of pulmonary rehabilitation in individuals with Chronic Obstructive Pulmonary Disease according to inhaled therapy: The Maugeri study](#)

[Michele Vitacca](#)¹, [Mara Paneroni](#)², [Antonio Spanevello](#)³, [Piero Ceriana](#)⁴, [Bruno Balbi](#)⁵, [Beatrice Salvi](#)², [Nicolino Ambrosino](#)⁶

Affiliations expand

- PMID: 36115316

- DOI: [10.1016/j.rmed.2022.106967](https://doi.org/10.1016/j.rmed.2022.106967)

Abstract

Background and aim: Real-life studies report discordant prescribing of inhaled triple therapy (TT) among individuals with COPD. Guidelines recommend pulmonary rehabilitation (PR) for persistent breathlessness and/or exercise limitation. This real-life study aimed to assess the effects of in-patient PR in individuals under TT as compared to other inhaled therapies (no TT).

Methods: Multicentric, retrospective analysis of data from individuals admitted to in-hospital PR. Baseline characteristics were recorded and lung function was assessed. Outcome measures were: 6-min walking test (6MWT: primary outcome), Medical Research Council (MRC) scale for dyspnoea, and COPD assessment test (CAT).

Results: Data of pre and post program 6MWT of 1139 individuals were available. Pulmonary rehabilitation resulted in significant improvement in 6MWT in both groups, however, the effect size (by 54.3 ± 69.7 vs 42.5 ± 64.2 m, $p = 0.004$) and proportion of individuals reaching the minimal clinically important difference (MCID) of 6MWT (64.2%, vs 54.3%, $p = 0.001$) were higher in TT group. Both groups significantly improved also the other outcome measures. The significant independent predictors of reaching the MCID of 6MWT were hospital provenience, TT use, and high eosinophils count.

Conclusion: Pulmonary rehabilitation results in significant benefits in individuals with COPD irrespective of the use of TT. However, individuals under TT report larger benefits in exercise tolerance than those under no TT.

Keywords: Airflow limitation; Bronchodilators; CAT; COPD triple therapy; Dyspnoea; Exercise capacity; Exercise training; Inhaled steroids.

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Conflict of interest statement

Declaration of competing interest The authors have no conflict of interest to disclose related to this manuscript.

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MeSH terms, Substancesexpand

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N Engl J Med

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. 2022 Sep 29;387(13):1230-1231.

doi: 10.1056/NEJMe2210347. Epub 2022 Sep 4.

[RETHINCKing COPD - Bronchodilators for Symptomatic Tobacco-Exposed Persons with Preserved Lung Function?](#)

[Don D Sin](#)¹

Affiliations expand

- PMID: 36066080
- DOI: [10.1056/NEJMe2210347](https://doi.org/10.1056/NEJMe2210347)

No abstract available

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Randomized Controlled Trial

N Engl J Med

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. 2022 Sep 29;387(13):1173-1184.

doi: 10.1056/NEJMoa2204752. Epub 2022 Sep 4.

Bronchodilators in Tobacco-Exposed Persons with Symptoms and Preserved Lung Function

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Collaborators, Affiliations expand

- PMID: 36066078
- DOI: [10.1056/NEJMoa2204752](https://doi.org/10.1056/NEJMoa2204752)

Abstract

Background: Many persons with a history of smoking tobacco have clinically significant respiratory symptoms despite an absence of airflow obstruction as assessed by spirometry. They are often treated with medications for chronic obstructive pulmonary disease (COPD), but supporting evidence for this treatment is lacking.

Methods: We randomly assigned persons who had a tobacco-smoking history of at least 10 pack-years, respiratory symptoms as defined by a COPD Assessment Test score of at least 10 (scores range from 0 to 40, with higher scores indicating worse symptoms), and preserved lung function on spirometry (ratio of forced expiratory volume in 1 second [FEV₁] to forced vital capacity [FVC] ≥0.70 and FVC ≥70% of the predicted value after bronchodilator use) to receive either indacaterol (27.5 μg) plus glycopyrrolate (15.6 μg) or placebo twice daily for 12 weeks. The primary outcome was at least a 4-point decrease (i.e., improvement) in the St. George's Respiratory Questionnaire (SGRQ) score (scores range from 0 to 100, with higher scores indicating worse health status) after 12 weeks without treatment failure (defined as an increase in lower respiratory symptoms treated with a long-acting inhaled bronchodilator, glucocorticoid, or antibiotic agent).

Results: A total of 535 participants underwent randomization. In the modified intention-to-treat population (471 participants), 128 of 227 participants (56.4%) in the treatment group and 144 of 244 (59.0%) in the placebo group had at least a 4-point decrease in the SGRQ score (difference, -2.6 percentage points; 95% confidence interval [CI], -11.6 to 6.3; adjusted odds ratio, 0.91; 95% CI, 0.60 to 1.37; P = 0.65). The mean change in the percent of predicted FEV₁ was 2.48 percentage points (95% CI, 1.49 to 3.47) in the treatment group and -0.09 percentage points (95% CI, -1.06 to 0.89) in the placebo group, and the mean change in the inspiratory capacity was 0.12 liters (95% CI, 0.07 to 0.18) in the treatment group and 0.02 liters (95% CI, -0.03 to 0.08) in the placebo group. Four serious adverse events occurred in the treatment group, and 11 occurred in the placebo group; none were deemed potentially related to the treatment or placebo.

Conclusions: Inhaled dual bronchodilator therapy did not decrease respiratory symptoms in symptomatic, tobacco-exposed persons with preserved lung function as assessed by spirometry. (Funded by the National Heart, Lung, and Blood Institute and others; RETHINC ClinicalTrials.gov number, [NCT02867761](https://clinicaltrials.gov/ct2/show/study/NCT02867761).)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated data, Grant supportexpand

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Respirology

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. 2022 Oct;27(10):810-811.

doi: 10.1111/resp.14350. Epub 2022 Aug 30.

[World Lung Day 2022-Lung health for all](#)

[David Chi-Leung Lam](#)¹

Affiliations expand

- PMID: 36039546
- DOI: [10.1111/resp.14350](https://doi.org/10.1111/resp.14350)

Free article

No abstract available

Keywords: COPD; air pollution; asthma; lung cancer; pneumonia; tobacco; tuberculosis.

- [7 references](#)

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS

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Review

Eur Respir Rev

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. 2022 Aug 23;31(165):220042.

doi: 10.1183/16000617.0042-2022. Print 2022 Sep 30.

[Does pulmonary rehabilitation address treatable traits? A systematic review](#)

[Anne E Holland](#)^{1,2,3}, [Bruna Wageck](#)⁴, [Mariana Hoffman](#)⁵, [Annemarie L Lee](#)^{3,6,7}, [Arwel W Jones](#)⁵

Affiliations expand

- PMID: 36002168
- DOI: [10.1183/16000617.0042-2022](https://doi.org/10.1183/16000617.0042-2022)

Free article

Abstract

Background: There is growing interest in a "treatable traits" approach to pulmonary rehabilitation in chronic airways disease. The frequency with which pulmonary rehabilitation programmes address treatable traits is unknown.

Methods: Randomised controlled trials of pulmonary rehabilitation compared to usual care in patients with stable chronic airways disease were included. The components of pulmonary rehabilitation delivered were extracted and mapped to treatable traits in pulmonary, extrapulmonary and behavioural/lifestyle domains. Meta-analysis was used to evaluate the impact of addressing >1 treatable trait on exercise capacity and health-related quality of life (HRQoL).

Results: 116 trials were included (6893 participants). Almost all pulmonary rehabilitation programmes addressed deconditioning (97% of trials). The most commonly addressed extrapulmonary traits were nutritional status (obesity and cachexia, 18% each) and mood disturbance (anxiety and depression, 10%

each). Behavioural/lifestyle traits most frequently addressed were nonadherence (46%), poor inhalation technique (24%) and poor family/social support (19%). Exercise capacity and HRQoL outcomes did not differ between studies that addressed deconditioning alone and those that targeted additional traits, but heterogeneity was high.

Conclusion: Aside from deconditioning, treatable traits are infrequently addressed in existing trials of pulmonary rehabilitation. The potential of the treatable traits approach to improve pulmonary rehabilitation outcomes remains to be explored.

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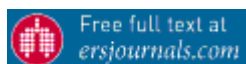
Conflict of interest statement

Provenance: Submitted article, peer reviewed. Conflict of interest: A.E. Holland, B. Wageck, M. Hoffman, A.L. Lee and A.W. Jones have no conflicts of interest to declare.

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Publication types, MeSH termsexpand

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[Review](#)

Eur Respir Rev

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. 2022 Aug 10;31(165):220059.

doi: 10.1183/16000617.0059-2022. Print 2022 Sep 30.

[Air pollution as an early determinant of COPD](#)

[Zhuylu Lu](#)¹, [Patrice Coll](#)², [Bernard Maitre](#)^{1,3}, [Ralph Epaud](#)^{1,4}, [Sophie Lanone](#)⁵

Affiliations expand

- PMID: 35948393

- DOI: [10.1183/16000617.0059-2022](https://doi.org/10.1183/16000617.0059-2022)

Free article

Abstract

COPD is a progressive and debilitating disease often diagnosed after 50 years of age, but more recent evidence suggests that its onset could originate very early on in life. In this context, exposure to air pollution appears to be a potential contributor. Although the potential role of air pollution as an early determinant of COPD is emerging, knowledge gaps still remain, including an accurate qualification of air pollutants (number of pollutants quantified and exact composition) or the "one exposure-one disease" concept, which might limit the current understanding. To fill these gaps, improvements in the field are needed, such as the use of atmosphere simulation chambers able to realistically reproduce the complexity of air pollution, consideration of the exposome, as well as improving exchanges between paediatricians and adult lung specialists to take advantage of reciprocal expertise. This review should lead to a better understanding of the current knowledge on air pollution as an early determinant of COPD, as well as identify the existing knowledge gaps and opportunities to fill them. Hopefully, this will lead to better prevention strategies to scale down the development of COPD in future generations.

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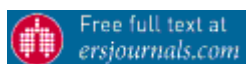
Conflict of interest statement

Conflict of interest: None of the authors have any conflict of interest to declare.

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Publication types, MeSH terms, Substancesexpand

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Eur J Intern Med

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. 2022 Oct;104:66-72.

doi: 10.1016/j.ejim.2022.07.019. Epub 2022 Jul 31.

[A machine learning approach to characterize patients with asthma exacerbation attending an acute care setting](#)

[Maria D'Amato](#)¹, [Pasquale Ambrosino](#)², [Francesca Simioli](#)³, [Sarah Adamo](#)⁴, [Anna Agnese Stanziola](#)³, [Giovanni D'Addio](#)⁵, [Antonio Molino](#)³, [Mauro Maniscalco](#)⁶

Affiliations expand

- PMID: 35922367
- DOI: [10.1016/j.ejim.2022.07.019](https://doi.org/10.1016/j.ejim.2022.07.019)

Abstract

Background: One of the main problems in poorly controlled asthma is the access to the Emergency Department (ED). Using a machine learning (ML) approach, the aim of our study was to identify the main predictors of severe asthma exacerbations requiring hospital admission.

Methods: Consecutive patients with asthma exacerbation were screened for inclusion within 48 hours of ED discharge. A k-means clustering algorithm was implemented to evaluate a potential distinction of different phenotypes. K-Nearest Neighbor (KNN) as instance-based algorithm and Random Forest (RF) as tree-based algorithm were implemented in order to classify patients, based on the presence of at least one additional access to the ED in the previous 12 months.

Results: To train our model, we included 260 patients (31.5% males, mean age 47.6 years). Unsupervised ML identified two groups, based on eosinophil count. A total of 86 patients with eosinophiles ≥ 370 cells/ μ L were significantly older, had a longer disease duration, more restrictions to daily activities, and lower rate of treatment compared to 174 patients with eosinophiles < 370 cells/ μ L. In addition, they reported lower values of predicted FEV₁ ($64.8 \pm 12.3\%$ vs. $83.9 \pm 17.3\%$) and FEV₁/FVC (71.3 ± 9.3 vs. 78.5 ± 6.8), with a higher amount of exacerbations/year. In supervised ML, KNN achieved the best performance in identifying frequent exacerbators (AUROC: 96.7%), confirming the importance of spirometry parameters and eosinophil count, along with the number of prior exacerbations and other clinical and demographic variables.

Conclusions: This study confirms the key prognostic value of eosinophiles in asthma, suggesting the usefulness of ML in defining biological pathways that can help plan personalized pharmacological and rehabilitation strategies.

Keywords: Asthma; Biomarker; Chronic disease; Chronic obstructive pulmonary disease; Disability; Exercise capacity; Occupational medicine; Outcome; Rehabilitation.

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Conflict of interest statement

Conflicts of interest The authors declare no conflicts of interest.

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Review

Int J Cardiol Heart Vasc

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. 2022 Jul 19;42:101086.

doi: 10.1016/j.ijcha.2022.101086. eCollection 2022 Oct.

[Dyspnea in patients with atrial fibrillation: Mechanisms, assessment and an interdisciplinary and integrated care approach](#)

[Rachel M J van der Velden](#)¹, [Astrid N L Hermans](#)¹, [Nikki A H A Pluymaekers](#)¹, [Monika Gawalko](#)^{1 2 3}, [Adrian Elliott](#)⁴, [Jeroen M Hendriks](#)^{4 5}, [Frits M E Franssen](#)^{6 7 8}, [Annelies M Slat](#)⁹, [Vanessa P M van Empel](#)¹, [Isabelle C Van Gelder](#)¹⁰, [Dick H J Thijssen](#)¹¹, [Thijs M H Eijssvogels](#)¹¹, [Carsten Leue](#)^{12 13}, [Harry J G M Crijns](#)¹, [Dominik Linz](#)^{1 4 14 15}, [Sami O Simons](#)^{7 8}

Affiliations expand

- PMID: 35873859
- PMCID: [PMC9304702](#)
- DOI: [10.1016/j.ijcha.2022.101086](#)

Free PMC article

Abstract

Atrial fibrillation (AF) is the most common sustained heart rhythm disorder and is often associated with symptoms that can significantly impact quality of life and daily functioning. Palpitations are the cardinal symptom of AF and many AF therapies are targeted towards relieving this symptom. However, up to two-third of patients also complain of dyspnea as a predominant self-reported symptom. In clinical practice it is often challenging to ascertain whether dyspnea represents an AF-related symptom or a symptom of concomitant cardiovascular and non-cardiovascular comorbidities, since common AF comorbidities such as heart failure and chronic obstructive pulmonary disease share similar symptoms. In addition, therapeutic

approaches specifically targeting dyspnea have not been well validated. Thus, assessing and treating dyspnea can be difficult. This review describes the latest knowledge on the burden and pathophysiology of dyspnea in AF patients. We discuss the role of heart rhythm control interventions as well as the management of AF risk factors and comorbidities with the goal to achieve maximal relief of dyspnea. Given the different and often complex mechanistic pathways leading to dyspnea, dyspneic AF patients will likely profit from an integrated multidisciplinary approach to tackle all factors and mechanisms involved. Therefore, we propose an interdisciplinary and integrated care pathway for the work-up of dyspnea in AF patients.

Keywords: Atrial fibrillation; Comorbidities; Dyspnea; Exercise intolerance; Mechanisms; Symptom assessment.

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Conflict of interest statement

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

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

SUPPLEMENTARY INFO

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Ann Allergy Asthma Immunol

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. 2022 Oct;129(4):490-496.

doi: 10.1016/j.anai.2022.06.028. Epub 2022 Jul 11.

[Plasma immunoglobulin E and risk of exacerbation and mortality in chronic obstructive pulmonary disease: A contemporary population-based cohort](#)

[Yunus Çolak](#)¹, [Truls S Ingebrigtsen](#)², [Børge G Nordestgaard](#)³, [Jacob L Marott](#)⁴, [Peter Lange](#)⁵, [Jørgen Vestbo](#)⁶, [Shoaib Afzal](#)⁷

Affiliations expand

- PMID: 35835293
- DOI: [10.1016/j.anai.2022.06.028](https://doi.org/10.1016/j.anai.2022.06.028)

Free article

Abstract

Background: Novel biomarkers and targeted treatments are needed for patients with chronic obstructive pulmonary disease (COPD).

Objective: To test the hypothesis that high plasma immunoglobulin (Ig)E concentrations associate with increased risk of exacerbation and mortality in individuals with COPD in the general population.

Methods: Among 46,598 adults in the Copenhagen General Population Study, we included 1559 with COPD, defined as forced expiratory volume in 1 second/forced vital capacity < 0.70 and forced expiratory volume in 1 second < 80% predicted in individuals aged ≥ 40 years with chronic respiratory symptoms and smoking exposure ≥ 10 pack-years, and without asthma. We assessed risk of future severe exacerbation and all-cause mortality according to baseline plasma IgE ≥ 76 IU/mL, a clinical cutoff for omalizumab treatment in severe asthma.

Results: During 14 years of follow-up (median, 6.9; interquartile range, 3.4), we recorded 224 severe exacerbations and 434 deaths in 1559 individuals with COPD. Individuals with COPD with IgE ≥ 76 IU/mL vs those with < 76 IU/mL had a multivariable adjusted hazard ratio (HR) of 1.43 (95% confidence interval, 1.07-1.89) for severe exacerbation and 1.30 (1.05-1.62) for all-cause mortality. Compared with individuals with IgE < 76 IU/mL and blood eosinophils < 300 cells/μL, the multivariable adjusted HR for severe exacerbation was 1.12 (0.76-1.67) for those with IgE < 76 IU/mL and blood eosinophils ≥ 300 cells/μL, 1.62 (1.17-2.24) for IgE ≥ 76 IU/mL and blood eosinophils < 300 cells/μL, and 1.06 (0.63-1.77) for those with IgE ≥ 76 IU/mL and blood eosinophils ≥ 300 cells/μL. Corresponding HRs for all-cause mortality were 1.27 (0.99-1.63), 1.47 (1.14-1.88), and 1.17 (0.83-1.64), respectively.

Conclusion: High plasma IgE was associated with an increased risk of severe exacerbation and all-cause mortality in individuals with COPD in the general population, independent of blood eosinophils.

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SUPPLEMENTARY INFO

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Magn Reson Imaging

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. 2022 Oct;92:140-149.

doi: 10.1016/j.mri.2022.06.016. Epub 2022 Jun 28.

Quantification of lung ventilation defects on hyperpolarized MRI: The Multi-Ethnic Study of Atherosclerosis (MESA) COPD study

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Affiliations expand

- PMID: 35777684
- DOI: [10.1016/j.mri.2022.06.016](https://doi.org/10.1016/j.mri.2022.06.016)

Abstract

Purpose: To develop an end-to-end deep learning (DL) framework to segment ventilation defects on pulmonary hyperpolarized MRI.

Materials and methods: The Multi-Ethnic Study of Atherosclerosis Chronic Obstructive Pulmonary Disease (COPD) study is a nested longitudinal case-control study in older smokers. Between February 2016 and July 2017, 56 participants (age, mean \pm SD, 74 ± 8 years; 34 men) underwent same breath-hold proton (^1H) and helium (^3He) MRI, which were annotated for non-ventilated, hypo-ventilated, and normal-ventilated lungs. In this retrospective DL study, 820 ^1H and ^3He slices from 42/56 (75%) participants were randomly selected for training, with the remaining 14/56 (25%) for test. Full lung masks were segmented using a traditional U-Net on ^1H MRI and were imported into a cascaded U-Net, which were used to segment ventilation defects on ^3He MRI. Models were trained with conventional data augmentation (DA) and generative adversarial networks (GAN)-DA.

Results: Conventional-DA improved ^1H and ^3He MRI segmentation over the non-DA model ($P = 0.007$ to 0.03) but GAN-DA did not yield further improvement. The cascaded U-Net improved non-ventilated lung segmentation ($P < 0.005$). Dice similarity coefficients (DSC) between manually and DL-segmented full lung, non-ventilated, hypo-ventilated, and normal-ventilated regions were 0.965 ± 0.010 , 0.840 ± 0.057 , 0.715 ± 0.175 , and 0.883 ± 0.060 , respectively. We observed no statistically significant difference in DCSs between participants with and without COPD ($P = 0.41$, 0.06 , and 0.18 for non-ventilated, hypo-ventilated, and normal-ventilated regions, respectively).

Conclusion: The proposed cascaded U-Net framework generated fully-automated segmentation of ventilation defects on ^3He MRI among older smokers with and without COPD that is consistent with our reference method.

Keywords: COPD; Deep learning; Hyperpolarized gas; MRI; Ventilation defects.

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- [Cited by 1 article](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grant supportexpand

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Respirology

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. 2022 Oct;27(10):844-853.

doi: 10.1111/resp.14309. Epub 2022 Jun 15.

[Effectiveness of influenza and pneumococcal vaccines on chronic obstructive pulmonary disease exacerbations](#)

[Yan Li](#)¹, [Pingshu Zhang](#)², [Zhijie An](#)¹, [Chenyan Yue](#)¹, [Yamin Wang](#)¹, [Yunqiu Liu](#)³, [Xiaodong Yuan](#)², [Ying Ma](#)², [Keli Li](#)¹, [Zundong Yin](#)¹, [Liye Wang](#)³, [Huaqing Wang](#)¹

Affiliations expand

- PMID: 35705329
- DOI: [10.1111/resp.14309](https://doi.org/10.1111/resp.14309)

Abstract

Background and objective: Single-study evidence of separate and combined effectiveness of influenza and pneumococcal vaccination in patients with chronic obstructive pulmonary disease (COPD) is limited. To fill this gap, we studied the effectiveness of trivalent seasonal influenza vaccine (TIV) and 23-valent pneumococcal polysaccharide vaccine (PPSV23), separately and together, at preventing adverse COPD outcomes.

Methods: Our study used a self-controlled, before-and-after cohort design to assess the effectiveness of TIV and PPSV23 in COPD patients. Patients were recruited from hospitals in Tangshan City, Hebei Province, China. Subjects self-selected into one of the three vaccination schedules: TIV group, PPSV23 group and TIV&PPSV23 group. We used a physician-completed, medical record-verified questionnaire to obtain data on acute exacerbations of COPD (AECOPD), pneumonia and related hospitalization. Vaccine effectiveness was determined by comparing COPD outcomes before and after vaccination, controlling for potential confounding using Cox regression.

Results: We recruited 474 COPD patients, of whom 109 received TIV, 69 received PPSV23 and 296 received TIV and PPSV23. Overall effectiveness for preventing AECOPD, pneumonia and related hospitalization were respectively 70%, 59% and 58% in the TIV group; 54%, 53% and 46% in the PPSV23 group; and 72%, 73% and 69% in the TIV&PPSV23 group. The vaccine effectiveness without COVID-19 non-pharmaceutical intervention period were 84%, 77% and 88% in the TIV group; 63%, 74% and 66% in the PPSV23 group; and 82%, 83% and 91% in the TIV&PPSV23 group.

Conclusion: Influenza vaccination and PPSV23 vaccination, separately and together, can effectively reduce the risk of AECOPD, pneumonia and related hospitalization. Effectiveness for preventing AECOPD was the greatest.

Keywords: 23-valent pneumococcal polysaccharide vaccine; acute exacerbations of chronic obstructive pulmonary disease; hospitalization; immunization; pneumonia; trivalent seasonal influenza vaccine; vaccine effectiveness.

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Comment in

- [Vaccination in patients with COPD: COVID has raised the bar.](#)
Waterer G. *Respirology*. 2022 Oct;27(10):799-800. doi: 10.1111/resp.14331. Epub 2022 Jul 18. PMID: 35852029 **Free PMC article.**
- [26 references](#)

SUPPLEMENTARY INFO

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

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Ann Am Thorac Soc

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. 2022 Oct;19(10):1677-1686.

doi: 10.1513/AnnalsATS.202110-1174OC.

[Adverse Effects, Smoking, Alcohol Consumption, and Quality of Life during Long-Term Oxygen Therapy: A Nationwide Study](#)

[Filip Björklund](#)¹, [Magnus Ekström](#)^{1,2}

Affiliations expand

- PMID: 35657698
- DOI: [10.1513/AnnalsATS.202110-1174OC](https://doi.org/10.1513/AnnalsATS.202110-1174OC)

Abstract

Rationale: Long-term oxygen therapy (LTOT) is prescribed for at least 15 hours per day and often used by patients for several years, but knowledge is limited regarding adverse effects, risk exposures, and health-related quality of life (HrQoL) among those treated. **Objectives:** To determine the prevalence of adverse effects, smoking, and alcohol consumption and their relations to HrQoL among patients treated with LTOT. **Methods:** This was a cross-sectional survey of a randomized sample of adults with ongoing LTOT in the Swedish National Registry for Respiratory Failure (Swedevox). Patient characteristics and the prevalence of 26 prespecified adverse effects, smoking, and alcohol consumption, were compared between respondents with better and worse HrQoL on the chronic obstructive pulmonary disease assessment test. **Results:** A total of 151 respondents were included (mean age, 74.7 yr [standard deviation, 8.6 yr]; 58.9% women; median LTOT duration, 2.2 yr [interquartile range, 1.0-3.8 yr]). Characteristics upon starting LTOT were similar between respondents and nonrespondents. Active smoking was very rare ($n = 4$, 2.6%). For alcohol use, 67.2% of participants reported no consumption during an average week, whereas risk use was reported by 25.8% of men and 16.9% of women. The most prevalent adverse effects were reduced mobility or physical activity (70.9%), dry mouth (69.5%), congestion or nasal drip (61.6%), increased tiredness (57.0%), and dry nose (53.0%). Patients with higher numbers of total and systemic adverse effects experienced worse HrQoL, whereas no associations were found for smoking status or alcohol consumption. The majority (54.8%) of adverse effects were untreated and unreported to health professionals. **Conclusions:** Adverse effects are common among patients with LTOT and are associated with worse HrQoL. As the majority of adverse effects had not been discussed or treated, structured assessment and management of risk exposures and adverse effects is warranted.

Keywords: HrQoL; LTOT; adverse effects; alcohol consumption; smoking.

SUPPLEMENTARY INFO

Grant supportexpand

FULL TEXT LINKS



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Ann Am Thorac Soc

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. 2022 Oct;19(10):1661-1668.

doi: 10.1513/AnnalsATS.202112-1346OC.

[Race and Sex Differences in Mortality in Individuals with Chronic Obstructive Pulmonary Disease](#)

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Affiliations expand

- PMID: 35657680
- DOI: [10.1513/AnnalsATS.202112-1346OC](https://doi.org/10.1513/AnnalsATS.202112-1346OC)

Abstract

Rationale: Despite differences in chronic obstructive pulmonary disease (COPD) comorbidities, race- and sex-based differences in all-cause mortality and cause-specific mortality are not well described. **Objectives:** To examine mortality differences in COPD by race-sex and underlying mechanisms. **Methods:** Medicare claims were used to identify COPD among REGARDS (Reasons for Geographic and Racial Differences in Stroke) cohort participants. Mortality rates were calculated using adjudicated causes of death. Hazard ratios (HRs) for mortality comparing race-sex groups were modeled with Cox proportional hazards regression. **Results:** In the 2,148-member COPD subcohort, 49% were women, and 34% were Black individuals; 1,326 deaths occurred over a median 7.5 years (interquartile range, 3.9-10.5 yr) follow-up. All-cause mortality per 1,000 person-years comparing Black versus White men was 101.1 (95% confidence interval [CI], 88.3-115.8) versus 93.9 (95% CI, 86.3-102.3; $P = 0.99$); comparing Black versus White women, all-cause mortality per 1,000 person-years was 74.2 (95% CI, 65.0-84.8) versus 70.6 (95% CI, 63.5-78.5; $P = 0.99$). Cardiovascular disease (CVD) was the leading cause-specific mortality among all race-sex groups. HR for CVD and chronic lung disease mortality were nonsignificant comparing

Black versus White men. HR for CVD death was higher in Black compared with White women (HR, 1.44; 95% CI, 1.06-1.95), whereas chronic lung disease death was lower (HR, 0.44; 95% CI, 0.25-0.77). These differences were attributable to higher CVD risk factor burden among Black women. **Conclusions:** In the REGARDS COPD cohort, there were no race-sex differences in all-cause mortality. CVD was the most common cause of death for all race-sex groups with COPD. Black women with COPD had a higher risk of CVD-related mortality than White women. CVD comorbidity management, especially among Black individuals, may improve mortality outcomes.

Keywords: cardiovascular disease; chronic obstructive pulmonary disease; mortality; race.

SUPPLEMENTARY INFO

Grant supportexpand

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Am J Respir Crit Care Med

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. 2022 Oct 1;206(7):838-845.

doi: 10.1164/rccm.202201-0206OC.

[Clinical Trial of Losartan for Pulmonary Emphysema: Pulmonary Trials Cooperative Losartan Effects on Emphysema Progression Clinical Trial](#)

[Robert A Wise](#)¹, [Janet T Holbrook](#)², [Robert H Brown](#)¹, [Gerard J Criner](#)³, [Mark T Dransfield](#)⁴, [Jiaxian He](#)², [Robert J Henderson](#)², [David A Kaminsky](#)⁵, [Robert J Kaner](#)⁶, [Stephen C Lazarus](#)⁷, [Barry J Make](#)⁸, [Meredith C McCormack](#)¹, [Enid R Neptune](#)¹, [Loretta G Que](#)⁹

Affiliations expand

- PMID: 35649189
- DOI: [10.1164/rccm.202201-0206OC](https://doi.org/10.1164/rccm.202201-0206OC)

Abstract

Rationale: There are no pharmacologic agents that modify emphysema progression in patients with chronic obstructive pulmonary disease (COPD). **Objectives:** To evaluate the efficacy of losartan, an angiotensin receptor blocker, to reduce emphysema progression. **Methods:** The trial was a multicenter, randomized, placebo-controlled trial conducted between May 2017 and January 2021. Eligible participants were aged ≥ 40 years, had moderate to severe airflow obstruction, ≥ 10 pack-years of smoking, mild-moderate emphysema on high-resolution computed tomography, and no medical indication for or intolerance of angiotensin receptor blockers. Treatment with losartan 100 mg daily or matching placebo (1:1) was randomly assigned. The primary outcome was emphysema progression on high-resolution computed tomography over 48 weeks. Secondary outcomes included the St George's Respiratory Questionnaire, the modified Medical Research Council dyspnea scale, the COPD Assessment Test, and the Physical Function-Short Form 20a. **Measurements and Main Results:** A total of 220 participants were enrolled; 58% were men, 19% were African American, and 24% were current smokers. The medians (interquartile ranges) for age were 65 (61-73) years and 48 (36-59) for percent predicted FEV₁ after bronchodilator use. The mean (95% confidence interval) percentage emphysema progression was 1.35% (0.67-2.03) in the losartan group versus 0.66% (0.09-1.23) in the placebo group ($P = \text{NS}$). **Conclusions:** Losartan did not prevent emphysema progression in people with COPD with mild-moderate emphysema. Clinical trial registered with www.clinicaltrials.gov ([NCT02696564](https://clinicaltrials.gov/ct2/show/study/NCT02696564)).

Keywords: angiotensin receptor blocker; clinical trial; emphysema; losartan; quantitative image analysis.

Comment in

- [Use of Computed Tomography Lung Densitometry as an Outcome Measure for Emphysema Progression: The Case of Losartan.](#)

Miravittles M, Anzueto A. *Am J Respir Crit Care Med*. 2022 Oct 1;206(7):804-806. doi: 10.1164/rccm.202205-0927ED. PMID: 35653703 No abstract available.

SUPPLEMENTARY INFO

Associated data, Grant supportexpand

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Ann Allergy Asthma Immunol

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. 2022 Oct;129(4):461-466.

doi: 10.1016/j.anai.2022.05.024. Epub 2022 May 25.

[Could transthoracic ultrasound be useful to suggest a small airways disease in severe uncontrolled asthma?](#)

[Giulia Scioscia](#)¹, [Donato Lacedonia](#)¹, [Carla Maria Irene Quarato](#)², [Pasquale Tondo](#)¹, [Anna Del Colle](#)¹, [Marco Sperandeo](#)³, [Giovanna Elisiana Carpagnano](#)⁴, [Maria Pia Foschino Barbaro](#)¹

Affiliations expand

- PMID: 35643297
- DOI: [10.1016/j.anai.2022.05.024](#)

Abstract

Background: Transthoracic ultrasound (TUS) is an accepted complementary tool in the diagnostic process of several pleuro-pulmonary diseases. However, to the best of our knowledge, TUS findings in patients with severe asthma have never been systematically described.

Objective: To explore if TUS examination is a useful imaging method in suggesting the presence of a "small airways disease" in patients with severe uncontrolled asthma.

Methods: Seventy-two consecutive subjects with a diagnosis of severe uncontrolled asthma were enrolled. The presence of a "small airways disease" was assessed through the execution of pulmonary function tests. All the patients underwent a complete TUS examination and a chest high resolution computed tomography (HRCT), which was regarded as the reference standard for comparison with TUS findings.

Results: Pulmonary function tests results have confirmed a reduction in expiratory flows relative to the small airways and a condition of hyperinflation in 78% and 82% of our patients, respectively. The main signs observed in the TUS examination were a thickened and/or irregular pleural line and the lack or reduction of the "gliding sign." TUS showed high sensitivity and specificity in suggesting the presence of hyperinflation and distal airways inflammation according to the HRCT scan. K Cohen's coefficients showed substantial agreement between the 2 diagnostic tests.

Conclusion: TUS in patients with severe uncontrolled asthma can provide useful information on the state of the peripheral lung, suggesting the execution of a second-line HRCT scan for better assessment of eventual alterations that may represent the underlying causes of nonresponse to treatment.

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SUPPLEMENTARY INFO

MeSH termsexpand

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Environ Sci Pollut Res Int

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. 2022 Oct;29(47):71502-71510.

doi: 10.1007/s11356-022-20588-1. Epub 2022 May 21.

The effects of temperature variability on mortality in patients with chronic obstructive pulmonary disease: a time-series analysis in Hangzhou, China

[Simeng Gu](#)¹, [Xiaofeng Wang](#)¹, [Guangming Mao](#)¹, [Xuemin Huang](#)¹, [Yuanyang Wang](#)¹, [Peiwei Xu](#)¹, [Lizhi Wu](#)¹, [Xiaoming Lou](#)¹, [Zhijian Chen](#)¹, [Zhe Mo](#)²

Affiliations expand

- PMID: 35597825
- DOI: [10.1007/s11356-022-20588-1](https://doi.org/10.1007/s11356-022-20588-1)

Abstract

Chronic obstructive pulmonary disease (COPD) is a leading cause of death in people aged over 60 years old. Research has been reported that ambient temperature and diurnal temperature range (DTR), as representative indices of temperature variability, are contributors to the development and exacerbation of COPD. However, few studies are available in Chinese population. In this study, we aimed to assess the associations of temperature variability on COPD mortality in a fast developing city in China. Using the mortality surveillance system, we obtained a total of 7,863 deaths attributed to COPD from 2014 to 2016. Quasi-Poisson generalized linear regression with distributed lag non-linear model was applied to explore the associations between temperature variability and COPD deaths, after controlling for the potential confounders, including relative humidity, day of week, public holiday, and long-term trend. A J-shaped association of DTR and a reversely J-shaped association of temperature for COPD mortality were observed. Risk estimates showed that the relative risks (RRs) of COPD mortality with extreme high DTR at lag 0 and 0-7 days were 1.045 (95% CI: 0.949-1.151) and 1.460 (95% CI: 1.118-1.908), and the extreme high temperature at lag 0 and 0-7 days were 1.090 (95% CI: 0.945-1.256) and 1.352 (95% CI: 1.163-1.572). Our findings suggest that short-term exposure to extreme temperature was associated with mortality for COPD in Hangzhou. The evidence has implications for policy decision-making and targeted interventions.

Keywords: Ambient temperature; Chronic obstructive pulmonary disease; Distributed lag non-linear model; Mortality.

- [52 references](#)

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

FULL TEXT LINKS



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Ann Am Thorac Soc

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. 2022 Oct;19(10):1669-1676.

doi: 10.1513/AnnalsATS.202111-1221OC.

[Physical Activity, Exercise Capacity, and Body Composition in U.S. Veterans with Chronic Obstructive Pulmonary Disease](#)

[Emily S Wan](#)^{1,2,3}, [Madeline Polak](#)¹, [Rebekah L Goldstein](#)¹, [Antonio A Lazzari](#)^{4,5}, [Ana Kantorowski](#)¹, [Eric Garshick](#)^{1,2,3}, [Marilyn L Moy](#)^{1,3}

Affiliations expand

- PMID: 35536690
- DOI: [10.1513/AnnalsATS.202111-1221OC](https://doi.org/10.1513/AnnalsATS.202111-1221OC)

Abstract

Rationale: Differences in body composition may contribute to variability in exercise capacity (EC) and physical activity (PA) in individuals with chronic obstructive pulmonary disease (COPD). Most studies have used bioimpedance-based surrogates of muscle (lean) mass; relatively few studies have included consideration of fat mass, and limited studies have been performed using dual X-ray absorptiometry (DXA) to assess body composition. **Objectives:** To determine whether DXA-assessed muscle (lean) and fat mass exhibit differential correlations with EC and PA in subjects with COPD. **Methods:** U.S. veterans with COPD (defined as forced expiratory volume in 1 second/forced vital capacity < 0.7 or emphysema on clinical chest computed tomography) had DXA-assessed body composition, EC (6-minute-walk distance), objective PA

(average daily step counts), and self-reported PA measured at enrollment. Associations among EC, PA, and body composition were examined using Spearman correlations and multivariable models adjusted *a priori* for age, sex, race, and lung function. **Results:** Subjects ($n = 98$) were predominantly White (90%), obese (mean body mass index, $30.2 \pm 6.2 \text{ kg/m}^2$), and male (96%), with a mean age of 69.8 ± 7.9 years and moderate airflow obstruction (mean forced expiratory volume in 1 second percentage predicted, $68 \pm 20\%$). Modest inverse correlations of EC and PA with fat mass were observed (Spearman's rho range, -0.20 to -0.34), whereas measures of muscle (lean) mass were not significantly associated with EC or PA. The ratio of appendicular skeletal muscle mass (ASM) to weight, which considers both muscle (lean) and fat mass, was consistently associated with EC (8.4 [95% confidence interval, 2.9-13.8] meter increase in 6-minute walk distance per 1% increase in ASM-to-weight ratio), objective PA (194.8 [95% confidence interval, 15.2-374.4] steps per day per 1% increase in ASM-to-weight ratio), and self-reported PA in multivariable-adjusted models. **Conclusions:** DXA-assessed body composition measures that include consideration of both lean and fat mass are associated with cross-sectional EC and PA in COPD populations. Clinical trial registered with www.clinicaltrials.gov ([NCT02099799](https://doi.org/10.1186/11767-019-00000-0)).

Keywords: COPD; body composition; exercise tolerance; physical activity.

Comment in

- [The Paradox of Obesity in Patients with Chronic Obstructive Pulmonary Disease.](#)
Yohannes AM. *Ann Am Thorac Soc*. 2022 Oct;19(10):1638-1639. doi: 10.1513/AnnalsATS.202206-525ED.PMID: 36178401 No abstract available.

SUPPLEMENTARY INFO

Associated data, Grant supportexpand

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Ann Am Thorac Soc

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. 2022 Oct;19(10):1687-1696.

doi: 10.1513/AnnalsATS.202108-932OC.

[Comparing Self-Management Programs with and without Peer Support among Patients with Chronic Obstructive Pulmonary Disease: A Clinical Trial](#)

[Hanan Aboumatar](#)^{1,2,3,4}, [Emmanuel E Garcia Morales](#)^{1,5}, [Leah R Jager](#)⁶, [Mohammad Naqibuddin](#)¹, [Samuel Kim](#)¹, [Jamia Saunders](#)¹, [Lee Bone](#)⁴, [John Linnell](#)⁷, [Marjorie McBurney](#)⁸, [Joseph Neiman](#)⁹, [Margaret Riley](#)⁷, [Nancy Robinson](#)⁸, [Cynthia Rand](#)^{10,4}, [Robert Wise](#)¹⁰

Affiliations expand

- PMID: 35442179
- DOI: [10.1513/AnnalsATS.202108-932OC](https://doi.org/10.1513/AnnalsATS.202108-932OC)

Abstract

Rationale: Self-management support (SMS) is an essential component of care for patients who have chronic obstructive pulmonary disease (COPD), but there is little evidence on how to provide SMS most effectively to these patients. Peer support (i.e., support provided by a person with a similar medical condition) has been successfully used to promote self-management among patients with various chronic conditions, yet no randomized studies have focused on testing its effects for patients with COPD. **Objectives:** To assess whether adding peer support to healthcare professional (HCP) support to help patients with COPD self-management results in better health-related quality of life (HRQoL) and less acute care use. **Methods:** A two-arm randomized controlled trial was performed at one academic and one community hospital and their affiliate clinics. The study population included patients aged ≥ 40 years who had been diagnosed with COPD by a physician and were currently receiving daily treatment for it. Two self-management support strategies were compared over 6 months. One strategy relied on the HCP for COPD self-management (HCP support); the other used a dual approach involving both HCPs and peer supporters (HCP Plus Peer). The primary outcome was change in HRQoL measured by the St. George's Respiratory Questionnaire at 6 months (range, 0-100, lower is better; four-point meaningful difference). Secondary outcomes included COPD-related and all-cause hospitalizations and emergency department visits. Analysis was conducted under intention to treat. **Results:** The number of enrolled participants was 292. Mean age was 67.7 (standard deviation, 9.4) years; 70.9% of participants were White, and 61.3% were female. St. George's Respiratory Questionnaire scores were not significantly different between the study arms at 6 months. HCP Plus Peer arm participants had fewer COPD-related acute care events at 3 months (incidence rate ratio, 0.68; 95% confidence interval [CI], 0.50-0.93) and 6 months (incidence rate ratio, 0.84; 95% CI, 0.71-0.99). **Conclusions:** Adding peer support to HCP support to help patients self-manage COPD did not further improve HRQoL in this study. However, it did result in fewer COPD-related acute care events during the 6-month intervention period. Clinical trial registered with www.clinicaltrials.gov ([NCT02891200](https://doi.org/10.1186/1745-6215-10-1200)).

Keywords: delivery of health care; health care utilization; health-related behavior.

Comment in

- [Peer Support and Chronic Obstructive Pulmonary Disease Self-Management: A Promising Approach?](#)
Fan VS, Coultas DB. *Ann Am Thorac Soc*. 2022 Oct;19(10):1640-1641. doi: [10.1513/AnnalsATS.202207-591ED](https://doi.org/10.1513/AnnalsATS.202207-591ED). PMID: 36178399 No abstract available.

SUPPLEMENTARY INFO

Associated data, Grant support expand

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Ann Am Thorac Soc

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. 2022 Oct;19(10):1642-1649.

doi: 10.1513/AnnalsATS.202109-1042OC.

[Lung Function and the Risk of Exacerbation in the \$\beta\$ -Blockers for the Prevention of Acute Exacerbations of Chronic Obstructive Pulmonary Disease Trial](#)

[Trisha M Parekh¹](#), [Erika S Helgeson²](#), [John Connett³](#), [Helen Voelker³](#), [Sharon X Ling³](#), [Stephen C Lazarus⁴](#), [Surya P Bhatt¹](#), [David M MacDonald³](#), [Takudzwa Mkorombindo¹](#), [Ken M Kunisaki^{3,5}](#), [Spyridon Fortis⁶](#), [David Kaminsky⁷](#), [Mark T Dransfield¹](#)

Affiliations expand

- PMID: 35363600
- DOI: [10.1513/AnnalsATS.202109-1042OC](https://doi.org/10.1513/AnnalsATS.202109-1042OC)

Abstract

Rationale: The BLOCK COPD (β -Blockers for the Prevention of Acute Exacerbations of Chronic Obstructive Pulmonary Disease) study found that metoprolol was associated with a higher risk of severe exacerbation. **Objectives:** To determine the mechanism underlying these results, we compared changes in lung function over the course of the study between treatment groups and evaluated whether baseline bronchodilator response or early reduction in forced expiratory volume in 1 second (FEV₁) or forced vital capacity (FVC) was associated with exacerbation risk. **Methods:** We compared changes in lung function (FEV₁ and FVC) over the treatment period between treatment groups using linear mixed-effect models. Cox proportional hazards models were used to evaluate the association between baseline bronchodilator responsiveness (FEV₁, FVC, and combined FEV₁ and FVC), early post-randomization (14 d) change in lung function, and the interaction between treatment assignment and these measures with risk of any or severe or very severe exacerbations. Negative binomial models were used to evaluate the relationship between bronchodilator responsiveness, the interaction between bronchodilator responsiveness and treatment assignment, and exacerbation rate. **Results:** Over the 336-day treatment period, individuals in the metoprolol group had a significantly greater decrease in logarithmic FEV₁ from baseline to visit on Day 28 than individuals in the placebo group. Individuals in the metoprolol group had a significantly greater decrease in FVC from baseline to visits on Days 14 and 28, and also a significantly greater decrease in

logarithmic FVC from baseline to visits on Days 42 and 112 than individuals in the placebo group. There were no associations between early lung function reduction or interactions between lung function reduction and treatment assignment and time to any or severe or very severe exacerbations. There were no interactions between treatment arm and baseline bronchodilator responsiveness measures on risk or rate of exacerbations. However, those with baseline FVC bronchodilator responsiveness had a higher rate of severe or very severe exacerbations (adjusted rate ratio, 1.62; 95% confidence interval, 1.04-2.48). **Conclusions:** Metoprolol was associated with reduced lung function during the early part of the treatment period, but these effects were modest and did not persist. Early lung function reduction and baseline bronchodilator responsiveness did not interact with the treatment arm to predict exacerbations; however, baseline FVC bronchodilator responsiveness was associated with a 60% higher rate of severe or very severe exacerbations. Clinical trial registered with www.clinicaltrials.gov ([NCT02587351](https://clinicaltrials.gov/ct2/show/study/NCT02587351)).

Keywords: COPD; bronchodilator response; exacerbations; spirometry; β -blockers.

Comment in

- [To \$\beta\$ -Block or Not to \$\beta\$ -Block: That Is Still the Question in Chronic Obstructive Pulmonary Disease.](#) Hancox RJ. *Ann Am Thorac Soc*. 2022 Oct;19(10):1636-1637. doi: 10.1513/AnnalsATS.202207-609ED.PMID: 36178400 No abstract available.

SUPPLEMENTARY INFO

Associated data, Grant supportexpand

FULL TEXT LINKS



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J Thorac Cardiovasc Surg

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. 2022 Oct;164(4):1222-1233.e11.

doi: 10.1016/j.jtcvs.2021.11.086. Epub 2021 Dec 13.

[Lung transplantation for chronic obstructive pulmonary disease: A call to modify the lung allocation score to decrease waitlist mortality](#)

[Travis D Hull](#)¹, [Gregory A Leya](#)¹, [Andrea L Axtell](#)¹, [Philicia Moonsamy](#)¹, [Asishana Osho](#)¹, [David C Chang](#)², [Thoralf M Sundt](#)¹, [Mauricio A Villavicencio](#)³

Affiliations expand

- PMID: 35016781
- DOI: [10.1016/j.jtcvs.2021.11.086](https://doi.org/10.1016/j.jtcvs.2021.11.086)

Abstract

Objective: Approximately 40% of lung transplants for chronic obstructive pulmonary disease (COPD) in the lung allocation score era are single lung transplantations (SLTs). We hypothesized that double lung transplantation (DLT) results in superior survival, but that mortality on the waitlist may compel clinicians to perform SLT. We investigated both waitlist mortality in COPD patients with restricted versus unrestricted listing preferences and posttransplant survival in SLT versus DLT to identify key predictors of mortality.

Methods: A retrospective analysis of waitlist mortality and posttransplant survival in patients with COPD was conducted using post-lung allocation score data from the United Network for Organ Sharing database between 2005 and 2018.

Results: Of 6740 patients with COPD on the waitlist, 328 (4.87%) died and 320 (4.75%) were removed due to clinical deterioration. Median survival on the waitlist was significantly worse in patients listed as restricted for DLT (4.39 vs 6.09 years; $P = .002$) compared with patients listed as unrestricted (hazard ratio, 1.34; 95% CI, 1.13-1.57). Factors that increase waitlist mortality include female sex, increased pulmonary artery pressure, and increased wait time. Median posttransplant survival was 5.3 years in SLT versus 6.5 years in DLT ($P < .001$). DLT recipients are younger, male patients with a higher lung allocation score. The survival advantage of DLT persisted in adjusted analysis (hazard ratio, 0.819; 95% CI, 0.741-0.905).

Conclusions: Restricted listing preference is associated with increased waitlist mortality, but DLT recipients have superior posttransplant survival. Because the lung allocation score does not prioritize COPD, concern for increased waitlist mortality with restricted listing preference may drive continued use of SLT despite better posttransplant survival in DLT.

Keywords: chronic obstruction pulmonary disease; double-lung transplantation; lung allocation score; lung transplantation; single-lung transplantation; waitlist mortality.

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Comment in

- [Commentary: How best to dance tango in lung transplantation for chronic obstructive pulmonary disease?](#)
Van Raemdonck D, Ceulemans LJ, Vos R, Verleden GM. *J Thorac Cardiovasc Surg*. 2022 Oct;164(4):1234-1235. doi: 10.1016/j.jtcvs.2021.12.034. Epub 2021 Dec 24. PMID: 35000685 No abstract available.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

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Review

Physiol Rev

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. 2022 Oct 1;102(4):1757-1836.

doi: 10.1152/physrev.00004.2021. Epub 2022 Jan 10.

[Physiology and pathophysiology of human airway mucus](#)

[David B Hill](#)^{1,2}, [Brian Button](#)¹, [Michael Rubinstein](#)^{1,3}, [Richard C Boucher](#)¹

Affiliations expand

- PMID: 35001665
- DOI: [10.1152/physrev.00004.2021](https://doi.org/10.1152/physrev.00004.2021)

Abstract

The mucus clearance system is the dominant mechanical host defense system of the human lung. Mucus is cleared from the lung by cilia and airflow, including both two-phase gas-liquid pumping and cough-dependent mechanisms, and mucus transport rates are heavily dependent on mucus concentration. Importantly, mucus transport rates are accurately predicted by the gel-on-brush model of the mucociliary apparatus from the relative osmotic moduli of the mucus and periciliary-glycocalyx (PCL-G) layers. The fluid available to hydrate mucus is generated by transepithelial fluid transport. Feedback interactions between mucus concentrations and cilia beating, via purinergic signaling, coordinate Na⁺ absorptive vs Cl⁻ secretory rates to maintain mucus hydration in health. In disease, mucus becomes hyperconcentrated (dehydrated). Multiple mechanisms derange the ion transport pathways that normally hydrate mucus in muco-obstructive lung diseases, e.g., cystic fibrosis (CF), chronic obstructive pulmonary disease (COPD), non-CF bronchiectasis (NCFB), and primary ciliary dyskinesia (PCD). A key step in muco-obstructive disease pathogenesis is the osmotic compression of the mucus layer onto the airway surface with the formation of adherent mucus plaques and plugs, particularly in distal airways. Mucus plaques create locally hypoxic conditions and produce airflow obstruction, inflammation, infection, and, ultimately, airway wall damage.

Therapies to clear adherent mucus with hydrating and mucolytic agents are rational, and strategies to develop these agents are reviewed.

Keywords: airway ion transport; gel-on-brush model; mucins; muco-obstructive diseases; mucus.

- [Cited by 5 articles](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant support[expand](#)

FULL TEXT LINKS



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Editorial

J Thorac Cardiovasc Surg

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. 2022 Oct;164(4):1234-1235.

doi: 10.1016/j.jtcvs.2021.12.034. Epub 2021 Dec 24.

[Commentary: How best to dance tango in lung transplantation for chronic obstructive pulmonary disease?](#)

[Dirk Van Raemdonck](#)¹, [Laurens J Ceulemans](#)², [Robin Vos](#)³, [Geert M Verleden](#)³

Affiliations [expand](#)

- PMID: 35000685
- DOI: [10.1016/j.jtcvs.2021.12.034](https://doi.org/10.1016/j.jtcvs.2021.12.034)

No abstract available

Comment on

- [Lung transplantation for chronic obstructive pulmonary disease: A call to modify the lung allocation score to decrease waitlist mortality.](#)

Hull TD, Leya GA, Axtell AL, Moonsamy P, Osho A, Chang DC, Sundt TM, Villavicencio MA. J Thorac Cardiovasc Surg. 2022 Oct;164(4):1222-1233.e11. doi: 10.1016/j.jtcvs.2021.11.086. Epub 2021 Dec 13. PMID: 35016781

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS



ASTHMA

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Am J Respir Cell Mol Biol

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. 2022 Oct;67(4):506-511.

doi: 10.1165/rcmb.2022-0137LE.

[A Unique CD27⁺IgD⁺ B Cell Population in the Sputum of Severe Eosinophilic Asthma Associated with Airway Autoimmunity](#)

[Nadia Suray Tan](#)¹, [Manali Mukherjee](#)², [Sheau Yng Lim](#)¹, [Angeline Rouers](#)³, [You Yi Hwang](#)³, [Chung Hwee Thiam](#)¹, [W S Daniel Tan](#)¹, [Wupeng Liao](#)¹, [W S Fred Wong](#)¹, [Mei Fong Liew](#)^{1,4}, [Parameswaran Nair](#)², [Anis Larbi](#)³, [De Yun Wang](#)¹, [Katja Fink](#)³, [Veronique Angeli](#)¹, [Hui Fang Lim](#)^{1,4}

Affiliations expand

- PMID: 36178857
- DOI: [10.1165/rcmb.2022-0137LE](#)

No abstract available

SUPPLEMENTARY INFO

Publication types, Grant supportexpand

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Genome Med

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. 2022 Sep 29;14(1):112.

doi: 10.1186/s13073-022-01114-x.

[African-specific alleles modify risk for asthma at the 17q12-q21 locus in African Americans](#)

[Charles Washington 3rd](#)¹, [Matthew Dapas](#)¹, [Arjun Biddanda](#)¹, [Kevin M Magnaye](#)¹, [Ivy Aneas](#)¹, [Britney A Helling](#)¹, [Brooke Szczesny](#)², [Meher Preethi Boorgula](#)³, [Margaret A Taub](#)⁴, [Eimear Kenny](#)⁵, [Rasika A Mathias](#)², [Kathleen C Barnes](#)³, [CAAPA](#); [Gurjit K Khurana Hershey](#)⁶, [Carolyn M Kercksmar](#)⁶, [Jessica D Gereige](#)⁷, [Melanie Makhija](#)⁸, [Rebecca S Gruchalla](#)⁹, [Michelle A Gill](#)⁹, [Andrew H Liu](#)¹⁰, [Deepa Rastogi](#)¹¹, [William Busse](#)¹², [Peter J Gergen](#)¹³, [Cynthia M Visness](#)¹⁴, [Diane R Gold](#)¹⁵, [Tina Hartert](#)¹⁶, [Christine C Johnson](#)¹⁷, [Robert F Lemanske Jr](#)¹⁸, [Fernando D Martinez](#)¹⁹, [Rachel L Miller](#)²⁰, [Dennis Ownby](#)¹⁷, [Christine M Seroogy](#)¹⁸, [Anne L Wright](#)¹⁹, [Edward M Zoratti](#)²¹, [Leonard B Bacharier](#)²², [Meyer Kattan](#)²³, [George T O'Connor](#)²⁴, [Robert A Wood](#)²⁵, [Marcelo A Nobrega](#)¹, [Matthew C Altman](#)^{26 27}, [Daniel J Jackson](#)¹⁸, [James E Gern](#)¹⁸, [Christopher G McKennan](#)²⁸, [Carole Ober](#)²⁹

Collaborators, Affiliations expand

- PMID: 36175932
- DOI: [10.1186/s13073-022-01114-x](https://doi.org/10.1186/s13073-022-01114-x)

Abstract

Background: Asthma is the most common chronic disease in children, occurring at higher frequencies and with more severe disease in children with African ancestry.

Methods: We tested for association with haplotypes at the most replicated and significant childhood-onset asthma locus at 17q12-q21 and asthma in European American and African American children. Following this, we used whole-genome sequencing data from 1060 African American and 100 European American individuals to identify novel variants on a high-risk African American-specific haplotype. We characterized these variants in silico using gene expression and ATAC-seq data from airway epithelial cells, functional annotations from ENCODE, and promoter capture (pc)Hi-C maps in airway epithelial cells. Candidate causal variants were then assessed for correlation with asthma-associated phenotypes in African American children and adults.

Results: Our studies revealed nine novel African-specific common variants, enriched on a high-risk asthma haplotype, which regulated the expression of GSDMA in airway epithelial cells and were associated with

features of severe asthma. Using ENCODE annotations, ATAC-seq, and pcHi-C, we narrowed the associations to two candidate causal variants that are associated with features of T2 low severe asthma.

Conclusions: Previously unknown genetic variation at the 17q12-21 childhood-onset asthma locus contributes to asthma severity in individuals with African ancestries. We suggest that many other population-specific variants that have not been discovered in GWAS contribute to the genetic risk for asthma and other common diseases.

Keywords: Asthma; Fine mapping; Health disparities; Integrated omics; Whole-genome sequencing.

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- [63 references](#)

SUPPLEMENTARY INFO

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NPJ Prim Care Respir Med

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. 2022 Sep 29;32(1):37.

doi: 10.1038/s41533-022-00295-7.

[Short-acting \$\beta_2\$ -agonist prescription patterns for asthma management in the SABINA III primary care cohort](#)

[David Price](#)^{1,2}, [Kerry Hancock](#)³, [Joseph Doan](#)⁴, [Sri Wahyu Taher](#)⁵, [Chakaya J Muhwa](#)⁶, [Hisham Farouk](#)⁷, [Maarten J H I Beekman](#)⁸

Affiliations expand

- PMID: 36175556
- DOI: [10.1038/s41533-022-00295-7](https://doi.org/10.1038/s41533-022-00295-7)

Abstract

Short-acting β_2 -agonist (SABA) prescriptions and associated outcomes were assessed in 1440 patients with asthma from the SABA use IN Asthma (SABINA) III study treated in primary care. Data on asthma medications were collected, and multivariable regression models analysed the association of SABA prescriptions with clinical outcomes. Patients (mean age, 47.9 years) were mostly female (68.6%); 58.3% had uncontrolled/partly controlled asthma and 38.8% experienced ≥ 1 severe exacerbation (reported in 39% of patients with mild asthma). Overall, 44.9% of patients were prescribed ≥ 3 SABA canisters (over-prescription) and 21.5% purchased SABA over-the-counter. Higher SABA prescriptions (vs 1-2 canisters) were associated with significantly decreased odds of having at least partly controlled asthma (6-9 and 10-12 canisters) and an increased incidence rate of severe exacerbations (10-12 and ≥ 13 canisters). Findings revealed a high disease burden, even in patients with 'mild' asthma, emphasising the need for local primary care guidelines based on international recommendations.

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- [58 references](#)

SUPPLEMENTARY INFO

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Editorial

Eur Respir J

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. 2022 Sep 29;60(3):2201031.

doi: 10.1183/13993003.01031-2022. Print 2022 Sep.

[Moving the dial on identifying endotypes of asthma from early life](#)

[Lucy Perrem](#)^{1 2 3}, [Padmaja Subbarao](#)^{4 2 5}

Affiliations expand

- PMID: 36175027

- DOI: [10.1183/13993003.01031-2022](https://doi.org/10.1183/13993003.01031-2022)

No abstract available

Conflict of interest statement

Conflict of interest: L. Perrem reports advisory board honoraria from Sanofi. P. Subbarao reports grants from CIHR, Canada Research Chairs, Tier 1, Genome Ontario, Don and Debbie Morrison; participation on advisory board for OSMB NIH, outside of the submitted work.

Comment on

- [T2-high asthma phenotypes across lifespan.](#)
Maison N, Omony J, Illi S, Thiele D, Skevaki C, Dittrich AM, Bahmer T, Rabe KF, Weckmann M, Happle C, Schaub B, Meyer M, Foth S, Rietschel E, Renz H, Hansen G, Kopp MV, von Mutius E, Grychtol R; ALLIANCE Study Group. *Eur Respir J.* 2022 Sep 29;60(3):2102288. doi: 10.1183/13993003.02288-2021. Print 2022 Sep. PMID: 35210326

SUPPLEMENTARY INFO

Publication typesexpand

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Respirology

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. 2022 Sep 29.

doi: 10.1111/resp.14381. Online ahead of print.

[What have we learnt from real-life research in asthma and COPD? Standards and novel designs for the future](#)

[David Price](#)^{1 2 3}, [Thendral Uthaman](#)¹

Affiliations expand

- PMID: 36172950
- DOI: [10.1111/resp.14381](#)

No abstract available

Keywords: chronic obstructive pulmonary disease; clinical guidelines; real-life research; severe asthma.

- [13 references](#)

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ERJ Open Res

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. 2022 Sep 26;8(3):00361-2022.

doi: 10.1183/23120541.00361-2022. eCollection 2022 Jul.

[Reply: Key role of dysregulated airway epithelium in response to respiratory viral infections in asthma](#)

[René Lutter](#)^{1,2}, [Abilash Ravi](#)³

Affiliations expand

- PMID: 36171991
- PMID: [PMC9511152](#)
- DOI: [10.1183/23120541.00361-2022](#)

Free PMC article

Abstract

The defective translational control in bronchial epithelial cells from asthma patients is reflected by enhanced responses to viral infection and (temporarily?) worsened by a respiratory viral infection <https://bit.ly/3cInNDT>.

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Conflict of interest statement

Conflict of interest: None declared.

- [10 references](#)

FULL TEXT LINKS

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ERJ Open Res

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. 2022 Sep 26;8(3):00140-2022.

doi: 10.1183/23120541.00140-2022. eCollection 2022 Jul.

[SABA use as an indicator for asthma exacerbation risk: an observational cohort study \(SABINA Canada\)](#)

[Stephen G Noorduy](#)^{1,2}, [Christina Qian](#)³, [Karissa M Johnston](#)^{3,4}, [Mena Soliman](#)¹, [Manisha Talukdar](#)¹, [Brandie L Walker](#)⁵, [Paul Hernandez](#)⁶, [Erika Penz](#)⁷

Affiliations expand

- PMID: 36171990
- PMCID: [PMC9511146](#)
- DOI: [10.1183/23120541.00140-2022](#)

Free PMC article

Abstract

Background: Patients with asthma use short-acting β -agonists (SABA) to relieve symptoms but SABA alone does not treat underlying inflammation. Thus, over-reliance on SABA may result in poor asthma control and negative health outcomes.

Objective: To describe use of SABA and characterise the relationship with severe exacerbations in the Canadian provinces of Nova Scotia (NS) and Alberta (AB).

Methods: In this longitudinal Canadian SABA In Asthma (SABINA) study, patients with an asthma diagnosis were identified between 2016 and 2020 within two provincial administrative datasets (Health Data Nova Scotia and Alberta Health Services). All patients were followed for ≥ 24 months, with the first 12 months used to measure baseline asthma severity. Medication use and the relationship of SABA overuse (three or more canisters per year) with severe asthma exacerbations were characterised descriptively and *via* regression analysis.

Results: A total of 115 478 patients were identified (NS: $n=8034$; AB: $n=107\,444$). SABA overuse was substantial across both provinces (NS: 39.4%; AB: 28.0%) and across all baseline disease severity categories. Patients in NS with SABA overuse had a mean \pm sd annual rate of 0.46 ± 1.11 exacerbations, compared to 0.30 ± 1.36 for those using fewer than three canisters of SABA. Patients in AB had mean \pm sd exacerbation rates of 0.31 ± 0.86 and 0.17 ± 0.62 , respectively. The adjusted risk of severe exacerbation was associated with SABA overuse (NS: incidence ratio rate 1.36, 95% CI 1.18-1.56; AB: incidence ratio rate 1.32, 95% CI 1.27-1.38).

Conclusion: This study supports recent updates to Canadian Thoracic Society and Global Initiative for Asthma guidelines for asthma care. SABA overuse is associated with increased risk of severe exacerbations and can be used to identify patients at a higher risk for severe exacerbations.

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Conflict of interest statement

Conflict of Interest: S.G. Noorduynd, M. Soliman and M. Talukdar are employees of AstraZeneca Canada Inc. C. Qian and K. Johnston are employees of Broadstreet HEOR, which received funds from AstraZeneca Canada Inc. for this work. B.L. Walker has received advisory board and speaker's honoraria from AstraZeneca, GlaxoSmithKline, Boehringer Ingelheim and Sanofi, unrelated to this work. P. Hernandez received funding from AstraZeneca to his institution and company for data acquisition and covered costs to conduct the study at the local site. He has received grants paid to his institution from Canadian Institute of Health Research, Boehringer Ingelheim, Cyclomedica, Grifols and Vertex, and received speaker honoraria from AstraZeneca, Boehringer Ingelheim and Janssen. He received honoraria from and participated in advisory boards for Acceleron, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Janssen, Novartis, Sanofi, Takeda, Teva and Valeo. He volunteered at Canadian Thoracic Society as an executive committee and Board member unrelated to this work. E. Penz has received research funds paid to her institution from AstraZeneca and Saskatchewan Cancer Agency, Canadian Institutes of Health Research, Saskatchewan Health Research Foundation and Respiratory Research Centre unrelated to this work. She has received consulting fees from GlaxoSmithKline, AstraZeneca and Sanofi Genzyme unrelated to this work. She received honoraria for participation on advisory boards, lecture series and educational events from AstraZeneca, GlaxoSmithKline, Sanofi, Boehringer Ingelheim and the International Centre for Evidence-Based Medicine, unrelated to this work. She is a Co-Chair of the COPD Assembly of Canadian Thoracic Society, Medical Lead at the Lung Cancer Screening Prevention Program, Saskatchewan Cancer Agency and a member of the Institute for Cancer Research Advisory Board, Canadian Institute for Health Research.

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

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ERJ Open Res

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. 2022 Sep 26;8(3):00200-2022.

doi: 10.1183/23120541.00200-2022. eCollection 2022 Jul.

[Major cardiovascular events in patients with severe COPD with and without asthma: a nationwide cohort study](#)

[Barbara Bonnesen](#)¹, [Pradeesh Sivapalan](#)¹, [Anna Kjær Kristensen](#)¹, [Mats Christian Højbjerg Lassen](#)^{2,3}, [Kristoffer Grundtvig Skaarup](#)^{2,3}, [Ema Rastoder](#)¹, [Rikke Sørensen](#)⁴, [Josefin Eklöf](#)¹, [Tor Biering-Sørensen](#)^{2,3}, [Jens-Ulrik Stæhr Jensen](#)^{1,5}

Affiliations expand

- PMID: 36171987
- PMCID: [PMC9511138](#)
- DOI: [10.1183/23120541.00200-2022](#)

Free PMC article

Abstract

Background: Chronic low-grade inflammation as in asthma may lead to a higher risk of cardiovascular events. We evaluated whether patients with COPD and asthma have a higher risk of acute cardiovascular events than patients with COPD without asthma.

Methods: Nationwide multicentre retrospective cohort study of Danish outpatients with a specialist diagnosis of COPD with or without asthma. Patients with both COPD and asthma were propensity-score matched 1:2 to patients with COPD without asthma. The primary end-point was severe major adverse cardiac events (MACE), defined as mortal cardiovascular events and events requiring revascularisation or hospitalisation.

Results: A total of 52 386 Danish patients with COPD were included; 34.7% had pre-existing cardiovascular disease, and 20.1% had asthma in addition to their COPD. Patients with pre-existing cardiovascular disease were then propensity-score matched: 3690 patients with COPD and asthma *versus* 7236 patients with COPD without asthma, and similarly, for patients without pre-existing cardiovascular disease (6775 matched with 13 205). The risk of MACE was higher among patients with asthma and COPD *versus* COPD without asthma: hazard ratio (HR) 1.25 (95% CI 1.13-1.39, p<0.0001) for patients with pre-existing

cardiovascular disease and HR 1.22 (95% CI 1.06-1.41, p=0.005) for patients without pre-existing cardiovascular disease.

Conclusion: Among patients with COPD, asthma as a comorbid condition is associated with substantially increased risk of cardiovascular events. The signal was an increased risk of 20-25%. Based on our study and other smaller studies, asthma can be considered a risk factor for cardiovascular events among COPD patients.

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Conflict of interest statement

Conflict of interest: B. Bonnesen has nothing to disclose. Conflict of interest: P. Sivapalan has nothing to disclose. Conflict of interest: A.K. Kristensen has nothing to disclose. Conflict of interest: M.C.H. Lassen has nothing to disclose. Conflict of interest: K.G. Skaarup has nothing to disclose. Conflict of interest: E. Rastoder has nothing to disclose. Conflict of interest: R. Sørensen has nothing to disclose. Conflict of interest: J. Eklöf has nothing to disclose. Conflict of interest: T. Biering-Sørensen has nothing to disclose. Conflict of interest: J-U. Stæhr Jensen has nothing to disclose.

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

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. 2022 Sep 26;8(3):00138-2022.

doi: 10.1183/23120541.00138-2022. eCollection 2022 Jul.

[Eosinophilic cationic protein as marker for response to antibody therapy in severe asthma](#)

[Elisa Franceschi](#)¹, [Nora Drick](#)², [Jan Fuge](#)^{2,3}, [Tobias Welte](#)^{2,3}, [Hendrik Suhling](#)²

Affiliations expand

- PMID: 36171986
- PMCID: [PMC9511155](#)

- DOI: [10.1183/23120541.00138-2022](https://doi.org/10.1183/23120541.00138-2022)

Free PMC article

Abstract

This study of the eosinophil cationic protein (ECP) as predictor of clinical response to biological therapy in severe asthma found that ECP is not useful in unselected patients but may have a role in those not exposed to oral corticosteroids. <https://bit.ly/398RwEk>.

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Conflict of interest statement

Conflict of interest: The authors declare that they have no competing interests

- [10 references](#)

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. 2022 Sep 26;8(3):00213-2022.

doi: 10.1183/23120541.00213-2022. eCollection 2022 Jul.

[Demographic and clinical characteristics of patients with \$\alpha_1\$ -antitrypsin deficiency genotypes PI*ZZ and PI*SZ in the Spanish registry of EARCO](#)

[María Torres-Durán¹](#), [José Luis López-Campos^{2,3}](#), [Juan Luis Rodríguez-Hermosa^{4,5}](#), [Cristina Esquinas^{2,6}](#), [Cristina Martínez-González⁷](#), [José María Hernández-Pérez⁸](#), [Carlota Rodríguez⁹](#), [Ana Bustamante¹⁰](#), [Francisco Casas-Maldonado¹¹](#), [Miriam Barrecheguren^{2,6}](#), [Cruz González¹²](#), [Marc Miravittles^{2,6}](#)

Affiliations expand

- PMID: 36171983

- PMID: [PMC9511153](#)
- DOI: [10.1183/23120541.00213-2022](#)

Free PMC article

Abstract

Background: The Spanish registry of α_1 -antitrypsin deficiency (AATD) integrated in the European Alpha-1 Research Collaboration (EARCO) provides information about the characteristics of patients, in particular those with the PI*SZ genotype, which is frequent in Spain.

Method: Individuals with severe AATD defined as proteinase inhibitor (PI) genotypes PI*ZZ, PI*SZ and other rare deficient variants were included from February 1, 2020, to February 1, 2022. The analysis focused on a comparison of the characteristics of PI*ZZ and PI*SZ patients.

Results: 409 patients were included (53.8% men) with a mean \pm sd age of 53.5 \pm 15.9 years. Genotypes were PI*ZZ in 181 (44.7%), PI*SZ in 163 (40.2%), PI*SS in 29 (7.2%) and other in 32 (7.9%). 271 (67.4%) had lung disease: 175 chronic obstructive pulmonary disease (43.5%), 163 emphysema (40.5%) and 83 bronchiectasis (20.6%). Patients with the PI*SZ genotype were younger, more frequently non-index cases and had a lower frequency of respiratory diseases except asthma compared with PI*ZZ patients. Among patients with respiratory diseases, PI*SZ individuals were significantly older both at onset of symptoms and at diagnosis; only asthma was more frequent in PI*SZ than in PI*ZZ individuals. Twelve PI*SZ patients (15.4%) received augmentation therapy compared with 94 PI*ZZ patients (66.2%; $p < 0.001$).

Conclusions: There is a high prevalence of PI*SZ in Spain. Patients with the PI*SZ genotype were older at symptom onset and diagnosis and had less severe lung disease compared with PI*ZZ patients. The prevalence of asthma was higher in PI*SZ, and up to 15% of PI*SZ patients received augmentation therapy.

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Conflict of interest statement

Competing interests: M. Torres-Durán has received speaker fees from Chiesi, CSL Behring, Grifols and Resmed, and consulting fees from CSL Behring and Grifols. J.L. López-Campos has received honoraria during the last 3 years for lecturing, scientific advice, participation in clinical studies or writing for publications for AstraZeneca, Boehringer Ingelheim, Chiesi, CSL Behring, Esteve, Ferrer, Gebro, GlaxoSmithKline, Grifols, Menarini, Novartis, Rovi and Teva. J.L. Rodríguez-Hermosa has received speaker fees from Zambon, Bial, Gebro Pharma, GlaxoSmithKline, Chiesi, Boehringer Ingelheim, CSL Behring and Grifols. J.M. Hernández-Pérez has received speaker fees from Grifols, CSL Behring, AstraZeneca, GlaxoSmithKline, Bial laboratory and Teva laboratory, support for attending meetings from Grifols and CSL Behring, and consulting fees from CSL Behring. C. Rodríguez has received speaker fees from GlaxoSmithKline, AstraZeneca, Grifols, Chiesi, Ferrer, Menarini and Boehringer Ingelheim, has provided expert testimony for Chiesi, and has received support for attending meetings from FAES. A. Bustamante has received speaker fees from Boehringer Ingelheim, AstraZeneca, GlaxoSmithKline, Novartis and Ferrer, and funding for travelling or attending meetings from CSL Behring, AstraZeneca and Chiesi. F. Casas-Maldonado has received speaker fees from AstraZeneca, Bial, Boehringer Ingelheim, Chiesi, Gebro Pharma, GlaxoSmithKline, Laboratorios Esteve, Laboratorios Ferrer, Menarini, Novartis, Rovi, Teva, Vertex, Zambon, CSL Behring and Grifols, and consulting fees from AstraZeneca, Chiesi, GlaxoSmithKline, CSL Behring and Grifols. M. Barrecheguren has received speaker fees from Grifols, Menarini, CSL Behring, GlaxoSmithKline and Boehringer Ingelheim, and

consulting fees from GlaxoSmithKline, Novartis, CSL Behring and Boehringer Ingelheim. C. González has received speaker fees from Menarini, GlaxoSmithKline, Novartis, Boehringer Ingelheim and Chiesi. M. Miravittles has received speaker fees from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, Menarini, Rovi, Bial, Sandoz, Zambon, CSL Behring, Grifols and Novartis, consulting fees from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Bial, Gebro Pharma, Kamada, CSL Behring, Laboratorios Esteve, Ferrer, Mereo Biopharma, Verona Pharma, Teva, Spin Therapeutics, pH Pharma, Novartis, Sanofi and Grifols, and research grants from GlaxoSmithKline and Grifols. The remaining authors report no conflicts of interest.

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

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. 2022 Sep 26;8(3):00314-2022.

doi: 10.1183/23120541.00314-2022. eCollection 2022 Jul.

[Key role of dysregulated airway epithelium in response to respiratory viral infections in asthma](#)

[Fatemeh Moheimani](#)^{1,2}, [Nafeesa Shahdab](#)^{1,2}, [Stephen Cummings](#)^{2,3}, [Philip M Hansbro](#)⁴, [Christopher Ward](#)⁵

Affiliations [expand](#)

- PMID: 36171982
- PMID: [PMC9511154](#)
- DOI: [10.1183/23120541.00314-2022](#)

Free PMC article

Abstract

A differentiated air-liquid interface model shows that the airway epithelium plays a key role in response to respiratory viral infections in people with asthma <https://bit.ly/3yDgiX1>.

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Conflict of interest statement

Conflict of interest: None declared.

- [13 references](#)

FULL TEXT LINKS

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Intern Med

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. 2022 Sep 28.

doi: 10.2169/internalmedicine.0613-22. Online ahead of print.

[Long-term Safety and Efficacy of Benralizumab for Eosinophilic Granulomatosis with Polyangiitis Complicated with Severe Neuropathy](#)

[Yasuhiko Koga](#)¹, [Seishi Yoshimi](#)², [Takashi Harada](#)², [Satoshi Suzuki](#)³, [Takayuki Ohtsuka](#)³, [Kunio Dobashi](#)⁴, [Takeshi Hisada](#)⁵

Affiliations [expand](#)

- PMID: 36171130
- DOI: [10.2169/internalmedicine.0613-22](#)

Free article

Abstract

The efficacy of benralizumab, as well as mepolizumab, to granulomatosis with polyangiitis (EGPA) involved with mononeuritis multiplex remains unclear. We experienced a case of EGPA presenting neuropathy with severe asthma. Muscle weakness due to neuropathy involved with gait disturbance was partly ameliorated by intravenous immunoglobulin therapy. Mepolizumab (100 mg/day) did not promote further improvement of neuropathy. However, the administration of benralizumab instead of mepolizumab improved neuropathy quickly and enabled walking alone. The efficacy of benralizumab for EGPA and its

complication has been maintained for over four years. Benralizumab may be a possible treatment for EGPA presenting neuropathy with severe asthma.

Keywords: IL-5; asthma; benralizumab; eosinophilic granulomatosis with polyangiitis; mepolizumab; mononeuritis multiplex neuropathy.

FULL TEXT LINKS



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Cite

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Ann Am Thorac Soc

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. 2022 Sep 28.

doi: 10.1513/AnnalsATS.202204-368OC. Online ahead of print.

[Roflumilast May Increase Risk of Exacerbations When Used to Treat Poorly Controlled Asthma in People with Obesity](#)

[Anne E Dixon¹](#), [Loretta G Que²](#), [Ravi Kalhan³](#), [Mark T Dransfield⁴](#), [Linda Rogers⁵](#), [Lynn B Gerald⁶](#), [Monica Kraft⁷](#), [Jerry A Krishnan⁸](#), [Olivia Johnson⁹](#), [Heather Hazucha¹⁰](#), [Gem Roy¹⁰](#), [Janet T Holbrook¹⁰](#), [Robert A Wise¹¹](#)

Affiliations expand

- PMID: 36170654
- DOI: [10.1513/AnnalsATS.202204-368OC](https://doi.org/10.1513/AnnalsATS.202204-368OC)

Abstract

Rationale: People with obesity often have severe, difficult to control asthma. There is a need to develop better treatments in this population. One potential treatment is roflumilast, a phosphodiesterase 4 inhibitor, as it is reported to have efficacy for treatment of asthma and can promote weight loss.

Objective: to investigate the potential efficacy of roflumilast for the treatment of poorly controlled asthma in people with obesity.

Methods: A randomized, double-masked, placebo-controlled trial of 24 weeks of roflumilast versus placebo for the treatment of poorly controlled asthma in people with obesity (body mass index ≥ 30 kg/m²). The primary outcome was change in asthma control test score (ACT).

Results: Twenty-two people were randomized to roflumilast, 16 to placebo. Roflumilast had no effect on change in ACT (increased by 2.6 [IQR 0.5 to 4.4] in those on roflumilast versus 2.0 [IQR 0.7 to 3.3] in those on placebo). Participants assigned to roflumilast had a 3.5 fold (Relative risk [RR] 95% confidence interval [CI] 1.3 to 9.4) increased risk of an episode of poor asthma control and an 8.1-fold (RR 95% CI 1.01 to 65.0) increased risk of an urgent care visit for asthma. Ten participants (56%) assigned to roflumilast required a course of oral corticosteroids for asthma exacerbations and none in the placebo group. Participants losing $\geq 5\%$ of their body weight experienced a clinically and statistically significant improvement in asthma control (ACT increased by 4.4 [IQR 2.5, 6.3] versus 1.5 [IQR 0.0, 3.0] in those who lost $< 5\%$).

Conclusions: Roflumilast had no effect on asthma control. Of concern, roflumilast was associated with an increased risk of exacerbation in obese individuals with poorly controlled asthma. These results highlight the importance of studying interventions in different sub-populations of people with asthma, particularly people with obesity and asthma who may respond differently to medications than lean people with asthma. Weight loss of at least 5% was associated with improved asthma control indicating that interventions- other than roflumilast -promoting weight loss may have efficacy for treatment of poorly controlled asthma in people with obesity.

FULL TEXT LINKS



[Proceed to details](#)

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Am J Respir Crit Care Med

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. 2022 Sep 28.

doi: 10.1164/rccm.202209-1768ED. Online ahead of print.

[Bronchial Epithelial Cell CC16 mRNA: Novel Asthma Biomarker or the Same Book with a New Cover?](#)

[Brinda Desai](#)¹, [Praveen Akuthota](#)²

Affiliations expand

- PMID: 36169926

- DOI: [10.1164/rccm.202209-1768ED](https://doi.org/10.1164/rccm.202209-1768ED)

No abstract available

FULL TEXT LINKS



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J Sports Med Phys Fitness

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. 2022 Sep 28.

doi: [10.23736/S0022-4707.22.13825-9](https://doi.org/10.23736/S0022-4707.22.13825-9). Online ahead of print.

[Allergic diseases in German competitive athletes: results of a cross-sectional study](#)

[Christina Dornquast¹](#), [Gabriele Rotter²](#), [Lisa Schollbach³](#), [Sylvia Binting¹](#), [Johannes Scherr^{3,4}](#), [Florian Pfab^{3,5}](#), [Benno Brinkhaus¹](#)

Affiliations expand

- PMID: 36169393
- DOI: [10.23736/S0022-4707.22.13825-9](https://doi.org/10.23736/S0022-4707.22.13825-9)

Abstract

Background: Allergic diseases are common in the general population. Among the population of competitive athletes (hereafter referred to as athletes), previous studies have mostly focused on the prevalence of allergic diseases and further aspects of bronchial asthma. We aimed to examine the prevalence of allergic diseases and respective medication use in athletes in Germany.

Methods: We performed a cross-sectional study in athletes from different sport disciplines between March 2012 and September 2013 in Munich, Bavaria. Allergic diseases and medication use were descriptively determined using the standardized Allergy Questionnaire for Athletes (AQUA). Allergic predisposition was defined at an AQUA score (range 0 to 35) of at least 5.

Results: In total, 560 athletes (mean age 20.4 ± 6.7 years, males 73.4%, most frequent sport discipline soccer) were included in the analysis. The reported proportion of any allergic condition was 28%, and 46% of the athletes had an allergic predisposition. Sixteen percent of all athletes and 36% of athletes with an allergic predisposition reported the use of antiallergic or antiasthmatic medications.

Conclusions: Athletes had a high rate of allergic diseases, and almost half of them reported an allergic predisposition. Further research is needed to validate our results and investigate the impact of allergic diseases in athletes on the performance and specific aspects of their sport, such as training intensity and duration.

[Proceed to details](#)

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Randomized Controlled Trial

Trials

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. 2022 Sep 27;23(1):817.

doi: 10.1186/s13063-022-06720-z.

[Targeted AntiBiotics for Chronic pulmonary diseases \(TARGET ABC\): can targeted antibiotic therapy improve the prognosis of Pseudomonas aeruginosa-infected patients with chronic pulmonary obstructive disease, non-cystic fibrosis bronchiectasis, and asthma? A multicenter, randomized, controlled, open-label trial](#)

[Josefin Eklöf](#)¹, [Imane Achir Alispahic](#)², [Pradeesh Sivapalan](#)^{1,3}, [Torgny Wilcke](#)¹, [Niels Seersholm](#)¹, [Karin Armbruster](#)¹, [Jakob Lyngby Kjærgaard](#)¹, [Mohamad Isam Saeed](#)¹, [Thyge Lynghøj Nielsen](#)⁴, [Andrea Browatzki](#)⁴, [Rikke Holmen Overgaard](#)⁴, [Camilla Sund Fenlev](#)⁴, [Zitta Barella Harboe](#)⁴, [Helle Frost Andreassen](#)⁵, [Therese Sophie Lapperre](#)⁵, [Lars Pedersen](#)⁵, [Stine Johnsen](#)⁵, [Charlotte Suppli Ulrik](#)⁶, [Julie Janner](#)⁶, [Mia Moberg](#)⁶, [Maria Heidemann](#)⁶, [Ulla Møller Weinreich](#)⁷, [Roxana Vijdea](#)⁷, [Hans Linde](#)⁸, [Ingrid Titlestad](#)⁹, [Sofie Lock Johansson](#)⁹, [Flemming Schønning Rosenvinge](#)¹⁰, [Christian Østergaard](#)¹¹, [Khaled Saoud Ali Ghathian](#)¹¹, [Lise Gundersen](#)¹², [Christina Wellendorph Christensen](#)¹², [Jette Bangsborg](#)¹², [Torben Tranborg Jensen](#)¹³, [Vibeke Muff Sørensen](#)¹³, [Thilde Ellingsgaard](#)¹³, [Raluca Datcu](#)¹⁴, [John Eugenio Coia](#)¹⁴, [Uffe Bodtger](#)^{3,15}, [Jens Ulrik Stæhr Jensen](#)^{1,16}

Affiliations expand

- PMID: 36167555
- PMCID: [PMC9513970](#)

- DOI: [10.1186/s13063-022-06720-z](https://doi.org/10.1186/s13063-022-06720-z)

Free PMC article

Abstract

Background: *Pseudomonas aeruginosa* infection is seen in chronic pulmonary disease and is associated with exacerbations and poor long-term prognosis. However, evidence-based guidelines for the management and treatment of *P. aeruginosa* infection in chronic, non-cystic fibrosis (CF) pulmonary disease are lacking. The aim of this study is to investigate whether targeted antibiotic treatment against *P. aeruginosa* can reduce exacerbations and mortality in patients with chronic obstructive pulmonary disease (COPD), non-CF bronchiectasis, and asthma.

Methods: This study is an ongoing multicenter, randomized, controlled, open-label trial. A total of 150 patients with COPD, non-CF bronchiectasis or asthma, and *P. aeruginosa*-positive lower respiratory tract samples will be randomly assigned with a 1:1 ratio to either no antibiotic treatment or anti-pseudomonal antibiotic treatment with intravenous beta-lactam and oral ciprofloxacin for 14 days. The primary outcome, analyzed with two co-primary endpoints, is (i) time to prednisolone and/or antibiotic requiring exacerbation or death, in the primary or secondary health sector, within days 20-365 from study allocation and (ii) days alive and without exacerbation within days 20-365 from the study allocation.

Discussion: This trial will determine whether targeted antibiotics can benefit future patients with chronic, non-CF pulmonary disease and *P. aeruginosa* infection in terms of reduced morbidity and mortality, thus optimizing therapeutic approaches in this large group of chronic patients.

Trial registration: ClinicalTrials.gov [NCT03262142](https://clinicaltrials.gov/ct2/show/study/NCT03262142) . Registered on August 25, 2017.

Keywords: Antibiotics; Asthma; Chronic obstructive pulmonary disease; Non-CF bronchiectasis; *Pseudomonas aeruginosa*; Randomized controlled trial.

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Conflict of interest statement

The authors declare that they have no competing interests. Pradeesh Sivapalan reports personal fees from Boehringer Ingelheim, outside the submitted work.

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

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated data, Grant support[expand](#)

FULL TEXT LINKS



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JAMA

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. 2022 Sep 27;328(12):1170.

doi: 10.1001/jama.2022.14722.

[Asthma and Oil Spill Cleanup](#)

[Melissa Suran](#)

- PMID: 36166043
- DOI: [10.1001/jama.2022.14722](https://doi.org/10.1001/jama.2022.14722)

No abstract available

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS



[Proceed to details](#)

Cite

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JAMA

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. 2022 Sep 27;328(12):1171-1172.

doi: 10.1001/jama.2022.16965.

[Mepolizumab Cuts Asthma Exacerbations Among High-risk Kids](#)

[Anita Slomski](#)

- PMID: 36166028
- DOI: [10.1001/jama.2022.16965](#)

No abstract available

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS



[Proceed to details](#)

Cite

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JAAPA

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- . 2022 Oct 1;35(10):15-16.

doi: 10.1097/01.JAA.0000873824.54710.20.

[Albuterol: Still first-line in rescue therapy?](#)

[David G Pitonzo](#)¹

Affiliations expand

- PMID: 36165542
- DOI: [10.1097/01.JAA.0000873824.54710.20](#)

Abstract

Albuterol has been a cornerstone of asthma treatment for several decades, but evidence suggests that it may be overused at the expense of more efficacious treatment. Albuterol may not even be appropriate for sole first-line rescue medication in some patients. Inflammatory mechanisms have been shown to play a role early in the course of developing bronchospasm, suggesting that inhaled corticosteroids should be included as part of initial rescue treatment. Newer biologics target inflammatory cytokine pathways, which may be needed in patients with moderate to severe disease. Evidence-based recommendations for the management of asthma and bronchospasm are continuing to evolve.

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- [11 references](#)

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS



[Proceed to details](#)

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☐ 20

Curr Opin Allergy Clin Immunol

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. 2022 Sep 27.

doi: 10.1097/ACI.0000000000000861. Online ahead of print.

[Trends and determinants of epinephrine prescriptions: a proxy of anaphylaxis epidemiology?](#)

[Enrico Costa](#)^{1,2}, [Luciana Kase Tanno](#)^{3,4,5}, [Damiano Salazzari](#)⁶, [Federico Tedeschi](#)⁶, [Margherita Andretta](#)⁷, [Marco Caminati](#)⁸

Affiliations expand

- PMID: 36165443
- DOI: [10.1097/ACI.0000000000000861](https://doi.org/10.1097/ACI.0000000000000861)

Abstract

Purpose of review: Epinephrine autoinjectors (EAls) are recommended to all patients previously experiencing anaphylaxis reaction in order to prevent further reactions and fatalities. Under that perspective, EAI prescription could be considered as a proxy of anaphylaxis epidemiology. Nevertheless EAI prescription rates are still unacceptably low.

Recent findings: The review focuses on potential determinants, in addition to clinical indications, which might impact EAI prescription rates by exploring the scientific literature published within the past 18 months, wherever available. Although some controversial results, age, sex, ethnicity, geographical setting and socioeconomic conditions might influence both physician prescription behaviour and EAls' accessibility from the patient's side, which hampers the accuracy of EAI prescription as a proxy of anaphylaxis. Low EAI prescription and refill rates have been recorded even in the absence of significant socioeconomic barriers, suggesting that economical limitations only partially account for the issue, and cultural restrictions have also to be considered and addressed.

Summary: In addition to providing the same opportunities in terms of EAI availability in all countries worldwide, implementing the resources for anaphylaxis management in terms of practical knowledge, education, and allergy specialist networks is an urgent need, even in the absence of socioeconomic barriers.

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- [48 references](#)

FULL TEXT LINKS



[Proceed to details](#)

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Ann Allergy Asthma Immunol

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. 2022 Sep 24;S1081-1206(22)01775-6.

doi: 10.1016/j.anai.2022.09.026. Online ahead of print.

[Airflow obstruction in real life is associated with small airways dysfunction in moderate to severe asthma](#)

[Rory Chan](#)¹, [Kirsten Stewart](#)², [Brian Lipworth](#)²

Affiliations expand

- PMID: 36162618

- DOI: [10.1016/j.anai.2022.09.026](https://doi.org/10.1016/j.anai.2022.09.026)

No abstract available

Keywords: airflow obstruction; asthma; small airways obstruction; type 2 inflammation.

FULL TEXT LINKS



[Proceed to details](#)

Cite

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☐ 22

Review

Cochrane Database Syst Rev

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. 2022 Sep 26;9(9):CD007524.

doi: 10.1002/14651858.CD007524.pub5.

[Increased versus stable doses of inhaled corticosteroids for exacerbations of chronic asthma in adults and children](#)

[Kayleigh M Kew](#)¹, [Ella Flemyng](#)², [Bradley S Quon](#)³, [Clarus Leung](#)³

Affiliations expand

- PMID: 36161875
- PMCID: PMC9512263 (available on 2023-09-26)
- DOI: [10.1002/14651858.CD007524.pub5](https://doi.org/10.1002/14651858.CD007524.pub5)

Abstract

Background: People with asthma may experience exacerbations, or 'attacks', during which their symptoms worsen and additional treatment is required. Written action plans sometimes advocate a short-term increase in the dose of inhaled corticosteroids (ICS) at the first sign of an exacerbation to reduce the severity of the attack and to prevent the need for oral steroids or hospital admission.

Objectives: To compare the clinical effectiveness and safety of increased versus stable doses of ICS as part of a patient-initiated action plan for the home management of exacerbations in children and adults with persistent asthma.

Search methods: We searched the Cochrane Airways Group Specialised Register, which is derived from searches of the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, and CINAHL (Cumulative Index to Nursing and Allied Health Literature), and handsearched abstracts to 20 December 2021. We also searched major trial registries for ongoing trials.

Selection criteria: We included parallel and cross-over randomised controlled trials (RCTs) that allocated people with persistent asthma to take a blinded inhaler in the event of an exacerbation which either increased their daily dose of ICS or kept it stable (placebo).

Data collection and analysis: Two review authors independently selected trials, assessed quality, and extracted data. We reassessed risk of bias for all studies at the result level using the revised risk of bias tool for RCTs (Risk of Bias 2), and employed the GRADE approach to assess our confidence in the synthesised effect estimates. The primary outcome was treatment failure, defined as the need for rescue oral steroids in the randomised population. Secondary outcomes were treatment failure in the subset who initiated the study inhaler (treated population), unscheduled physician visits, unscheduled acute care, emergency department or hospital visits, serious and non-serious adverse events, and duration of exacerbation.

Main results: This review update added a new study that increased the number of people in the primary analysis from 1520 to 1774, and incorporates the most up-to-date methods to assess the likely impact of bias within the meta-analyses. The updated review now includes nine RCTs (1923 participants; seven parallel and two cross-over) conducted in Europe, North America, and Australasia and published between 1998 and 2018. Five studies evaluated adult populations ($n = 1247$; ≥ 15 years), and four studies evaluated child or adolescent populations ($n = 676$; < 15 years). All study participants had mild to moderate asthma. Studies varied in the dose of maintenance ICS, age, fold increase of ICS in the event of an exacerbation, criteria for initiating the study inhaler, and allowed medications. Approximately 50% of randomised participants initiated the study inhaler (range 23% to 100%), and the included studies reported treatment failure in a variety of ways, meaning assumptions were required to permit the combining of data. Participants randomised to increase their ICS dose at the first signs of an exacerbation had similar odds of needing rescue oral corticosteroids to those randomised to a placebo inhaler (odds ratio (OR) 0.97, 95% confidence interval (CI) 0.76 to 1.25; 8 studies; 1774 participants; $I^2 = 0\%$; moderate quality evidence). We could draw no firm conclusions from subgroup analyses conducted to investigate the impact of age, time to treatment initiation, baseline dose, smoking history, and fold increase of ICS on the primary outcome. Results for the same outcome in the subset of participants who initiated the study inhaler were unchanged from the previous version, which provides a different point estimate with very low confidence due to heterogeneity, imprecision, and risk of bias (OR 0.84, 95% CI 0.54 to 1.30; 7 studies; 766 participants; $I^2 = 42\%$; random-effects model). Confidence was reduced due to risk of bias and assumptions that had to be made to include study data in the intention-to-treat and treated-population analyses. Sensitivity analyses that tested the impact of assumptions made for synthesis and to exclude cross-over studies, studies at overall high risk of bias, and those with commercial funding did not change our conclusions. Pooled effects for unscheduled physician visits, unscheduled acute care, emergency department or hospital visits, and duration of exacerbation made it very difficult to determine where the true effect may lie, and confidence

was reduced by risk of bias. Point estimates for both serious and non-serious adverse events favoured keeping ICS stable, but imprecision and risk of bias due to missing data and outcome measurement and reporting reduced our confidence in the effects (serious adverse events: OR 1.69, 95% CI 0.77 to 3.71; 2 studies; 394 participants; $I^2 = 0\%$; non-serious adverse events: OR 2.15, 95% CI 0.68 to 6.73; 2 studies; 142 participants; $I^2 = 0\%$).

Authors' conclusions: Evidence from double-blind trials of adults and children with mild to moderate asthma suggests there is unlikely to be an important reduction in the need for oral steroids from increasing a patient's ICS dose at the first sign of an exacerbation. Other clinically important benefits and potential harms of increased doses of ICS compared with keeping the dose stable cannot be ruled out due to wide confidence intervals, risk of bias in the trials, and assumptions that had to be made for synthesis. Included studies conducted between 1998 and 2018 reflect evolving clinical practice and study methods, and the data do not support thorough investigation of effect modifiers such as baseline dose, fold increase, asthma severity and timing. The review does not include recent evidence from pragmatic, unblinded studies showing benefits of larger dose increases in those with poorly controlled asthma. A systematic review is warranted to examine the differences between the blinded and unblinded trials using robust methods for assessing risk of bias to present the most complete view of the evidence for decision makers.

Trial registration: ClinicalTrials.gov [NCT00394329](#) [NCT03769090](#).

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Conflict of interest statement

Kayleigh Kew: former employee of the Cochrane Central Executive Team (2020 to 2021), during which time most of the work for the update was completed, and former employee of the Cochrane Airways editorial team (2012 to 2016). No commercial or non-commercial conflicts of interest relevant to this review.
Ella Flemyng: employee of the Cochrane Central Executive Team. No commercial or non-commercial conflicts of interest relevant to this review.

Bradley Quon: none known

Clarus Leung: none known

Update of

- [Increased versus stable doses of inhaled corticosteroids for exacerbations of chronic asthma in adults and children.](#)

Kew KM, Quinn M, Quon BS, Ducharme FM. *Cochrane Database Syst Rev.* 2016 Jun 7;2016(6):CD007524. doi: 10.1002/14651858.CD007524.pub4. PMID: 27272563 **Free PMC article. Updated.** Review.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated dataexpand

FULL TEXT LINKS



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Respirology

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. 2022 Sep 26.

doi: 10.1111/resp.14377. Online ahead of print.

[Choosing and switching biological agents in severe asthma](#)

[Muhammad Adrish](#)¹, [Nicola A Hanania](#)¹

Affiliations expand

- PMID: 36161677
- DOI: [10.1111/resp.14377](https://doi.org/10.1111/resp.14377)

Free article

No abstract available

Keywords: asthma control; asthma exacerbations; biologics; severe asthma; type 2 inflammation.

- [7 references](#)

FULL TEXT LINKS



[Proceed to details](#)

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Editorial

Ann Allergy Asthma Immunol

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. 2022 Oct;129(4):401-402.

doi: 10.1016/j.anai.2022.07.011.

[Can current hospitalization rates for asthma be decreased?](#)

[Miles Weinberger](#)¹

Affiliations expand

- PMID: 36155697
- DOI: [10.1016/j.anai.2022.07.011](https://doi.org/10.1016/j.anai.2022.07.011)

No abstract available

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS



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Editorial

Ann Allergy Asthma Immunol

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. 2022 Oct;129(4):399-400.

doi: 10.1016/j.anai.2022.07.003.

[Should asthma evaluation include assessment of small airway function?](#)

[Miles Weinberger](#)¹

Affiliations expand

- PMID: 36155696
- DOI: [10.1016/j.anai.2022.07.003](https://doi.org/10.1016/j.anai.2022.07.003)

No abstract available

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS



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Review

J Med Internet Res

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. 2022 Sep 26;24(9):e38030.

doi: 10.2196/38030.

[Digital Health Interventions for Depression and Anxiety Among People With Chronic Conditions: Scoping Review](#)

[Amika Shah](#)^{1,2}, [Neesha Hussain-Shamsy](#)^{1,2}, [Gillian Strudwick](#)^{1,3}, [Sanjeev Sockalingam](#)^{3,4,5}, [Robert P Nolan](#)^{5,6,7}, [Emily Seto](#)^{1,2}

Affiliations expand

- PMID: 36155409
- DOI: [10.2196/38030](https://doi.org/10.2196/38030)

Free article

Abstract

Background: Chronic conditions are characterized by their long duration (≥ 1 year), need for ongoing medical attention, and limitations in activities of daily living. These can often co-occur with depression and anxiety as common and detrimental comorbidities among the growing population living with chronic conditions. Digital health interventions (DHIs) hold promise in overcoming barriers to accessing mental health support for these individuals; however, the design and implementation of DHIs for depression and anxiety in people with chronic conditions are yet to be explored.

Objective: This study aimed to explore what is known in the literature regarding DHIs for the prevention, detection, or treatment of depression and anxiety among people with chronic conditions.

Methods: A scoping review of the literature was conducted using the Arksey and O'Malley framework. Searches of the literature published in 5 databases between 1990 and 2019 were conducted in April 2019 and updated in March 2021. To be included, studies must have described a DHI tested with, or designed for, the prevention, detection, or treatment of depression or anxiety in people with common chronic conditions (arthritis, asthma, diabetes mellitus, heart disease, chronic obstructive pulmonary disease, cancer, stroke, and Alzheimer disease or dementia). Studies were independently screened by 2 reviewers against the inclusion and exclusion criteria. Both quantitative and qualitative data were extracted, charted, and synthesized to provide a descriptive summary of the trends and considerations for future research.

Results: Database searches yielded 11,422 articles across the initial and updated searches, 53 (0.46%) of which were included in this review. DHIs predominantly sought to provide treatment (44/53, 83%), followed by detection (5/53, 9%) and prevention (4/53, 8%). Most DHIs were focused on depression (36/53, 68%), guided (32/53, 60%), tailored to chronic physical conditions (19/53, 36%), and delivered through web-based platforms (20/53, 38%). Only 2 studies described the implementation of a DHI.

Conclusions: As a growing research area, DHIs offer the potential to address the gap in care for depression and anxiety among people with chronic conditions; however, their implementation in standard care is scarce. Although stepped care has been identified as a promising model to implement efficacious DHIs, few studies have investigated the use of DHIs for depression and anxiety among chronic conditions using such models. In developing stepped care, we outlined DHI tailoring, guidance, and intensity as key considerations that require further research.

Keywords: anxiety; chronic disease; depression; digital health; eHealth; mHealth; mental health; mobile health; multiple chronic conditions; psychiatry; telehealth; telemedicine.

©Amika Shah, Neesha Hussain-Shamsy, Gillian Strudwick, Sanjeev Sockalingam, Robert P Nolan, Emily Seto. Originally published in the Journal of Medical Internet Research (<https://www.jmir.org>), 26.09.2022.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS



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Cite

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Am J Respir Crit Care Med

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. 2022 Sep 26.

doi: 10.1164/rccm.202107-1583RR. Online ahead of print.

[The Effects of Air Pollution in Pediatric Respiratory Disease](#)

[Sarah E Bauer](#)^{1,2}, [Eli Rhoads](#)^{1,2}, [Brittany L Wall](#)^{1,2}, [Don B Sanders](#)^{1,3}

Affiliations expand

- PMID: 36154892
- DOI: [10.1164/rccm.202107-1583RR](https://doi.org/10.1164/rccm.202107-1583RR)

No abstract available

Keywords: Air pollution; Asthma; Bronchopulmonary dysplasia; Respiratory outcomes.

FULL TEXT LINKS



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Cite

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 28

Randomized Controlled Trial

BMC Pulm Med

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. 2022 Sep 24;22(1):363.
doi: 10.1186/s12890-022-02152-2.

[A pragmatic randomised controlled trial of tailored pulmonary rehabilitation in participants with difficult-to-control asthma and elevated body mass index](#)

[Helen Clare Ricketts](#)¹, [Varun Sharma](#)¹, [Femke Steffensen](#)², [Anna Goodfellow](#)², [Elaine Mackay](#)³, [Gordon MacDonald](#)⁴, [Duncan S Buchan](#)⁵, [Rekha Chaudhuri](#)⁶, [Douglas C Cowan](#)⁷

Affiliations expand

- PMID: 36153525
- PMCID: [PMC9509551](#)
- DOI: [10.1186/s12890-022-02152-2](#)

Free PMC article

Abstract

Background: Difficult-to-control asthma associated with elevated body mass index (BMI) is challenging with limited treatment options. The effects of pulmonary rehabilitation (PR) in this population are uncertain.

Methods: This is a randomised controlled trial of an eight-week asthma-tailored PR programme versus usual care (UC) in participants with difficult-to-control asthma and BMI ≥ 25 kg/m². PR comprised two hours of education and supervised exercise per week, with encouragement for two individual exercise sessions. Primary outcome was difference in change in Asthma Quality of Life Questionnaire (AQLQ) in PR versus UC groups between visits. Secondary outcomes included difference in change in Asthma Control Questionnaire-6 (ACQ6), and a responder analysis comparing proportion reaching minimum clinically important difference for AQLQ and ACQ6.

Results: 95 participants were randomised 1:1 to PR or UC. Median age was 54 years, 60% were female and median BMI was 33.8 kg/m². Mean (SD) AQLQ was 3.9 (+/-1.2) and median (IQR) ACQ6 2.8(1.8-3.6). 77 participants attended a second visit and had results analysed. Median (IQR) change in AQLQ was not significantly different: 0.3 (- 0.2 to 0.6) in PR and - 0.1 (- 0.5 to 0.4) in UC, $p = 0.139$. Mean change in ACQ6 was significantly different: - 0.4 (95% CI - 0.6 to - 0.2) in PR and 0 (- 0.3 to + 0.3) in UC, $p = 0.015$, but below minimum clinically important difference. In ACQ6 responder analysis, minimum clinically important difference was reached by 18 PR participants (54.5%) versus 10 UC (22.7%), $p = 0.009$. Dropout rate was 31% between visits in PR group, and time to completion was significantly prolonged in PR group at 94 (70-107) days versus 63 (56-73) in UC, $p < 0.001$.

Conclusions: PR improved asthma control and reduced perceived breathlessness in participants with difficult-to-control asthma and elevated BMI. However, this format appears to be suboptimal for this population with high drop-out rates and prolonged time to completion. Trial registration Clinicaltrials.gov. ID [NCT03630432](#). Retrospectively registered, submitted May 26th 2017, posted August 14th 2018.

Keywords: Asthma; Difficult-to-control asthma; Obesity; Pulmonary rehabilitation.

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Conflict of interest statement

HCR, VS, FS, AG, EM, GM, DSB and DCC have no conflicts of interest. RC has received grants from AstraZeneca for being an investigator on an MRC study, payments from GSK, AstraZeneca, Teva, Chiesi for lecturing, support from Teva, Chiesi, Napp Sanofi, Boehringer for attending conferences and from GSK, AstraZeneca, Teva, Chiesi, Novartis for advisory board meetings.

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

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Adv Ther

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. 2022 Sep 24.

doi: 10.1007/s12325-022-02307-x. Online ahead of print.

[A Review of Anti-IL-5 Therapies for Eosinophilic Granulomatosis with Polyangiitis](#)

[Haruki Koike](#)¹, [Ryoji Nishi](#)^{2,3}, [Satoru Yagi](#)², [Soma Furukawa](#)², [Yuki Fukami](#)², [Masahiro Iijima](#)², [Masahisa Katsuno](#)^{2,4}

Affiliations [expand](#)

- PMID: 36152266

- DOI: [10.1007/s12325-022-02307-x](https://doi.org/10.1007/s12325-022-02307-x)

Abstract

Eosinophilic granulomatosis with polyangiitis (EGPA), previously known as Churg-Strauss syndrome, is a systemic disorder characterized by asthma, eosinophilia, and vasculitis primarily affecting small vessels. Although this disease is classified as an anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis along with microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA), observations suggest that eosinophils play a vital role in the pathophysiology of EGPA. Therefore, biopsy specimens derived from patients with EGPA demonstrated an increase in eosinophils within the vascular lumen and extravascular interstitium, especially in patients negative for ANCA. In addition, active secretion of eosinophil intracellular components by cytolysis and piecemeal degranulation occurs in the extravascular interstitium and bloodstream. Although the treatment for EGPA is described in the context of ANCA-associated vasculitis along with MPA and GPA, a therapeutic approach to suppress eosinophils is also considered. Monoclonal antibodies directed against interleukin-5 (IL-5) or its receptors are good therapeutic agents because IL-5 plays an important role in eosinophil growth, activation, and survival. Currently, mepolizumab (Nucala), reslizumab (Cinqair), and benralizumab (Fasenra) have been studied for use in patients with EGPA. These monoclonal antibodies were initially approved for use in patients with severe eosinophilic asthma. Mepolizumab is now approved for treating EGPA following the success of phase 3 randomized controlled trial. Therefore, further studies are needed to clarify long-term safety and efficacy of anti-IL-5 agents and establish indications of individual therapeutic agents tailored to individual conditions of patients with EGPA.

Keywords: Allergy; Coagulation; EETosis; ETosis; Electron microscopy; Extracellular trap; NETosis; Pathology; Thrombosis; Ultrastructure.

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- [105 references](#)

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BJA Educ

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. 2022 Oct;22(10):402-410.

doi: 10.1016/j.bjae.2022.07.001. Epub 2022 Sep 10.

[Perioperative management of the child with asthma](#)

[S Bali](#)¹, [S Seglani](#)², [J Challands](#)³

Affiliations expand

- PMID: 36132877
- PMCID: PMC9482867 (available on 2023-10-01)
- DOI: [10.1016/j.bjae.2022.07.001](https://doi.org/10.1016/j.bjae.2022.07.001)

No abstract available

Keywords: asthma; paediatrics; perioperative care.

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Prehosp Emerg Care

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. 2022 Sep 29;1-7.

doi: 10.1080/10903127.2022.2126041. Online ahead of print.

[Implementing Oral Systemic Corticosteroids for Pediatric Asthma into EMS Treatment Guidelines: A Qualitative Study](#)

[Kayla McManus¹](#), [Alexandra Cheetham²](#), [Lauren Riney²](#), [Jennifer Brailsford³](#), [Jennifer N Fishe^{1,3}](#)

Affiliations expand

- PMID: 36125194
- DOI: [10.1080/10903127.2022.2126041](https://doi.org/10.1080/10903127.2022.2126041)

Abstract

Introduction: Respiratory distress accounts for approximately 14% of all pediatric emergency medical services (EMS) encounters, with asthma being the most common diagnosis. In the emergency department (ED), early administration of systemic corticosteroids decreases hospital admission and speeds resolution of symptoms. For children treated by EMS, there is an opportunity for earlier corticosteroid administration. Most EMS agencies carry intravenous (IV) corticosteroids; yet given the challenges and low rates of EMS pediatric IV placement, oral corticosteroids (OCS) are a logical alternative. However, previous single-agency studies showed low adoption of OCS. Therefore, qualitative study of OCS implementation by EMS is warranted. **Methods:** This study's objective was to explore uptake and implementation of OCS for pediatric asthma treatment through semi-structured interviews and focus groups with EMS clinicians. We thematically coded and analyzed transcripts using the domains and constructs of the Consolidated Framework for Implementation Research (CFIR) to identify barriers and facilitators that most strongly influenced OCS implementation and adoption by EMS clinicians. **Results:** We conducted five focus groups with a total of ten EMS clinicians from four EMS systems: one urban region with multiple agencies that hosted two focus groups, one suburban agency, one rural agency, and a mixed rural/suburban agency. Of the 36 CFIR constructs, 31 were addressed in the interviews. Most constructs coded were in the CFIR domains of the inner setting and characteristics of individuals, indicating that EMS agency factors as well as EMS clinician characteristics were impactful for implementation. Barriers to OCS adoption included unfamiliarity and inexperience with pediatric patients and pediatric dosing, and lack of knowledge of the benefits of corticosteroids. Facilitators included friendly competition with colleagues, having a pediatric medical director, and feedback from receiving EDs on patient outcomes. **Conclusion:** This qualitative focus group study of OCS implementation by EMS clinicians for the treatment of pediatric asthma found many barriers and facilitators that mapped to the structure of EMS agencies and characteristics of individual EMS clinicians. To fully implement this evidence-based intervention for pediatric asthma, more education on the intervention is required, and EMS clinicians will benefit from further pediatric training.

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Observational Study

Respir Med

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. 2022 Oct;202:106982.

doi: 10.1016/j.rmed.2022.106982. Epub 2022 Sep 9.

Luminal mucus plugs are spatially associated with airway wall thickening in severe COPD and asthma: A single-centered, retrospective, observational study

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Affiliations expand

- PMID: 36116144
- DOI: [10.1016/j.rmed.2022.106982](https://doi.org/10.1016/j.rmed.2022.106982)

Abstract

Background: Airway wall thickening and excess airway mucus occur in asthma and chronic obstructive pulmonary disease (COPD), but few studies have investigated the relationship between them. Our objective was to determine the association between computed tomography (CT) airway wall thickening in segmental airways proximal to airways with or without mucus plugging in patients with asthma and COPD.

Methods: Mucus plugging was scored using a CT bronchopulmonary segment-based scoring system in asthma and COPD patients. For each of the 19 segmental airways, a mucus plug was defined as complete occlusion of one or more of the daughter branches (sub-segmental airways) by mucus. CT airway measurements were generated for each of the 19 segmental airways: wall-area-percentage (WA%), lumen area (LA), and total airway count (TAC) (VIDA Diagnostics Inc.). Multivariable logistic regression models were constructed for the presence of mucus plugs with corresponding CT measurement and adjusted by covariates; each of the 19 segments was treated as a nested variable.

Results: A total of 33 participants were evaluated. Participants had a mean age of 60 ± 15 yrs and there were $n = 14$ (42%) males. There were 16 (48%) participants with a diagnosis of asthma and 17 (52%) with a COPD diagnosis. The mean FEV_1 was $53 \pm 21\%$ pred and FEV_1/FVC was $54 \pm 15\%$. The mean mucus score in all participants was 15 ± 4 (min = 0, max = 19). Multivariable logistic regression analysis showed the presence of airway mucus was significantly associated with increased CT WA% ($\beta = 7.30$, $p = 0.004$) and reduced TAC ($\beta = -0.06$, $p = 0.045$).

Conclusions: There was increased airway wall thickness and reduced airway counts on CT in segments where there was a distal mucus plug compared to segments without mucus plugs in asthma and COPD.

Keywords: Airway wall thickening; Asthma; COPD; Computed tomography (CT); Imaging; Mucus plugs.

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Conflict of interest statement

Declaration of competing interest TH reports grants from Fisher and Paykel and personal fees from Sanofi, outside the submitted work. PN reports grants from AstraZeneca, Teva, Roche, Novartis, Sanofi and Foresee, and personal fees from AstraZeneca, Teva, Roche, Novartis, Merck and Equillium, outside the submitted work. SS reports grants from Cyclomedica and personal fees from AstraZeneca, Novartis, Polarean, and Arrowhead Pharmaceuticals, all outside the submitted work. All other authors do not have any potential conflicts of interest to declare.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Respir Med

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. 2022 Oct;202:106942.

doi: 10.1016/j.rmed.2022.106942. Epub 2022 Aug 4.

[Is asthma control more than just an absence of symptoms? An expert consensus statement](#)

[Giorgio Walter Canonica](#)¹, [Antonio Spanevello](#)², [Luis Pérez de Llano](#)³, [Christian Domingo Ribas](#)⁴, [John D Blakey](#)⁵, [Gabriel Garcia](#)⁶, [Hiromasa Inoue](#)⁷, [Margareth Dalcolmo](#)⁸, [Dong Yang](#)⁹, [Soniya Mokashi](#)¹⁰, [Abhishek Kurne](#)¹¹, [Aman Kapil Butta](#)¹²

Affiliations expand

- PMID: 36096072
- DOI: [10.1016/j.rmed.2022.106942](https://doi.org/10.1016/j.rmed.2022.106942)

Abstract

Purpose: Definitions and measures of asthma control used in clinical trials and in clinical practice vary considerably. There is also misalignment between patients and healthcare professionals (HCPs) in terms of understanding and managing asthma control. This study aimed to progress towards a consensus definition of asthma control, and evaluate disparities between HCP and patient perspectives.

Basic procedures: A two-stage Delphi questionnaire involving asthma specialists sought to identify areas of consensus on aspects of asthma control in clinical practice. Results were compared with those of a structured literature review to assess if existing guidance and measures of asthma control used in studies correlated with practice. Eighty-two panelists took part in the Delphi questionnaire. The structured literature review included 185 manuscripts and 31 abstracts.

Main findings: Panelists agreed that there was no standard definition of asthma control, confirmed by a total of 19 different composite consensus/guideline definitions and/or validated measures of control being identified across the Delphi study and literature review. Panelists agreed on the positive associations of well-controlled asthma with patient outcomes, but not on the components or thresholds of a working definition of control.

Principal conclusions: A universally accepted definition and measure of asthma control that is utilized and understood by patients, HCPs, and researchers is required.

Keywords: Asthma; Asthma control; Delphi consensus; Exacerbations; Quality of life; Symptom control.

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SUPPLEMENTARY INFO

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J Asthma

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. 2022 Sep 29;1-7.

doi: 10.1080/02770903.2022.2123741. Online ahead of print.

[Reduced forced expiratory flow between 25% and 75% of vital capacity in children with allergic rhinitis without asthmatic symptoms](#)

[Jue Seong Lee](#)¹, [Sang Hyun Park](#)¹, [Han Ho Kim](#)¹, [So Hyun Ahn](#)², [Eunji Kim](#)², [Seunghyun Kim](#)², [Wonsuck Yoon](#)², [Young Yoo](#)^{1,2}

Affiliations expand

- PMID: 36093643
- DOI: [10.1080/02770903.2022.2123741](https://doi.org/10.1080/02770903.2022.2123741)

Abstract

Allergic rhinitis (AR) and asthma are closely associated in children. Reduced FEF_{25%-75%} which reflects small airway airflow limitation is frequently observed in asthma. This study aimed to examine the proportion of small airway dysfunction in children with AR and to determine its associated factors. **Methods:** The medical records of 144 aged 6-18-year children with AR without overt asthmatic symptoms were retrospectively reviewed. Subjects were divided into 2 groups according to the FEF_{25%-75%} values; normal FEF_{25%-75%} group ($n = 129$) and reduced FEF_{25%-75%} group ($n = 15$). Clinical data, allergen sensitization profile, exhaled nitric oxide, spirometry, and methacholine provocation test results were compared between the two groups. **Results:** The mean FEV₁ and FEF_{25%-75%} values in the reduced FEF_{25%-75%} group ($73.5 \pm 9.4\%$ pred and $56.0 \pm 7.7\%$ pred, respectively) were significantly lower than in the normal FEF_{25%-75%} group ($87.0 \pm 12.5\%$ pred and $99.1 \pm 21.4\%$ pred, respectively). The mean disease duration was significantly longer in the reduced FEF_{25%-75%} group than in the normal FEF_{25%-75%} group (5.39 ± 1.85 y vs 3.14 ± 1.80 y, $p < 0.001$). Subjects with positive bronchial hyperresponsiveness (MChPC₂₀ < 16 mg/mL) were more frequently detected in the reduced FEF_{25%-75%} group than in the normal FEF_{25%-75%} group (26.7% vs 8.52%, $p = 0.013$). Long disease duration and severity of AR were significantly associated with impaired FEF_{25%-75%} values. **Conclusions:** Subjects with AR alone may have impaired FEF_{25%-75%} values which is considered as a marker of early bronchial involvement. Longer disease duration and severity of AR are important risk factors for progressive declines in small airway function. Physicians should be aware of need for the measurement of FEF_{25%-75%} values for early detection of small airway dysfunction, particularly in children with severe long-lasting allergic rhinitis.

Keywords: Children; allergy; asthma; pulmonary function; rhinitis.

FULL TEXT LINKS



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Respir Med

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. 2022 Oct;202:106938.

doi: 10.1016/j.rmed.2022.106938. Epub 2022 Aug 11.

Dupilumab efficacy in subgroups of type 2 asthma with high-dose inhaled corticosteroids at baseline

[Arnaud Bourdin](#)¹, [J Christian Virchow](#)², [Alberto Papi](#)³, [Njira L Lugogo](#)⁴, [Philip Bardin](#)⁵, [Martti Antila](#)⁶, [David M G Halpin](#)⁷, [Nadia Daizadeh](#)⁸, [Michel Djandji](#)⁹, [Benjamin Ortiz](#)¹⁰, [Juby A Jacob-Nara](#)¹¹, [Rebecca Gall](#)¹², [Yamo Deniz](#)¹³, [Paul J Rowe](#)¹⁴

Affiliations expand

- PMID: 36087550
- DOI: [10.1016/j.rmed.2022.106938](https://doi.org/10.1016/j.rmed.2022.106938)

Abstract

Background and objective: Dupilumab blocks the shared receptor component for interleukin (IL)-4/IL-13, key and central drivers of type 2 inflammation in multiple diseases. In phase 3 QUEST ([NCT02414854](#)), add-on dupilumab 200 and 300 mg every 2 weeks reduced severe exacerbations, improved pre-bronchodilator forced expiratory volume in 1 s (FEV₁), and was generally well tolerated in patients with uncontrolled moderate-to-severe asthma. This post hoc analysis assessed dupilumab efficacy in subpopulations of patients with type 2 asthma and high-dose inhaled corticosteroids (ICS).

Methods: Adjusted annualized severe exacerbation rates over the treatment period, least squares (LS) mean change from baseline at Week 12 in pre-bronchodilator FEV₁, and LS mean change from baseline at Week 24 in 5-item Asthma Control Questionnaire (ACQ-5) scores were analyzed in subgroups of patients receiving high-dose (>500 µg) ICS with baseline blood eosinophils ≥150 cells/µL and/or fractional exhaled nitric oxide ≥25 ppb. Subgroups included allergic phenotype (with/without), comorbid chronic rhinosinusitis and/or nasal polyposis (with/without), pre-bronchodilator FEV₁/forced vital capacity (<70%/≥70%), blood eosinophil level, exacerbation history, median baseline pre-bronchodilator FEV₁, age at asthma onset (≤40/>40 years), median FEV₁ reversibility, body mass index (<30/≥30 kg/m²), and sex.

Results: Dupilumab vs placebo reduced exacerbations and improved pre-bronchodilator FEV₁ at Week 12 and ACQ-5 at Week 24 across subgroups of patients with type 2 asthma and high-dose ICS at baseline. Dupilumab was also effective in patients receiving medium-dose ICS.

Conclusion: Dupilumab reduced severe exacerbations and improved lung function and asthma control in subgroups of patients with type 2 asthma and high-dose ICS at baseline.

Clinical trial registration number: [NCT02414854](#).

Keywords: Exacerbations; Inhaled corticosteroids; Moderate-to-severe asthma; Pre-bronchodilator FEV₁(1); Type 2 inflammation.

Conflict of interest statement

Declaration of competing interest Bourdin A: GSK – non-financial support during the conduct of the study; Acceleron Pharma, Actelion, Galapagos, Merck Sharp & Dohme, Nuvaira, Pulmonx, United Therapeutics, Vertex Pharmaceuticals – other; Boehringer Ingelheim – grants, personal fees; AstraZeneca, Chiesi, GSK, Regeneron Pharmaceuticals, Inc., Sanofi – personal fees. Virchow JC: Altana, AstraZeneca, Avontec, Bayer, Bencard Allergie, Bionorica, Boehringer Ingelheim, Chiesi, Essex Pharma Development, GSK, Hexal, Janssen-Cilag, Leti, Meda Pharmaceuticals, Merck, MSD, Mundipharma, Novartis, Nycomed, Pfizer, Revotar Biopharmaceuticals, Sandoz, Stallergenes Greer, Schwarz Pharma, Teva, UCB, Zydus Cadila – honoraria. Avontec, Boehringer Ingelheim, Chiesi, Essex Pharma Development, GSK, Hexal, Janssen-Cilag, Meda Pharmaceuticals, MSD, Mundipharma, Novartis, Regeneron Pharmaceuticals, Inc., Revotar Biopharmaceuticals, Roche, sanofi-aventis, Sandoz, Schwarz Pharma, Teva, UCB – advisory board participant. Deutsche Forschungsgesellschaft, GSK, Land Mecklenburg-Vorpommern, MSD – research grants. Papi A: AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Mundipharma, Teva – report grants, personal fees, nonfinancial support, other; Menarini, Novartis, Zambon – personal fees, nonfinancial support; Sanofi – grants (all outside the submitted work). Lugogo NL: Amgen, AstraZeneca, Avillion, Genentech, Gossamer Bio, GSK, Regeneron Pharmaceuticals, Inc., Sanofi, Teva – research support paid to institution; Amgen, AstraZeneca, Genentech, GSK, Novartis, Regeneron Pharmaceuticals, Inc., Sanofi, Teva – advisory board member, consultant; AstraZeneca – travel support; AstraZeneca, GSK – honoraria for non-speaker's bureau presentations. Bardin P: AstraZeneca, Boehringer Ingelheim, GSK, Novartis, Sanofi – consultant, speaker fees. Antila M: AbbVie, Angion Biomedica Corp, AstraZeneca, BeiGene, EMS, Eurofarma, GSK, Humanigen, Janssen, Novartis, Sanofi – clinical trial funding; Aché, AstraZeneca, Chiesi, Eurofarma, IPI ASAC Brasil, Sanofi – honoraria; AstraZeneca, GSK, Novartis, Sanofi – meeting or travel support; Abbott, AstraZeneca, Chiesi, Sanofi, Zambon – data safety monitoring board and/or advisory board member. Halpin DMG: AstraZeneca, Boehringer Ingelheim, Chiesi, CSL Behring, GSK, Novartis, Pfizer, Sandoz, Sanofi – advisory board member, speaker fees. Daizadeh N: Sanofi – former employee, may hold stock and/or stock options in the company. Djandji M, Jacob-Nara JA, Rowe PJ: Sanofi – employees, may hold stock and/or stock options in the company. Ortiz B: Regeneron – former employee, may hold stock and/or stock options in the company. Gall R, Deniz Y: Regeneron Pharmaceuticals, Inc. – employees and shareholders.

SUPPLEMENTARY INFO

MeSH terms, Substances, Associated dataexpand

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. 2022 Oct;202:106949.

doi: 10.1016/j.rmed.2022.106949. Epub 2022 Sep 2.

[The impact of inhaler technique on clinical outcomes in adolescents and adults with asthma: A systematic review](#)

[N Roche](#)¹, [B Aggarwal](#)², [I Boucot](#)³, [L Mittal](#)⁴, [A Martin](#)⁴, [H Chrystyn](#)⁵

Affiliations expand

- PMID: 36063773
- DOI: [10.1016/j.rmed.2022.106949](https://doi.org/10.1016/j.rmed.2022.106949)

Free article

Abstract

Background: Many patients with asthma use their inhalers incorrectly, which can lead to sub-optimal asthma control and an increased risk of exacerbations. The Accuhaler/Diskus and Turbuhaler are arguably two of the most commonly used dry powder inhalers worldwide.

Methods: A systematic literature review (SLR) was conducted to assess the impact of inhalation errors with these dry powder inhalers on clinical outcomes in asthma. Database searches were conducted in MEDLINE, Embase and proceedings from scientific conferences. Observational studies in adults and adolescents with asthma, reporting data for Accuhaler/Diskus and Turbuhaler devices and at least one outcome of interest, were included. Dual-independent screening and validation of studies was performed.

Results: The search identified 35 studies. A range of inhaler errors was observed across studies and devices. In 8 out of the 9 studies that involved the two devices, the percentage of overall inhaler error rates was numerically (7 studies) or significantly (1 study) higher for Turbuhaler than Diskus, ranging from 3.7% to 71.9% for Diskus and 1.2%-83% for Turbuhaler. Critical errors, reported in three studies using similar definitions, ranged from 20% to 43% for Diskus and 32%-100% for Turbuhaler. Five studies reported a significant association between inhaler errors and worse asthma control, while one showed no difference.

Conclusions: This SLR identified a large range of inhaler errors with both devices. Across devices, a better inhalation technique was associated with better asthma outcomes. This systematic review confirms the importance of patients using their inhalers correctly as an integral part of achieving optimal asthma outcomes.

Keywords: Asthma; Clinical outcomes; Diskus; Inhaler errors.

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SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Review

J Pharm Technol

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. 2022 Oct;38(5):289-296.

doi: 10.1177/87551225221105749. Epub 2022 Jul 11.

[Efficacy and Safety of Biologics for Chronic Rhinosinusitis With Nasal Polyps](#)

[Renee R Koski](#)^{1,2}, [Luke Hill](#)², [Kylee Taavola](#)³

Affiliations expand

- PMID: 36046351
- PMCID: PMC9420916 (available on 2023-07-11)
- DOI: [10.1177/87551225221105749](https://doi.org/10.1177/87551225221105749)

Abstract

Objective: To review published literature for biologic treatment of nasal polyps. **Data Sources:** PubMed search performed on February 16, 2022, using search terms: biologics, benralizumab, dupilumab, mepolizumab, omalizumab, or reslizumab AND nasal polyps, nasal polyposis, or chronic rhinosinusitis with nasal polyposis (CRSwNP). Inclusion criteria were English language, published randomized controlled trials, post hoc analyses, and meta-analyses evaluating biologics for nasal polyposis, with or without comorbid asthma, and no date limits. Additional studies were found through references of primary and tertiary literature. **Study Selection and Data Extraction:** Nineteen studies, including 8 randomized controlled trials, 2 meta-analyses, and 9 post hoc analyses, examined the efficacy and safety of biologics for nasal polyposis. Agents studied included benralizumab, dupilumab, mepolizumab, omalizumab, and reslizumab. Studies had

similar inclusion (refractory and recurrent CRSwNP) and exclusion criteria. All studies included the use of an intranasal corticosteroid (mometasone or fluticasone) in addition to the biologic or placebo. The most commonly studied primary endpoint was change in endoscopic nasal polyp score. **Data Synthesis:** All studies, post hoc analyses, and meta-analyses found improvement in endoscopic, clinical, and/or radiographic endpoints with benralizumab, dupilumab, mepolizumab, omalizumab, or reslizumab in patients with CRSwNP with or without comorbid asthma. Dupilumab has the most published data. Dupilumab, mepolizumab, and omalizumab are the only biologics currently Food and Drug Administration-approved for CRSwNP. **Conclusion:** Biologics are beneficial for treating nasal polyps with or without comorbid asthma. The choice depends on patient and provider preference and insurance coverage.

Keywords: benralizumab; biologics; chronic rhinosinusitis with nasal polyposis; dupilumab; mepolizumab; omalizumab; or reslizumab.

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Conflict of interest statement

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

SUPPLEMENTARY INFO

Publication types expand

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Review

Eur J Clin Pharmacol

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. 2022 Oct;78(10):1613-1622.

doi: 10.1007/s00228-022-03374-3. Epub 2022 Aug 26.

[Use of ketamine in patients with refractory severe asthma exacerbations: systematic review of prospective studies](#)

[Luigi La Via](#) ^{#1}², [Filippo Sanfilippo](#) ^{#3}, [Giuseppe Cuttone](#) ⁴, [Veronica Dezio](#) ³⁴, [Monica Falcone](#) ⁵, [Serena Brancati](#) ⁶, [Claudia Crimi](#) ⁷, [Marinella Astuto](#) ³

Affiliations expand

- PMID: 36008492
- PMCID: [PMC9482594](#)
- DOI: [10.1007/s00228-022-03374-3](#)

Free PMC article

Abstract

Purpose: Asthma is a heterogeneous disease with a wide range of symptoms. Severe asthma exacerbations (SAEs) are characterized by worsening symptoms and bronchospasm requiring emergency department visits. In addition to conventional strategies for SAEs (inhaled β -agonists, anticholinergics, and systemic corticosteroids), another pharmacological option is represented by ketamine. We performed a systematic review to explore the role of ketamine in refractory SAEs.

Methods: We performed a systematic search on PubMed and EMBASE up to August 12th, 2021. We selected prospective studies only, and outcomes of interest were oxygenation/respiratory parameters, clinical status, need for invasive ventilation and effects on weaning.

Results: We included a total of seven studies, five being randomized controlled trials (RCTs, population range 44-92 patients). The two small prospective studies ($n = 10$ and $n = 11$) did not have a control group. Four studies focused on adults, and three enrolled a pediatric population. We found a large heterogeneity regarding sample size, age and gender distribution, inclusion criteria (different severity scores, if any) and ketamine dosing (bolus and/or continuous infusion). Of the five RCTs, three compared ketamine to placebo, while one used fentanyl and the other aminophylline. The outcomes evaluated by the included studies were highly variable. Despite paucity of data and large heterogeneity, an overview of the included studies suggests absence of clear benefit produced by ketamine in patients with refractory SAE, and some signals towards side effects.

Conclusion: Our systematic review does not support the use of ketamine in refractory SAE. A limited number of prospective studies with large heterogeneity was found. Well-designed multicenter RCTs are desirable.

Keywords: Aminophylline; Asthma; Bronchospasm; Fentanyl; Inflammation; Mechanical ventilation.

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Conflict of interest statement

The authors declare no competing interests.

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

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS



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Review

Lancet Child Adolesc Health

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. 2022 Oct;6(10):713-724.

doi: 10.1016/S2352-4642(22)00185-7. Epub 2022 Aug 19.

[Obesity-related asthma in children and adolescents](#)

[Jessica Reyes-Angel](#)¹, [Parisa Kaviany](#)², [Deepa Rastogi](#)², [Erick Forno](#)³

Affiliations expand

- PMID: 35988550
- DOI: [10.1016/S2352-4642\(22\)00185-7](https://doi.org/10.1016/S2352-4642(22)00185-7)

Abstract

There is substantial epidemiological and experimental evidence of an obesity-related asthma phenotype. Compared to children of healthy weight, children with obesity are at higher risk of asthma. Children with obesity who have asthma have greater severity and poorer control of their asthma symptoms, more frequent asthma exacerbations, and overall lower asthma-related quality of life than children with asthma who have a healthy weight. In this Review, we examine some of the latest evidence on the characteristics of this phenotype and its main underlying mechanisms, including genetics and genomics, changes in airway mechanics and lung function, sex hormone differences, alterations in immune responses, systemic and airway inflammation, metabolic dysregulation, and modifications in the microbiome. We also review current recommendations for the treatment of these children, including in the management of their asthma, and current evidence for weight loss interventions. We then discuss initial evidence for potential novel therapeutic approaches, such as dietary modifications and supplements, antidiabetic medications, and statins. Finally, we identify knowledge gaps and future directions to improve our understanding of asthma in children with obesity, and to improve outcomes in these susceptible children. We highlight

important needs, such as designing paediatric-specific studies, implementing large multicentric trials with standardised interventions and outcomes, and including racial and ethnic groups along with other under-represented populations that are particularly affected by obesity and asthma.

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Conflict of interest statement

Declaration of interests We declare no competing interests.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grant supportexpand

FULL TEXT LINKS



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☐ 40

Randomized Controlled Trial

Eur J Pediatr

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. 2022 Oct;181(10):3701-3709.

doi: 10.1007/s00431-022-04576-8. Epub 2022 Aug 3.

[Efficacy of a loading dose of IV salbutamol in children with severe acute asthma admitted to a PICU: a randomized controlled trial](#)

[Shelley A Boeschoten](#)¹, [Corinne M P Buysse](#)², [Brenda C M de Winter](#)³, [Joost van Rosmalen](#)^{4,5}, [Johan C de Jongste](#)⁶, [Rogier C de Jonge](#)², [Sabien G J Heisterkamp](#)⁷, [Job B van Woensel](#)⁷, [Martin C J Kneyber](#)⁸, [Annelies van Zwol](#)⁹, [Annemie L M Boehmer](#)^{10,11}, [Matthijs de Hoog](#)², [Dutch collaborative PICU research network \(SKIC\)](#)

Affiliations expand

- PMID: 35922522

- PMID: [PMC9508206](#)
- DOI: [10.1007/s00431-022-04576-8](#)

Free PMC article

Abstract

The optimal dose regimen for intravenous (IV) treatment in children with severe acute asthma (SAA) is still a matter of debate. We assessed the efficacy of adding a salbutamol loading dose to continuous infusion with salbutamol in children admitted to a pediatric intensive care unit (PICU) with SAA. This multicentre, placebo-controlled randomized trial in the PICUs of four tertiary care children's hospitals included children (2-18 years) with SAA admitted between 2017 and 2019. Children were randomized to receive either a loading dose IV salbutamol (15 mcg/kg, max. 750 mcg) or normal saline while on continuous salbutamol infusion. The primary outcome was the asthma score (Qureshi) 1 h after the intervention. Analysis of covariance models was used to evaluate sensitivity to change in asthma scores. Serum concentrations of salbutamol were obtained. Fifty-eight children were included (29 in the intervention group). Median baseline asthma score was 12 (IQR 10-13) in the intervention group and 11 (9-12) in the control group ($p = 0.032$). The asthma score 1 h after the intervention did not differ significantly between the groups ($p = 0.508$, β -coefficient = 0.283). The median increase in salbutamol plasma levels 10 min after the intervention was 13 $\mu\text{g/L}$ (IQR 5-24) in the intervention group and 4 $\mu\text{g/L}$ (IQR 0-7) in the control group ($p = 0.001$). Side effects were comparable between both groups.

Conclusion: We found no clinical benefit of adding a loading dose IV salbutamol to continuous infusion of salbutamol, in children admitted to the PICU with SAA. Clinically significant side effects from the loading dose were not encountered.

What is known: • Pediatric asthma guidelines struggle with an evidence-based approach for the treatment of SAA beyond the initial steps of oxygen suppletion, repetitive administration of inhaled β_2 -agonists, and systemic steroids. • During an SAA episode, effective delivery of inhaled drugs is unpredictable due to severe airway obstruction.

What is new: • This study found no beneficial effect of an additional loading dose IV salbutamol in children admitted to the PICU. • This study found no clinically significant side effects from the loading dose.

Keywords: Children; IV salbutamol bolus; Intensive care; Severe acute asthma, Therapy; Status asthmaticus.

© 2022. The Author(s).

Conflict of interest statement

The authors declare no competing interests.

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

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand



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☐ 41

Eur J Intern Med

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. 2022 Oct;104:66-72.

doi: 10.1016/j.ejim.2022.07.019. Epub 2022 Jul 31.

[A machine learning approach to characterize patients with asthma exacerbation attending an acute care setting](#)

[Maria D'Amato](#)¹, [Pasquale Ambrosino](#)², [Francesca Simioli](#)³, [Sarah Adamo](#)⁴, [Anna Agnese Stanziola](#)³, [Giovanni D'Addio](#)⁵, [Antonio Molino](#)³, [Mauro Maniscalco](#)⁶

Affiliations expand

- PMID: 35922367
- DOI: [10.1016/j.ejim.2022.07.019](https://doi.org/10.1016/j.ejim.2022.07.019)

Abstract

Background: One of the main problems in poorly controlled asthma is the access to the Emergency Department (ED). Using a machine learning (ML) approach, the aim of our study was to identify the main predictors of severe asthma exacerbations requiring hospital admission.

Methods: Consecutive patients with asthma exacerbation were screened for inclusion within 48 hours of ED discharge. A k-means clustering algorithm was implemented to evaluate a potential distinction of different phenotypes. K-Nearest Neighbor (KNN) as instance-based algorithm and Random Forest (RF) as tree-based algorithm were implemented in order to classify patients, based on the presence of at least one additional access to the ED in the previous 12 months.

Results: To train our model, we included 260 patients (31.5% males, mean age 47.6 years). Unsupervised ML identified two groups, based on eosinophil count. A total of 86 patients with eosinophiles ≥ 370 cells/ μ L were significantly older, had a longer disease duration, more restrictions to daily activities, and lower rate of treatment compared to 174 patients with eosinophiles < 370 cells/ μ L. In addition, they reported lower values of predicted FEV₁ (64.8 \pm 12.3% vs. 83.9 \pm 17.3%) and FEV₁/FVC (71.3 \pm 9.3 vs. 78.5 \pm 6.8), with a higher

amount of exacerbations/year. In supervised ML, KNN achieved the best performance in identifying frequent exacerbators (AUROC: 96.7%), confirming the importance of spirometry parameters and eosinophil count, along with the number of prior exacerbations and other clinical and demographic variables.

Conclusions: This study confirms the key prognostic value of eosinophiles in asthma, suggesting the usefulness of ML in defining biological pathways that can help plan personalized pharmacological and rehabilitation strategies.

Keywords: Asthma; Biomarker; Chronic disease; Chronic obstructive pulmonary disease; Disability; Exercise capacity; Occupational medicine; Outcome; Rehabilitation.

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Conflict of interest statement

Conflicts of interest The authors declare no conflicts of interest.

FULL TEXT LINKS



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Case Reports

J Immunother

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. 2022 Oct 1;45(8):370-373.

doi: 10.1097/CJI.0000000000000430. Epub 2022 Aug 2.

[Nivolumab-associated Nasal Polyposis and Eosinophilic Asthma Responsive to Benralizumab, An Anti-IL5R Biologic](#)

[Steven Rembalski¹](#), [Joshua A Steinberg^{1,2}](#)

Affiliations expand

- PMID: 35913799

- DOI: [10.1097/CJI.0000000000000430](https://doi.org/10.1097/CJI.0000000000000430)

Abstract

We present a case report of nivolumab-aggravated treatment-resistant chronic rhinosinusitis with nasal polyposis with asthma, suggestive of aspirin-exacerbated respiratory disease, normalized with the IL-5R antagonist benralizumab. For patients experiencing symptomatic complications of immunotherapy-associated eosinophilia, this case suggests anti-IL-5(R) biologics may durably resolve nasal polyposis and asthma symptoms, permitting continuity of checkpoint inhibitor therapy and sparing of systemic corticosteroids. Postulated mechanisms of checkpoint inhibition favoring eosinophilia and polyposis, and the uncertain effect of eosinophil reduction upon malignancy progression, are reviewed.

- [26 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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☐ 43

Editorial

Am J Respir Cell Mol Biol

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. 2022 Oct;67(4):419-420.

doi: 10.1165/rcmb.2022-0287ED.

[Anxiolytics for Bronchodilation: Refinements to GABA_A Agonists for Asthma Relief](#)

[Ajay P Nayak](#)^{1,2}, [Steven S An](#)^{3,4}

Affiliations expand

- PMID: 35901197

- DOI: [10.1165/rcmb.2022-0287ED](https://doi.org/10.1165/rcmb.2022-0287ED)

No abstract available

Comment on

- [Imidazobenzodiazepine PI320 Relaxes Mouse Peripheral Airways by Inhibiting Calcium Mobilization.](#)

Perez-Zoghbi JF, Sajorda DR, Webb DA, Arnold LA, Emala CW, Yocum GT. Am J Respir Cell Mol Biol. 2022 Oct;67(4):482-490. doi: 10.1165/rcmb.2022-0084OC. PMID: 35776523

SUPPLEMENTARY INFO

Publication types, Grant supportexpand

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☐ 44

Allergy Asthma Proc

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. 2022 Sep 25;43(5):e25-e30.

doi: 10.2500/aap.2022.43.220029. Epub 2022 Jul 25.

[Effects of mechanical washing and drying on the removal of pet allergens](#)

[Young-Jin Choi](#)¹, [Sujiin Seong](#)², [Kyung Suk Lee](#)¹, [Kisup Lee](#)², [Hyeongjoon Seo](#)², [Jae-Won Oh](#)¹

Affiliations expand

- PMID: 35879023

- DOI: [10.2500/aap.2022.43.220029](https://doi.org/10.2500/aap.2022.43.220029)

Abstract

Background: In Korea, the number of households with indoor pets is rapidly increasing in parallel with changes in cultural lifestyles. The sensitization rate of pet allergens is also increasing in Korea. **Objective:** We evaluated the effectiveness of washing machines to remove dog and cat hair and their allergens. In addition, this study aimed to investigate whether only a mechanical dryer without mechanical washing could be used for pet allergen removal. **Method:** We brushed cats and dogs, and thereafter collected their hair and used a residential vacuum cleaner to obtain dust and other particulate matter from a household. The contents of the vacuum bag were sifted through a 300-µm sieve filter. Some of the contents were placed in phosphate-buffered saline solution with 0.5% Tween 20 to make a liquid extract. Hair, dust, and liquid extract-contaminated fabric samples after mechanical washing or after drying without mechanical washing were analyzed for pet allergens (Fel d 1 [cat], Can f 1 [dog]) by using a two-site enzyme-linked immunosorbent assay. We assessed the remaining allergens in the contaminated fabrics after mechanical drying and washing. **Results:** The mean Fel d 1 and mean Can f 1 removal ratios after mechanical washing with detergent were > 99.99% for the dust, hair, and liquid extract. The removal ratios after mechanical washing without a detergent were lower for both Fel d 1 and Can f 1, for hair, dust, and their respective liquid extracts ($p < 0.05$). Mechanical drying was just as effective as mechanical washing with detergent for removing Can f 1 but was less effective for Fel d 1 ($p < 0.05$). **Conclusion:** Mechanical washing with detergent is important to remove pet allergens from contaminated fabrics. If washing is difficult, then using just a dryer without washing can be an alternative method to remove allergens from contaminated bedding or clothing.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS



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Cite

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☐ 45

J Clin Sleep Med

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. 2022 Oct 1;18(10):2377-2385.

doi: 10.5664/jcsm.10114.

[Associations between sleep, obesity, and asthma in urban minority children](#)

[Laura A Conrad](#)¹, [Kiran Nandalike](#)², [Seema Rani](#)³, [Deepa Rastogi](#)⁴

Affiliations expand

- PMID: 35801341

- DOI: [10.5664/jcsm.10114](https://doi.org/10.5664/jcsm.10114)

Abstract

Study objectives: Although obesity, asthma, and sleep-disordered breathing are interrelated, there is limited understanding of the independent contributions of body-mass index and pulmonary function on polysomnography in children with asthma.

Methods: We conducted a retrospective chart review on 448 7- to 18-year-old children with asthma who had undergone polysomnography testing between 1/2007-12/2011 to elucidate the association between spirometry variables, body-mass index, and polysomnography parameters, adjusting for asthma and antiallergic medications.

Results: Obese children had poorer sleep architecture and more severe gas exchange abnormalities compared to healthy weight children. Multivariate analysis revealed an independent association of body-mass index with sleep efficiency, with more light and less deep sleep in both obese and healthy-weight children, and with baseline oxygen saturation and oxygen nadir in obese children. In obese children, forced vital capacity was independently associated with less deep sleep (time in N3 sleep) as well as with oxygen nadir, while among healthy-weight children, forced expiratory volume directly correlated but forced vital capacity inversely correlated with deep sleep. In obese children, inhaled corticosteroid was associated with baseline oxygen saturation, and montelukast was associated with lower end-tidal carbon dioxide. In healthy-weight children, inhaled corticosteroid was associated with arousal awakening index, and montelukast was associated with light sleep. Antiallergic medications were not independently associated with polysomnography parameters.

Conclusions: Pulmonary function, body-mass index, and asthma medications have independent and differing influences on sleep architecture and gas exchange polysomnography parameters in obese and healthy-weight children with asthma. Asthma medications are associated with improved gas exchange in obese children and improved sleep architecture in healthy-weight children with asthma.

Citation: Conrad LA, Nandalike K, Rani S, Rastogi D. Associations between sleep, obesity, and asthma in urban minority children. *J Clin Sleep Med*. 2022;18(10):2377-2385.

Keywords: asthma; lung function; obesity; polysomnography; sleep-disordered breathing.

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SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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Cite

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46

Ann Allergy Asthma Immunol

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. 2022 Oct;129(4):475-480.e2.

doi: 10.1016/j.anai.2022.06.022. Epub 2022 Jun 30.

[16-year trends in asthma hospital admissions in Canada](#)

[Tae Yoon Lee](#)¹, [John Petkau](#)², [Nevrose Mangat](#)³, [Abdollah Safari](#)⁴, [Jacquelyn J Cragg](#)³, [Larry D Lynd](#)⁵, [J Mark FitzGerald](#)⁶, [Stuart E Turvey](#)⁷, [Mohsen Sadatsafavi](#)⁸

Affiliations expand

- PMID: 35779843
- DOI: [10.1016/j.anai.2022.06.022](https://doi.org/10.1016/j.anai.2022.06.022)

Abstract

Background: Asthma hospitalizations declined rapidly in many parts of the world, including Canada, in the 1990s and early 2000s.

Objective: To examine whether the declining trend of asthma hospitalizations persisted in recent years in Canada.

Methods: Using the Canadian comprehensive nationwide hospitalization data (2002-2017), we identified hospital admissions with the main International Classification of Diseases codes for asthma. We analyzed sex-specific age-standardized trends in annual hospitalization rates among pediatric (< 19 years) and adult (19+ years) patients. We used change-point analysis to evaluate any substantial changes in the trends in the sex-age groups.

Results: There were 254,672 asthma-related hospital admissions (59% pediatric, 50% female) during the study period. Among children, age-adjusted annual rates per 100,000 decreased by 55% in females (152-69) and by 60% in males (270-108) from 2002 to 2017. Among adults, the rates decreased by 59% in both sexes (females: 61-25; males: 27-11). Change-point analysis indicated a substantial plateauing of the annual rate in both pediatric (from -15.3 [females] and -25.8 [males] before 2010 to -0.6 [females] and -0.8 [males] after 2010) and adult (from -5.4 [females] and -2.6 [males] before 2008 to -0.6 [females] and -0.2 [males] after 2008) groups.

Conclusion: After a substantial decline in hospital admissions for acute asthma, there has been minimal further decline since 2010 for children and 2008 for adults. In addition to adhering to the contemporary standards of asthma care, novel, disruptive strategies are likely needed to further reduce the burden of asthma.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS



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Cite

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47

Allergy Asthma Proc

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. 2022 Sep 27;43(5):383-387.

doi: 10.2500/aap.2022.43.220038. Epub 2022 Jun 27.

[Biomarker underuse contributes to an inability to phenotype patients with severe uncontrolled asthma](#)

[Najm S Khan¹](#), [Elizabeth Rubin²](#), [Bernard McKenna³](#), [Bernard L Palowitch³](#), [Frank Sonnenberg⁴](#), [Judith Argon⁵](#), [Reynold A Panettieri Jr⁵](#)

Affiliations expand

- PMID: 35760498
- DOI: [10.2500/aap.2022.43.220038](https://doi.org/10.2500/aap.2022.43.220038)

Abstract

Background: Biomarker measurements improve the phenotyping of patients with severe uncontrolled asthma (SUA) and predict therapeutic responses. The use of biomarkers in asthma, however, remains underused. **Objective:** To test the hypothesis that biomarker measurements of patients with SUA remain markedly underused and contributes to asthma morbidity and oral corticosteroid use. **Methods:** Leveraging claims data linked to electronic health record data, we calculated biomarker use by providers treating patients with SUA from January 2017 to August 2020. **Results:** From 3.6 million clients, 3817 had a primary diagnosis of asthma; most were between 50 and 60 years old. Also, 63.2% were female patients; those under ages 10 years were primarily boys. Of the 728 patients who reported race, 69.9% were white and 21.8% were African American. Of the 840 who reported ethnicity, 14% were Latinx. A predetermined

definition of SUA identified 348 patients with SUA. In a nested sample of 151 patients with SUA, 43% were managed by primary care physicians (PCP), 4% by specialists, and 49.7% by both. Of this sample, 61.5% had a measurement of serum eosinophils, 9.9% total immunoglobulin E values, and 9.3% radioallergosorbent skin tests; 38% received no tests, whereas 9.9% had more than one. Specialists ordered a biomarker test 4.6 times more often than did PCPs, whereas PCPs ordered 70% of the prednisone prescriptions for recurrent asthma exacerbations. **Conclusion:** Specialists were more likely to order biomarkers than were PCPs. Patients managed exclusively by PCPs were more likely prescribed oral prednisone. Real-world evidence shows that biomarkers are infrequently used to characterize patients with SUA, especially among patients exclusively managed by PCPs. Programs that encouraged biomarker use may improve SUA management and oral corticosteroid burden.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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Cite

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☐ 48

Allergy

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. 2022 Oct;77(10):2888-2908.

doi: 10.1111/all.15412. Epub 2022 Jun 30.

[Omics technologies in allergy and asthma research: An EAACI position paper](#)

[Urszula Radzikowska](#)^{1,2}, [Katja Baerenfaller](#)^{1,3}, [José Antonio Cornejo-García](#)⁴, [Cagatay Karaaslan](#)⁵, [Elena Barletta](#)^{1,3}, [Basak Ezgi Sarac](#)⁵, [Damir Zhakparov](#)^{1,3}, [Alma Villaseñor](#)^{6,7}, [Ibon Eguiluz-Gracia](#)^{8,9}, [Cristobalina Mayorga](#)^{8,9,10}, [Milena Sokolowska](#)^{1,2}, [Coral Barbas](#)⁶, [Domingo Barber](#)⁷, [Markus Ollert](#)^{11,12}, [Tomas Chivato](#)^{7,13}, [Ioana Agache](#)¹⁴, [Maria M Escribese](#)⁷

Affiliations expand

- PMID: 35713644
- DOI: [10.1111/all.15412](https://doi.org/10.1111/all.15412)

Abstract

Allergic diseases and asthma are heterogenous chronic inflammatory conditions with several distinct complex endotypes. Both environmental and genetic factors can influence the development and progression of allergy. Complex pathogenetic pathways observed in allergic disorders present a challenge in patient management and successful targeted treatment strategies. The increasing availability of high-throughput omics technologies, such as genomics, epigenomics, transcriptomics, proteomics, and metabolomics allows studying biochemical systems and pathophysiological processes underlying allergic responses. Additionally, omics techniques present clinical applicability by functional identification and validation of biomarkers. Therefore, finding molecules or patterns characteristic for distinct immune-inflammatory endotypes, can subsequently influence its development, progression, and treatment. There is a great potential to further increase the effectiveness of single omics approaches by integrating them with other omics, and nonomics data. Systems biology aims to simultaneously and longitudinally understand multiple layers of a complex and multifactorial disease, such as allergy, or asthma by integrating several, separated data sets and generating a complete molecular profile of the condition. With the use of sophisticated biostatistics and machine learning techniques, these approaches provide in-depth insight into individual biological systems and will allow efficient and customized healthcare approaches, called precision medicine. In this EAACI Position Paper, the Task Force "Omics technologies in allergic research" broadly reviewed current advances and applicability of omics techniques in allergic diseases and asthma research, with a focus on methodology and data analysis, aiming to provide researchers (basic and clinical) with a desk reference in the field. The potential of omics strategies in understanding disease pathophysiology and key tools to reach unmet needs in allergy precision medicine, such as successful patients' stratification, accurate disease prognosis, and prediction of treatment efficacy and successful prevention measures are highlighted.

Keywords: allergy; biomarker; omic; precision medicine; systems biology.

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- [223 references](#)

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS



[Proceed to details](#)

Cite

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 49

Editorial

Am J Respir Crit Care Med

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. 2022 Oct 1;206(7):803-804.

doi: 10.1164/rccm.202206-1063ED.

[When Health Disparities Hit Home: Redlining Practices, Air Pollution, and Asthma](#)

[Sonali Bose](#)^{1,2}, [Jaime Madrigano](#)³, [Nadia N Hansel](#)^{2,3}

Affiliations expand

- PMID: 35696342
- DOI: [10.1164/rccm.202206-1063ED](https://doi.org/10.1164/rccm.202206-1063ED)

No abstract available

Comment on

- [Historical Redlining Impacts Contemporary Environmental and Asthma-related Outcomes in Black Adults.](#)
Schuyler AJ, Wenzel SE. Am J Respir Crit Care Med. 2022 Oct 1;206(7):824-837. doi: 10.1164/rccm.202112-2707OC. PMID: 35612914

SUPPLEMENTARY INFO

Publication types expand

FULL TEXT LINKS



[Proceed to details](#)

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☐ 50

Allergy

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. 2022 Oct;77(10):3141-3144.

doi: 10.1111/all.15403. Epub 2022 Jun 20.

Impact of time-varying confounders on the association between early-life allergy sensitization and the risk of current asthma: A post hoc analysis of a birth cohort

[Arthur H Owora](#)^{1,2}, [Rui Li](#)¹, [Robert S Tepper](#)³, [Clare D Ramsey](#)⁴, [Moira Chan-Yeung](#)⁵, [Wade T A Watson](#)⁶, [Allan B Becker](#)²

Affiliations expand

- PMID: 35686384
- DOI: [10.1111/all.15403](https://doi.org/10.1111/all.15403)

No abstract available

Keywords: allergy sensitization; childhood asthma; marginal structural models.

- [6 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grant supportexpand

FULL TEXT LINKS



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Cite

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☐ 51

Pediatr Pulmonol

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. 2022 Oct;57(10):2313-2319.

doi: 10.1002/ppul.26033. Epub 2022 Jun 13.

Dupilumab in children with moderate-to-severe asthma: A cost utility analysis

[Jefferson A Buendía](#)¹, [Diana G Patiño](#)¹

Affiliations expand

- PMID: 35668042
- DOI: [10.1002/ppul.26033](https://doi.org/10.1002/ppul.26033)

Abstract

Introduction: Dupilumab is an effective and safe medicine for the management of severe asthma. Due to its high cost, concerns are generated regarding its cost-effectiveness. This study aimed to estimate the cost-utility of dupilumab plus standard of care (SoC) versus SoC alone in children between 6 and 11 years old with severe asthma and eosinophilic phenotype.

Methods: A Markov-type model was developed to estimate costs and health outcomes of a simulated cohort of pediatric patients with persistent asthma treated over a 6-year period. To determine the robustness of the model deterministic and probabilistic sensitivity analyses were conducted.

Results: The quality-adjusted life-years (QALYs) per patient estimated were 0.85 with dupilumab and 0.84 with SoC. The total mean of discounted costs per patient per cycle were US\$ 379 for dupilumab and US\$ 19 for SoC. The incremental cost-effectiveness ratio estimated was \$24 660 US\$ per QALY CONCLUSION: Dupilumab is not cost-effective in Colombia in children between 6 and 11 years old with severe asthma and eosinophilic phenotype. Our evidence should motivate regulatory agencies to improve negotiations for new drugs with better information and evidence.

Keywords: health economics; healthcare; public health.

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- [29 references](#)

SUPPLEMENTARY INFO

MeSH terms, Substances expand

FULL TEXT LINKS



[Proceed to details](#)

Cite

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☐ 52

Allergy

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. 2022 Oct;77(10):3137-3141.

doi: 10.1111/all.15401. Epub 2022 Jun 16.

[Soluble ST2 enhances IL-33-induced neutrophilic and pro-type 2 inflammation in the lungs](#)

[Masato Watanabe](#)¹, [Keitaro Nakamoto](#)¹, [Toshiya Inui](#)¹, [Mitsuru Sada](#)¹, [Kazuyuki Chibana](#)², [Chika Miyaoka](#)¹, [Yuki Yoshida](#)¹, [Jumpei Aso](#)¹, [Hiroki Nunokawa](#)¹, [Kojiro Honda](#)¹, [Masuo Nakamura](#)¹, [Masaki Tamura](#)¹, [Aya Hirata](#)¹, [Miku Oda](#)¹, [Saori Takata](#)¹, [Takeshi Saraya](#)¹, [Daisuke Kurai](#)³, [Haruyuki Ishii](#)¹, [Hajime Takizawa](#)¹

Affiliations expand

- PMID: 35661175
- DOI: [10.1111/all.15401](#)

No abstract available

Keywords: COPD; asthma; asthma-COPD overlap; neutrophil; sputum.

- [6 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grant supportexpand

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Ann Allergy Asthma Immunol

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. 2022 Oct;129(4):461-466.

doi: 10.1016/j.anai.2022.05.024. Epub 2022 May 25.

[Could transthoracic ultrasound be useful to suggest a small airways disease in severe uncontrolled asthma?](#)

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Affiliations expand

- PMID: 35643297
- DOI: [10.1016/j.anai.2022.05.024](#)

Abstract

Background: Transthoracic ultrasound (TUS) is an accepted complementary tool in the diagnostic process of several pleuro-pulmonary diseases. However, to the best of our knowledge, TUS findings in patients with severe asthma have never been systematically described.

Objective: To explore if TUS examination is a useful imaging method in suggesting the presence of a "small airways disease" in patients with severe uncontrolled asthma.

Methods: Seventy-two consecutive subjects with a diagnosis of severe uncontrolled asthma were enrolled. The presence of a "small airways disease" was assessed through the execution of pulmonary function tests. All the patients underwent a complete TUS examination and a chest high resolution computed tomography (HRCT), which was regarded as the reference standard for comparison with TUS findings.

Results: Pulmonary function tests results have confirmed a reduction in expiratory flows relative to the small airways and a condition of hyperinflation in 78% and 82% of our patients, respectively. The main signs observed in the TUS examination were a thickened and/or irregular pleural line and the lack or reduction of the "gliding sign." TUS showed high sensitivity and specificity in suggesting the presence of hyperinflation and distal airways inflammation according to the HRCT scan. K Cohen's coefficients showed substantial agreement between the 2 diagnostic tests.

Conclusion: TUS in patients with severe uncontrolled asthma can provide useful information on the state of the peripheral lung, suggesting the execution of a second-line HRCT scan for better assessment of eventual alterations that may represent the underlying causes of nonresponse to treatment.

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SUPPLEMENTARY INFO

MeSH termsexpand

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Allergy

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. 2022 Oct;77(10):2974-2986.

doi: 10.1111/all.15376. Epub 2022 May 25.

Airway remodelling rather than cellular infiltration characterizes both type2 cytokine biomarker-high and -low severe asthma

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Affiliations expand

- PMID: 35579040
- DOI: [10.1111/all.15376](https://doi.org/10.1111/all.15376)

Abstract

Background: The most recognizable phenotype of severe asthma comprises people who are blood eosinophil and FeNO-high, driven by type 2 (T2) cytokine biology, which responds to targeted biological therapies. However, in many people with severe asthma, these T2 biomarkers are suppressed but poorly controlled asthma persists. The mechanisms driving asthma in the absence of T2 biology are poorly understood.

Objectives: To explore airway pathology in T2 biomarker-high and -low severe asthma.

Methods: T2 biomarker-high severe asthma (T2-high, n = 17) was compared with biomarker-intermediate (T2-intermediate, n = 21) and biomarker-low (T2-low, n = 20) severe asthma and healthy controls (n = 28). Bronchoscopy samples were processed for immunohistochemistry, and sputum for cytokines, PGD₂ and LTE₄ measurements.

Results: Tissue eosinophil, neutrophil and mast cell counts were similar across severe asthma phenotypes and not increased when compared to healthy controls. In contrast, the remodelling features of airway smooth muscle mass and MUC5AC expression were increased in all asthma groups compared with health, but similar across asthma subgroups. Submucosal glands were increased in T2-intermediate and T2-low asthma. In spite of similar tissue cellular inflammation, sputum IL-4, IL-5 and CCL26 were increased in T2-

high versus T2-low asthma, and several further T2-associated cytokines, PGD₂ and LTE₄, were increased in T2-high and T2-intermediate asthma compared with healthy controls.

Conclusions: Eosinophilic tissue inflammation within proximal airways is suppressed in T2 biomarker-high and T2-low severe asthma, but inflammatory and structural cell activation is present, with sputum T2-associated cytokines highest in T2 biomarker-high patients. Airway remodelling persists and may be important for residual disease expression beyond eosinophilic exacerbations. Registered at ClinicalTrials.gov: [NCT02883530](https://clinicaltrials.gov/ct2/show/study/NCT02883530).

Keywords: FeNO; Th2; cytokine; eosinophil; severe asthma.

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- [Cited by 1 article](#)
- [68 references](#)

SUPPLEMENTARY INFO

MeSH terms, Substances, Associated data, Grant support [expand](#)

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Allergy

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. 2022 Oct;77(10):3002-3014.

doi: 10.1111/all.15371. Epub 2022 Jun 13.

[Comparison of rhinitis treatments using MASK-air® data and considering the minimal important difference](#)

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[Costa](#)³⁴, [Alvaro A Cruz](#)³⁵, [Stefano Del Giacco](#)³⁶, [Philippe Devillier](#)³⁷, [Patrik Eklund](#)³⁸, [Wytke J Fokkens](#)³⁹, [Bilun Gemicioglu](#)⁴⁰, [Tari Haahtela](#)⁴¹, [Juan Carlos Ivancevich](#)⁴², [Zhanat Ispayeva](#)⁴³, [Marek Jutel](#)^{44 45}, [Piotr Kuna](#)⁴⁶, [Igor Kaidashev](#)⁴⁷, [Musa Khaitov](#)⁴⁸, [Helga Kraxner](#)⁴⁹, [Daniel Laune](#)⁵⁰, [Brian Lipworth](#)⁵¹, [Renaud Louis](#)⁵², [Michael Makris](#)⁵³, [Riccardo Monti](#)⁵⁴, [Mario Morais-Almeida](#)⁵⁵, [Ralph Mösges](#)⁵⁶, [Marek Niedoszytko](#)⁵⁷, [Nikolaos G Papadopoulos](#)⁵⁸, [Vincenzo Patella](#)⁵⁹, [Nhân Pham-Thi](#)⁶⁰, [Frederico S Regateiro](#)⁶¹, [Sietze Reitsma](#)⁶², [Philip W Rouadi](#)^{63 64}, [Boleslaw Samolinski](#)⁶⁵, [Aziz Sheikh](#)⁶⁶, [Milan Sova](#)⁶⁷, [Ana Todo-Bom](#)⁶⁸, [Luis Taborda-Barata](#)^{69 70 71}, [Sanna Toppila-Salmi](#)⁴¹, [Joaquin Sastre](#)⁷², [Ioanna Tsiligianni](#)⁷³, [Arunas Valiulis](#)⁷⁴, [Olivier Vandenplas](#)⁷⁵, [Dana Wallace](#)⁷⁶, [Susan Waserman](#)⁷⁷, [Arzu Yorgancioglu](#)⁷⁸, [Mihaela Zidarn](#)^{79 80}, [Torsten Zuberbier](#)^{21 22}, [Joao A Fonseca](#)^{1 2 3}, [Jean Bousquet](#)^{21 22 81}

Affiliations expand

- PMID: 35567393
- DOI: [10.1111/all.15371](https://doi.org/10.1111/all.15371)

Abstract

Background: Different treatments exist for allergic rhinitis (AR), including pharmacotherapy and allergen immunotherapy (AIT), but they have not been compared using direct patient data (i.e., "real-world data"). We aimed to compare AR pharmacological treatments on (i) daily symptoms, (ii) frequency of use in co-medication, (iii) visual analogue scales (VASs) on allergy symptom control considering the minimal important difference (MID) and (iv) the effect of AIT.

Methods: We assessed the MASK-air® app data (May 2015–December 2020) by users self-reporting AR (16–90 years). We compared eight AR medication schemes on reported VAS of allergy symptoms, clustering data by the patient and controlling for confounding factors. We compared (i) allergy symptoms between patients with and without AIT and (ii) different drug classes used in co-medication.

Results: We analysed 269,837 days from 10,860 users. Most days (52.7%) involved medication use. Median VAS levels were significantly higher in co-medication than in monotherapy (including the fixed combination azelastine-fluticasone) schemes. In adjusted models, azelastine-fluticasone was associated with lower average VAS global allergy symptoms than all other medication schemes, while the contrary was observed for oral corticosteroids. AIT was associated with a decrease in allergy symptoms in some medication schemes. A difference larger than the MID compared to no treatment was observed for oral steroids. Azelastine-fluticasone was the drug class with the lowest chance of being used in co-medication (adjusted OR = 0.75; 95% CI = 0.71–0.80).

Conclusion: Median VAS levels were higher in co-medication than in monotherapy. Patients with more severe symptoms report a higher treatment, which is currently not reflected in guidelines.

Keywords: allergen immunotherapy; allergic rhinitis; co-medication; multivariable mixed-effects model; real-world data.

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- [26 references](#)

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MeSH terms, Substances, Grant supportexpand

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Case Reports

Allergol Int

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. 2022 Oct;71(4):548-551.

doi: 10.1016/j.alit.2022.03.005. Epub 2022 Apr 18.

[Two cases of dupilumab-associated eosinophilic pneumonia in asthma with eosinophilic chronic rhinosinusitis: IL-5-driven pathology?](#)

[Yuki Nishiyama](#)¹, [Toshiyuki Koya](#)², [Kei Nagano](#)¹, [Seitaro Abe](#)¹, [Yosuke Kimura](#)¹, [Kenjiro Shima](#)¹, [Mio Toyama-Kosaka](#)¹, [Takashi Hasegawa](#)³, [Takanobu Sasaki](#)⁴, [Kaori Shinbori](#)⁴, [Shigeharu Ueki](#)⁵, [Kaori Takamura](#)⁶, [Toshiaki Kikuchi](#)¹

Affiliations expand

- PMID: 35443910
- DOI: [10.1016/j.alit.2022.03.005](https://doi.org/10.1016/j.alit.2022.03.005)

Free article

No abstract available

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Publication types, MeSH terms, Substancesexpand

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Eur Respir J

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. 2022 Sep 29;60(3):2102288.

doi: 10.1183/13993003.02288-2021. Print 2022 Sep.

[T2-high asthma phenotypes across lifespan](#)

[Nicole Maison](#)^{1,2,3}, [Jimmy Omony](#)^{1,3}, [Sabina Illi](#)^{1,3}, [Dominik Thiele](#)^{4,5}, [Chrysanthi Skevaki](#)^{6,7}, [Anna-Maria Dittrich](#)^{8,9}, [Thomas Bahmer](#)^{5,10,11}, [Klaus Friedrich Rabe](#)^{5,11}, [Markus Weckmann](#)^{5,12}, [Christine Happle](#)^{8,9}, [Bianca Schaub](#)^{2,3}, [Meike Meyer](#)¹³, [Svenja Foth](#)^{7,14}, [Ernst Rietschel](#)¹³, [Harald Renz](#)^{6,7,15}, [Gesine Hansen](#)^{8,9}, [Matthias Volkmar Kopp](#)^{5,12,16}, [Erika von Mutius](#)^{17,2,3}, [Ruth Grychtol](#)^{8,9}, [ALLIANCE Study Group](#)

Affiliations expand

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- DOI: [10.1183/13993003.02288-2021](https://doi.org/10.1183/13993003.02288-2021)

Abstract

Rationale: In adults, personalised asthma treatment targets patients with type 2 (T2)-high and eosinophilic asthma phenotypes. It is unclear whether such classification is achievable in children.

Objectives: To define T2-high asthma with easily accessible biomarkers and compare resulting phenotypes across all ages.

Methods: In the multicentre clinical All Age Asthma Cohort (ALLIANCE), 1125 participants (n=776 asthmatics, n=349 controls) were recruited and followed for 2 years (1 year in adults). Extensive clinical characterisation (questionnaires, blood differential count, allergy testing, lung function and sputum induction (in adults)) was performed at baseline and follow-ups. Interleukin (IL)-4, IL-5 and IL-13 were measured after stimulation of whole blood with lipopolysaccharide (LPS) or anti-CD3/CD28.

Measurements and main results: Based on blood eosinophil counts and allergen-specific serum IgE antibodies, patients were categorised into four mutually exclusive phenotypes: "atopy-only", "eosinophils-only", "T2-high" (eosinophilia + atopy) and "T2-low" (neither eosinophilia nor atopy). The T2-high

phenotype was found across all ages, even in very young children in whom it persisted to a large degree even after 2 years of follow-up. T2-high asthma in adults was associated with childhood onset, suggesting early origins of this asthma phenotype. In both children and adults, the T2-high phenotype was characterised by excessive production of specific IgE to allergens ($p < 0.0001$) and, from school age onwards, by increased production of IL-5 after anti-CD3/CD28 stimulation of whole blood.

Conclusions: Using easily accessible biomarkers, patients with T2-high asthma can be identified across all ages delineating a distinct phenotype. These patients may benefit from therapy with biologicals even at a younger age.

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Conflict of interest statement

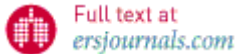
Conflict of interest: N. Maison, J. Omony, S. Illi, D. Thiele, A.M. Dittrich, C. Happle, M. Meyer, S. Foth and R. Grychtol have nothing to disclose. C. Skevaki reports grants and personal fees from Hycor Biomedical, Bencard Allergie, Thermo Fisher Scientific as well as grants from Mead Johnson Nutrition (MJN), Universities Giessen and Marburg Lung Centre, the German Centre for Lung Research (DZL), University Hospital Giessen and Marburg, Deutsche Forschungsgemeinschaft (DFG). T. Bahmer reports grants from the Federal Ministry for Education and Research (BMBF) for the German Center for Lung Research (DZL) and personal fees from AstraZeneca, GlaxoSmithKline, Novartis, Roche and Chiesi. M. Weckmann reports grants from Federal Ministry for Education and Research (BMBF), University of Luebeck and German Academic Exchange Service. B. Schaub reports grants from DFG, BMBF, the EU as well from GlaxoSmithKline, Sanofi and Novartis. H. Renz reports grants from German Center for Lung Disease (DZL) and Universities Giessen Marburg Lung Center. M.V. Kopp reports grants and personal fees from Allergopharma GmbH and Vertex GmbH; additional, personal fees from Sanofi GmbH, Infectopharm GmbH and Leti GmbH. E. Rietschel reports personal lecture payments for Nutricia Milupa GmbH and Novartis Pharma, and honoraria for participation in advisory boards for MICE-Mylan, Novartis Pharma GmbH and Boehringer Ingelheim GmbH. K.F. Rabe received personal payments or honoraria from AstraZeneca, Boehringer Ingelheim, Chiesi Pharmaceuticals, Novartis, Sanofi & Regeneron, GlaxoSmithKline, Berlin Chemie and Roche; K.F. Rabe also discloses participation on data safety monitoring boards/advisory boards for AstraZeneca and Sanofi Regeneron, and leadership or fiduciary role in the German Center for Lung Research (DZL), German Chest Society (DGP) and American Thoracic Society (ATS). G. Hansen reports grants from German Federal Ministry of Education and Research (BMBF) and German Research Foundation (DFG) as well as personal fees from Sanofi GmbH, MedUpdate, and Abbvie. E. von Mutius reports grants from the German Center for Lung Research (DZL) as well as royalties/licenses held by Elsevier GmbH, Gerog Thieme Verlag, Springer Verlag GmbH, Elsevier Ltd; furthermore, consultation fees were received from the Chinese University of Hong Kong, European Commission, HiPP GmbH and AstraZeneca; E. von Mutius also received payments and/or support for meetings/travel from the Massachusetts Medical Society, Springer-Verlag GmbH, Elsevier Ltd, Böhringer Ingelheim International GmbH, European Respiratory Society (ERS), University Utrecht, Salzburg, Colorado and Imperial College London, Springer Medizin Verlag GmbH, Japanese Society of Pediatric Allergy and Clinical Immunology, Klinikum Rechts der Isar, Paul-Martini-Stiftung; further support for meetings/travel was granted by Verein zur Förderung der Pneumologie am Krankenhaus Groshansdorf, Pneumologie Development Mondial Congress & Events GmbH, American Academy of Allergy, Asthma & Immunology, Margaux Orange, Volkswagen Stiftung, Österreichische Gesellschaft für Allergologie & Immunologie, OM Pharma SA, Hanson Wade Ltd, iKOMM GmbH, DSI Dansk Bornestma Center, American Thoracic Society, HiPP GmbH; E. von Mutius has patent EP2361632, EP1411977, EP1637147 and EP 1964570 (licensed to Protectimmun), furthermore patent LU101064 is pending; E. von Mutius participates in the following data monitoring or advisory boards: EXPANSE, BEAMS External Scientific Advisory Board, Journal of Allergy and Clinical Immunology: in Practice, Children's Respiratory and Environmental Workgroup (CREW), International Scientific & Societal Advisory Board of Utrecht Life Sciences, External Review Panel of the Faculty of Veterinary Science (University of Utrecht), Gottfried Wilhelm Leibniz

Programme, Asthma UK for Applied Research, Advisory Board of The Lancet Respiratory Medicine, CHILD (Canadian Healthy Infant Longitudinal Development Study).

Comment in

- [Moving the dial on identifying endotypes of asthma from early life.](#)
Perrem L, Subbarao P. Eur Respir J. 2022 Sep 29;60(3):2201031. doi: 10.1183/13993003.01031-2022. Print 2022 Sep. PMID: 36175027 No abstract available.

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Am J Perinatol

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. 2022 Oct;39(13):1410-1417.

doi: 10.1055/s-0040-1722604. Epub 2021 Jan 17.

[Cardiopulmonary Function Abnormalities in Cohort of Adults following Bronchopulmonary Dysplasia as Preterm Infants](#)

[Ariane Lasry](#)¹, [Patrick Kavabushi](#)¹, [Anne-Marie Canakis](#)², [Thuy M Luu](#)³, [Anne-Monique Nuyt](#)⁴, [Thérèse Perreault](#)⁵, [Jessica Simoneau](#)⁵, [Jennifer Landry](#)⁶, [Gabriel Altit](#)⁵

Affiliations expand

- PMID: 33454944
- DOI: [10.1055/s-0040-1722604](#)

Abstract

Objective: This study was aimed to describe the cardiopulmonary profiles of adult patients with bronchopulmonary dysplasia (BPD), comparing them to normative adult values.

Study design: This study presents a retrospective chart review of all BPD patients followed in the adult BPD clinic, identified from institutional and archive databases, born preterm at ≤ 33 weeks of estimated gestational age (EGA) between January 1980 and December 2000.

Results: Forty-four patients with BPD (26.4 ± 2.7 weeks of EGA) were included. Average age at follow-up was 19 years. Majority (61.4%) of the patients had a diagnosis of asthma. Mean spirometry values were: first second of forced expiration (FEV1) 74.1%, forced vital capacity (FVC) 80.7%, and FEV1/FVC 82.5%. Echocardiography (ECHO) images were reviewed, left ventricular (LV) structure and performance did not differ between obstructive and nonobstructive pulmonary function test (PFT) groups, but values of LV longitudinal strain were 4.8% lower than expected normal for adults. Patients with obstructive PFT had additional decreased right ventricular (RV) function by ECHO.

Conclusion: BPD patients in this study were found to have a burden of cardiorespiratory alterations that persisted into adulthood, with RV performance abnormalities found among patients with obstructive PFT.

Key points: · BPD patients born at extremes of prematurity have cardiorespiratory alterations in adulthood.. · Among patients with obstructive lung function, subtle cardiac performance abnormalities were found.. · Future directions should include systematic follow-up of premature newborns with BPD..

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Conflict of interest statement

None declared.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS



RHINITIS

Curr Stem Cell Res Ther

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. 2022 Sep 26.

doi: 10.2174/1574888X17666220926105744. Online ahead of print.

[Human Amniotic Fluid Stem cells exert immunosuppressive effects on T lymphocytes in Allergic rhinitis](#)

[Ling Zong](#)¹, [De Wang](#)², [Yanbo Long](#)¹, [Xiaolan Liu](#)³, [Ailin Tao](#)², [Lanzhen Zhang](#)³, [Jinming Zhai](#)¹

Affiliations expand

- PMID: 36165522

- DOI: [10.2174/1574888X17666220926105744](https://doi.org/10.2174/1574888X17666220926105744)

Abstract

Aim: To investigate the immunomodulatory effect of Amniotic fluid stem (AFS) cells to Th2-skewed allergic rhinitis (AR) on T-lymphocyte proliferation, viability, activation and cytokine production.

Background: AFS cells can suppress peripheral blood mononuclear cells (PBMCs) Proliferation and display immunomodulatory properties, but AFS cells immunoregulation on AR has not been defined.

Methods: Human AFS cells were derived from magnetic cell sorting and co-cultured with PBMCs from AR patients stimulated by phytohemagglutinin (PHA). The AFS cells-associated suppressive proliferation was analyzed using CellTrace™ Violet assay; the T lymphocytes proliferation, viability, activation and the Foxp3+ Treg cells were determined by flow cytometry; cytokine levels were measured using an enzyme-linked immunosorbent assay.

Results: We determined that AFS cells significantly inhibited PHA-induced CD3+ T lymphocyte proliferation at the ratio higher than 1:50 (AFS cells: PBMCs) ($P<0.05$); AFS cells obviously increased the T lymphocytes viability ($P<0.01$), inhibited the apoptosis of T lymphocytes ($P<0.001$), compared to PBMCs alone; AFS cells suppressed CD3+CD25+ T lymphocytes activated by PHA ($P<0.05$); AFS cells significantly promote Treg cells expansion in house dust mite (HDM)-stimulated PBMCs from AR patients ($P<0.05$). Compared with HDM-stimulated PBMCs, AFS cells co-culture predominantly decreased IL-4 level ($P<0.05$), but increased IFN- γ and IL-10 level ($P<0.01$).

Conclusion: AFS cells modulate the T-cells immune imbalance towards Th2 suppression in AR, which can be used as a new cell banking for allergic airway diseases.

Keywords: Allergic rhinitis; Amniotic fluid Stem cells; Immunomodulation; Mesenchymal stem cells; PBMCs; Treg cells.

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J Leukoc Biol

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. 2022 Sep 26.

doi: 10.1002/JLB.3MA0822-436RR. Online ahead of print.

[ILC3-like ILC2 subset increases in minimal persistent inflammation after acute type II inflammation of allergic rhinitis and inhibited by Biminkang: Plasticity of ILC2 in minimal persistent inflammation](#)

[Xiang-Jing Chen](#)¹, [Cheng Liu](#)², [Shan Zhang](#)², [Li-Feng Zhang](#)¹, [Wei Meng](#)¹, [Xin Zhang](#)¹, [Meng Sun](#)¹, [Yue Zhang](#)², [Ren-Zhong Wang](#)¹, [Cheng-Fang Yao](#)²

Affiliations expand

- PMID: 36161355
- DOI: [10.1002/JLB.3MA0822-436RR](#)

Abstract

Minimal persistent inflammation (MPI), the local inflammation that occurs after an acute type II immune response in patients with allergic rhinitis (AR), is responsible for airway hyperreactivity and the recurrence of AR. Innate lymphoid cells (ILCs) play a crucial role in mucosal immune homeostasis, but the changes of ILC subsets in the MPI stage remain unclear. In this study, the levels of ILC-secreting cytokines in nasal lavages were analyzed from 19 AR patients and 8 healthy volunteers. AR and MPI model mice were established to study the ILC subsets. The results showed that IL-17A was significantly increased in nasal lavage of AR patients in the MPI stage by MSD technology. When compared with the AR model mice, the frequency of IL-13⁺ ILC2 in the nasal mucosa and lungs decreased, while IL-5⁺ ILC2 remain high in MPI model mice. A part of the IL-5⁺ ILC2 subset displayed ILC3-like characteristics with elevated RORγt, IL-17A and IL-23R expression. Especially, these ILC3-like ILC2 exhibited up-regulation of GATA3⁺ RORγt⁺ were increased in MPI model mice. After the treatment of Biminkang, the frequencies of IL-5⁺ ILC2, IL-17A⁺ ILC3, and GATA3⁺ RORγt⁺ ILC3-like ILC2 were significantly reduced, and IL-23R expression was also decreased on ILC3-like-ILC2 subset. These results suggested that the elevated IL-17A in the MPI stage has been related to or at least partly due to the increased of ILC3-like ILC2. Biminkang could effectively decrease IL-17A⁺ ILC3 and inhibit ILC3-like ILC2 subset in the MPI stage. Biminkang is effective in administrating MPI by regulating airway ILC homeostasis.

Keywords: Biminkang; ILC3-like ILC2; minimal persistent inflammation; type II Inflammation.

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- [29 references](#)

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. 2022 Oct 1;244:114076.

doi: 10.1016/j.ecoenv.2022.114076. Epub 2022 Sep 13.

Effects of early life exposure to home environmental factors on childhood allergic rhinitis: Modifications by outdoor air pollution and temperature

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Affiliations expand

- PMID: 36113271
- DOI: [10.1016/j.ecoenv.2022.114076](https://doi.org/10.1016/j.ecoenv.2022.114076)

Free article

Abstract

Background: There is growing evidence that allergic rhinitis (AR) is associated with indoor environmental factors, but their role in childhood AR during early life remains unclear.

Objective: To investigate the association of preconceptional, prenatal, early postnatal, and current exposure to home environmental factors with childhood AR, and to further explore whether this association can be interacted by outdoor air pollution and temperature.

Methods: A retrospective cohort study of 8689 preschool children was conducted during 2019-2020 in Changsha, China. A standard questionnaire was used to collect data on each family's health outcomes and home environments. We considered home environmental exposures during one year before conception, pregnancy, first year of life, and past year. Associations of indoor air pollution and allergens with AR were assessed by multiple logistic regression models.

Results: Pre-birth exposure to indoor air pollution emitted by new furniture or redecoration and dampness related allergen derived from mold/damp stains and mold/damp clothes or bedding during 1 year before conception and pregnancy was significantly associated with increased AR, with adjusted ORs (95% CI) ranging from 1.35 (1.05-1.75) to 1.87 (1.55-2.27). Childhood AR was also significantly related with post-birth exposure to dampness related indoor allergen including mold/damp stains and mold/damp clothes or bedding in first year and past year and pollen allergen including total and nonflowering plants in past year, with a range of ORs (95% CI) from 1.20 (1.01-1.42) to 1.79 (1.42-2.27). We identified that pre-birth, particularly in utero exposure to both indoor air pollution from renovation and dampness related allergens, played a key role in AR development compared to post-birth exposures, and accumulative effect was observed with the highest risk of AR. High exposure to traffic-related air pollution (TRAP) including outdoor PM_{2.5}, NO₂, CO, and O₃, as well as living near traffic road not only significantly increased adverse effect of home environmental factors but also decreased protective effect of household dogs on childhood AR. Early life exposure to low temperature in pregnancy and high temperature in first year significantly increased AR

risk of home environmental exposure. Sensitivity analysis indicated that some sub-groups were more susceptible to AR risk of home environmental exposure.

Conclusion: Our study suggests that pre-birth exposure to home environmental factors played an important role in AR development and this effect can be interacted by TRAP and temperature, which supports a hypothesis of "(pre)fetal origin of childhood AR".

Keywords: Ambient air pollution; Childhood allergic rhinitis; Early life exposure; Environmental temperature; Indoor environments; Interaction effect.

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Conflict of interest statement

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

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS



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Cite

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J Asthma

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. 2022 Sep 29;1-7.

doi: 10.1080/02770903.2022.2123741. Online ahead of print.

[Reduced forced expiratory flow between 25% and 75% of vital capacity in children with allergic rhinitis without asthmatic symptoms](#)

[Jue Seong Lee](#)¹, [Sang Hyun Park](#)¹, [Han Ho Kim](#)¹, [So Hyun Ahn](#)², [Eunji Kim](#)², [Seunghyun Kim](#)², [Wonsuck Yoon](#)², [Young Yoo](#)^{1,2}

Affiliations expand

- PMID: 36093643

- DOI: [10.1080/02770903.2022.2123741](https://doi.org/10.1080/02770903.2022.2123741)

Abstract

Allergic rhinitis (AR) and asthma are closely associated in children. Reduced $FEF_{25\%-75\%}$ which reflects small airway airflow limitation is frequently observed in asthma. This study aimed to examine the proportion of small airway dysfunction in children with AR and to determine its associated factors. **Methods:** The medical records of 144 aged 6-18-year children with AR without overt asthmatic symptoms were retrospectively reviewed. Subjects were divided into 2 groups according to the $FEF_{25\%-75\%}$ values; normal $FEF_{25\%-75\%}$ group ($n = 129$) and reduced $FEF_{25\%-75\%}$ group ($n = 15$). Clinical data, allergen sensitization profile, exhaled nitric oxide, spirometry, and methacholine provocation test results were compared between the two groups. **Results:** The mean FEV_1 and $FEF_{25\%-75\%}$ values in the reduced $FEF_{25\%-75\%}$ group ($73.5 \pm 9.4\%$ pred and $56.0 \pm 7.7\%$ pred, respectively) were significantly lower than in the normal $FEF_{25\%-75\%}$ group ($87.0 \pm 12.5\%$ pred and $99.1 \pm 21.4\%$ pred, respectively). The mean disease duration was significantly longer in the reduced $FEF_{25\%-75\%}$ group than in the normal $FEF_{25\%-75\%}$ group (5.39 ± 1.85 y vs 3.14 ± 1.80 y, $p < 0.001$). Subjects with positive bronchial hyperresponsiveness ($MChPC_{20} < 16$ mg/mL) were more frequently detected in the reduced $FEF_{25\%-75\%}$ group than in the normal $FEF_{25\%-75\%}$ group (26.7% vs 8.52% , $p = 0.013$). Long disease duration and severity of AR were significantly associated with impaired $FEF_{25\%-75\%}$ values. **Conclusions:** Subjects with AR alone may have impaired $FEF_{25\%-75\%}$ values which is considered as a marker of early bronchial involvement. Longer disease duration and severity of AR are important risk factors for progressive declines in small airway function. Physicians should be aware of need for the measurement of $FEF_{25\%-75\%}$ values for early detection of small airway dysfunction, particularly in children with severe long-lasting allergic rhinitis.

Keywords: Children; allergy; asthma; pulmonary function; rhinitis.

FULL TEXT LINKS



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☐ 5

Clin Immunol

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. 2022 Oct;243:109101.

doi: 10.1016/j.clim.2022.109101. Epub 2022 Aug 24.

[5-HT is associated with the dysfunction of regulating T cells in patients with allergic rhinitis](#)

[Gui Yang](#)¹, [Gaohui Wu](#)², [Wenkai Yao](#)³, [Li Guan](#)², [Xiaorui Geng](#)⁴, [Jiangqi Liu](#)⁴, [Zhiqiang Liu](#)⁴, [Liteng Yang](#)², [Qinmiao Huang](#)⁵, [Xianhai Zeng](#)⁶, [Pingchang Yang](#)⁷

Affiliations expand

- PMID: 36029976
- DOI: [10.1016/j.jclim.2022.109101](https://doi.org/10.1016/j.jclim.2022.109101)

Abstract

The dysfunction of regulating T lymphocytes (Treg) is associated with the pathogenesis of many diseases. 5-hydroxytryptamine (5-HT) is capable of interacting with immune cells. The objective of the present study is to shed light on the role of 5-HT in regulating Treg activities. Blood samples were collected from patients with perennial allergic rhinitis (AR). Tregs were isolated from blood samples by magnetic cell sorting. The levels of 5-HT and other cytokines were determined by enzyme-linked immunosorbent assay. The results showed that serum 5-HT levels in patients with AR were higher than in healthy control (HC) subjects. A positive correlation was identified in the data between 5-HT concentrations and AR-related cytokine concentrations in the serum. A negative correlation was found between serum levels of 5-HT and the peripheral frequency of Treg. Exposure to 5-HT enhanced the expression of IL-6 and IL-21 in dendritic cells (DC). Co-culture of 5-HT-primed DCs with Tregs led to the conversion of Th17 cells. STAT3 blockade efficiently abolished the 5-HT-associated conversion of Th17 cells from Tregs. In summary, patients with AR exhibited higher serum concentrations of 5-HT. 5-HT-primed DCs could convert Tregs to Th17 cells.

Keywords: 5-HT; Allergy; Dendritic cells; Nose; Regulatory T cells.

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Conflict of interest statement

Declaration of Competing Interest None to declare.

SUPPLEMENTARY INFO

MeSH terms, Substances expand

FULL TEXT LINKS



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☐ 6

Allergy

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. 2022 Oct;77(10):3002-3014.

doi: 10.1111/all.15371. Epub 2022 Jun 13.

Comparison of rhinitis treatments using MASK-air® data and considering the minimal important difference

[Bernardo Sousa-Pinto](#)^{1 2 3}, [Holger J Schünemann](#)⁴, [Ana Sá-Sousa](#)^{1 2 3}, [Rafael José Vieira](#)^{1 2 3}, [Rita Amaral](#)^{1 2 3}, [Josep M Anto](#)^{5 6 7 8}, [Ludger Klimek](#)⁹, [Wienczysława Czarlewski](#)¹⁰, [Joaquim Mullol](#)¹¹, [Oliver Pfaar](#)¹², [Anna Bedbrook](#)¹³, [Luisa Brussino](#)¹⁴, [Violeta Kvedariene](#)¹⁵, [Desirée Larenas-Linnemann](#)¹⁶, [Yoshitaka Okamoto](#)¹⁷, [Maria Teresa Ventura](#)¹⁸, [Ioana Agache](#)¹⁹, [Ignacio J Ansotegui](#)²⁰, [Karl C Bergmann](#)^{21 22}, [Sinthia Bosnic-Anticevich](#)²³, [Jan Brozek](#)⁴, [G Walter Canonica](#)^{24 25}, [Victoria Cardona](#)²⁶, [Pedro Carreiro-Martins](#)^{27 28}, [Thomas Casale](#)²⁹, [Lorenzo Cecchi](#)³⁰, [Tomas Chivato](#)³¹, [Derek K Chu](#)³², [Cemal Cingi](#)³³, [Elísio M Costa](#)³⁴, [Alvaro A Cruz](#)³⁵, [Stefano Del Giacco](#)³⁶, [Philippe Devillier](#)³⁷, [Patrik Eklund](#)³⁸, [Wyske J Fokkens](#)³⁹, [Bilun Gemicioglu](#)⁴⁰, [Tari Haahtela](#)⁴¹, [Juan Carlos Ivancevich](#)⁴², [Zhanat Ispayeva](#)⁴³, [Marek Jutel](#)^{44 45}, [Piotr Kuna](#)⁴⁶, [Igor Kaidashev](#)⁴⁷, [Musa Khaitov](#)⁴⁸, [Helga Kraxner](#)⁴⁹, [Daniel Laune](#)⁵⁰, [Brian Lipworth](#)⁵¹, [Renaud Louis](#)⁵², [Michael Makris](#)⁵³, [Riccardo Monti](#)⁵⁴, [Mario Morais-Almeida](#)⁵⁵, [Ralph Mösges](#)⁵⁶, [Marek Niedoszytko](#)⁵⁷, [Nikolaos G Papadopoulos](#)⁵⁸, [Vincenzo Patella](#)⁵⁹, [Nhân Pham-Thi](#)⁶⁰, [Frederico S Regateiro](#)⁶¹, [Sietze Reitsma](#)⁶², [Philip W Rouadi](#)^{63 64}, [Boleslaw Samolinski](#)⁶⁵, [Aziz Sheikh](#)⁶⁶, [Milan Sova](#)⁶⁷, [Ana Todo-Bom](#)⁶⁸, [Luis Taborda-Barata](#)^{69 70 71}, [Sanna Toppila-Salmi](#)⁴¹, [Joaquin Sastre](#)⁷², [Ioanna Tsiligianni](#)⁷³, [Arunas Valiulis](#)⁷⁴, [Olivier Vandenplas](#)⁷⁵, [Dana Wallace](#)⁷⁶, [Susan Waserman](#)⁷⁷, [Arzu Yorgancioglu](#)⁷⁸, [Mihaela Zidarn](#)^{79 80}, [Torsten Zuberbier](#)^{21 22}, [Joao A Fonseca](#)^{1 2 3}, [Jean Bousquet](#)^{21 22 81}

Affiliations expand

- PMID: 35567393
- DOI: [10.1111/all.15371](https://doi.org/10.1111/all.15371)

Abstract

Background: Different treatments exist for allergic rhinitis (AR), including pharmacotherapy and allergen immunotherapy (AIT), but they have not been compared using direct patient data (i.e., "real-world data"). We aimed to compare AR pharmacological treatments on (i) daily symptoms, (ii) frequency of use in co-medication, (iii) visual analogue scales (VASs) on allergy symptom control considering the minimal important difference (MID) and (iv) the effect of AIT.

Methods: We assessed the MASK-air® app data (May 2015–December 2020) by users self-reporting AR (16–90 years). We compared eight AR medication schemes on reported VAS of allergy symptoms, clustering data by the patient and controlling for confounding factors. We compared (i) allergy symptoms between patients with and without AIT and (ii) different drug classes used in co-medication.

Results: We analysed 269,837 days from 10,860 users. Most days (52.7%) involved medication use. Median VAS levels were significantly higher in co-medication than in monotherapy (including the fixed combination azelastine-fluticasone) schemes. In adjusted models, azelastine-fluticasone was associated with lower average VAS global allergy symptoms than all other medication schemes, while the contrary was observed for oral corticosteroids. AIT was associated with a decrease in allergy symptoms in some medication

schemes. A difference larger than the MID compared to no treatment was observed for oral steroids. Azelastine-fluticasone was the drug class with the lowest chance of being used in co-medication (adjusted OR = 0.75; 95% CI = 0.71-0.80).

Conclusion: Median VAS levels were higher in co-medication than in monotherapy. Patients with more severe symptoms report a higher treatment, which is currently not reflected in guidelines.

Keywords: allergen immunotherapy; allergic rhinitis; co-medication; multivariable mixed-effects model; real-world data.

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- [26 references](#)

SUPPLEMENTARY INFO

MeSH terms, Substances, Grant supportexpand

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Eur Arch Otorhinolaryngol

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. 2022 Oct;279(10):4953-4959.

doi: 10.1007/s00405-022-07320-y. Epub 2022 Mar 19.

[BMI as a risk factor for the development of chronic rhinosinusitis: a prospective population-based study](#)

[Ulrika K E Clarhed](#)^{1,2}, [Linus Schiöler](#)³, [Kjell Torén](#)³, [Anne Kristin M Fell](#)^{4,5}, [Johan Hellgren](#)^{6,7}

Affiliations expand

- PMID: 35305138
- PMCID: [PMC9474381](#)

- DOI: [10.1007/s00405-022-07320-y](https://doi.org/10.1007/s00405-022-07320-y)

Free PMC article

Abstract

Purpose: Obesity is a growing, global health problem and previous cross-sectional studies have demonstrated an association between obesity and chronic rhinosinusitis (CRS). There is, however, a lack of prospective studies regarding the impact of obesity on developing (new-onset) CRS.

Methods: Questionnaire-based data (n = 5769) relating to new-onset CRS and Body Mass Index (BMI) were collected in 2013 and 2018 from the Telemark population study in Telemark, Norway. Odds ratios for the risk of new-onset CRS in 2018 in relation to BMI in 2013 were calculated, adjusted for smoking habits, asthma, gender and age.

Results: When comparing the group with normal weight ($18.5 \leq \text{BMI} < 25$) with the obese group ($\text{BMI} \geq 30$), the odds of new-onset CRS was 53% higher [OR 1.53 (1.11, 2.10)] in the obese group.

Conclusion: CRS is a multifactorial disease with different phenotypes and it is important to consider obesity when assessing patients with CRS in a clinical setting.

Keywords: Body mass index; Inflammation; Obesity; Population; Sinusitis.

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Conflict of interest statement

The authors declare that they have no competing interests.

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

SUPPLEMENTARY INFO

MeSH terms, Grant support[expand](#)

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Int Forum Allergy Rhinol

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. 2022 Oct;12(10):1299-1302.

doi: 10.1002/alr.22983. Epub 2022 Feb 23.

[Similarities between allergen sensitivity patterns of central compartment atopic disease and allergic rhinitis](#)

[Siddhant H Tripathi](#)¹, [Heather N Ungerer](#)¹, [Bianca Rullan-Oliver](#)¹, [Tapan Patel](#)¹, [Auddie M Sweis](#)¹, [Ivy W Maina](#)¹, [Michael A Kohanski](#)¹, [James N Palmer](#)¹, [Nithin D Adappa](#)¹, [John V Bosso](#)¹

Affiliations expand

- PMID: 35132826
- DOI: [10.1002/alr.22983](https://doi.org/10.1002/alr.22983)

No abstract available

Keywords: allergens; allergic rhinitis; chronic rhinosinusitis; skin prick testing.

- [5 references](#)

SUPPLEMENTARY INFO

MeSH terms, Substances expand

FULL TEXT LINKS



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Ann Otol Rhinol Laryngol

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. 2022 Oct;131(10):1137-1143.

doi: 10.1177/00034894211058135. Epub 2021 Nov 15.

[Increased Risk of Postpartum Depression in Women With Allergic Rhinitis During Pregnancy: A Population-Based Case-Control Study](#)

[Zhi-Chao Yang](#)¹, [Li-Xin Wang](#)², [Yang Yu](#)¹, [Huan-Yu Lin](#)³, [Liang-Chun Shih](#)³

Affiliations expand

- PMID: 34779274
- DOI: [10.1177/00034894211058135](https://doi.org/10.1177/00034894211058135)

Abstract

Objectives: Allergic rhinitis (AR) is associated with increased risk of major depression in the general population, however, no previous study has evaluated its role among pregnant women. We aimed to investigate the potential impact of AR during pregnancy on the development of postpartum depression (PPD).

Methods: This is a population-based case-control study. Data were retrieved from the National Health Insurance Research Database (NHIRD). Medical records of a total of 199 470 deliveries during 2000 and 2010 were identified. Among which, 1416 women with PPD within 12 months after delivery were classified as the case group, while 198 054 women without PPD after delivery formed the control group. Univariate and multivariate regression analyses were conducted to determine the associations between AR during pregnancies and other study variables with PPD.

Results: AR during pregnancy was found in 9.53% women who developed PPD and 5.44% in women without PPD. After adjusting for age at delivery, income level, various pregnancy and delivery-related conditions, asthma, atopic dermatitis and other medical comorbidities in the multivariate analysis, AR was significantly associated with increased odds of PPD (aOR: 1.498, 95% CI: 1.222-1.836).

Conclusion: AR during pregnancy was independently and significantly associated with an approximately 50% increased risk of PPD among women giving birth. Closely monitoring of AR is warranted in the future in order to optimize mother and child outcomes after delivery.

Keywords: National Health Insurance Research Database; allergic rhinitis; postpartum depression; pregnancy.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS



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Observational Study

Ann Otol Rhinol Laryngol

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. 2022 Oct;131(10):1130-1136.

doi: 10.1177/00034894211054948. Epub 2021 Nov 14.

Chronic Rhinosinusitis Outcomes of Patients With Aspirin-Exacerbated Respiratory Disease Treated With Budesonide Irrigations: A Case Series

[Rehab Talat](#)¹, [Isabelle Gengler](#)¹, [Katie M Phillips](#)¹, [David S Caradonna](#)^{2,3}, [Stacey T Gray](#)^{2,4}, [Ahmad R Sedaghat](#)¹

Affiliations expand

- PMID: 34775833
- DOI: [10.1177/00034894211054948](https://doi.org/10.1177/00034894211054948)

Abstract

Background: Pathophysiology-targeting treatments exist for aspirin-exacerbated respiratory disease (AERD) through aspirin desensitization and biologics, such as dupilumab. With increasing attention paid to these treatments, which may be associated with significant side effects and/or cost, there is little description of chronic rhinosinusitis with nasal polyps (CRSwNP) response to treatment with intranasal corticosteroids and saline irrigations in AERD.

Objective: To determine the effect of intranasal budesonide irrigations for the treatment of CRSwNP in AERD.

Methods: This is an observational study of 14 AERD patients presenting to a rhinology clinic for CRS who were treated with twice daily high volume, low pressure irrigations with 240 mL of saline to which a 0.5 mg/2 mL respule of budesonide was added. All participants completed a 22-item Sinonasal Outcome Test (SNOT-22) at enrollment and at follow up 1 to 6 months later. Polyp scores were also calculated at each time point.

Results: SNOT-22 scores ranged from 26 to 98 (median: 40.5) at enrollment and 3 to 85 (median: 38.5) at follow-up. Polyp scores ranged from 2 to 6 (median: 4) at enrollment at 0 to 6 (median: 2) at follow-up. Over the treatment period, change in SNOT-22 score ranged from -38 to 16 (median: -18) and change in polyp score ranged from -2 to 0 (median: -0.5). Approximately 57% of participants experienced at least 1

minimal clinically important difference in SNOT-22 score and 21% of participants had a SNOT-22 score <20 at follow-up.

Conclusion: Medical management with intranasal corticosteroids and saline irrigations alone leads to significant improvement in sinonasal symptomatology in a subset of AERD.

Keywords: AERD; SNOT-22; aspirin exacerbated respiratory disease; budesonide; chronic rhinosinusitis; intranasal corticosteroids; medical management; nasal polyps; polyp score.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS



CHRONIC COUGH

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Rev Med Suisse

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. 2022 Sep 28;18(797):1792-1797.

doi: 10.53738/REVMED.2022.18.797.1792.

[\[COPD: Guidelines for primary care physicians\]](#)

[Article in French]

[Mohammad Razban](#)^{#1}, [Manuel Diego Sztajzel](#)^{#1}, [Frédéric Lador](#)², [Johanna Sommer](#)³, [Dagmar M Haller](#)^{1,3}, [Thierry Favrod-Coune](#)¹

Affiliations expand

- PMID: 36170131
- DOI: [10.53738/REVMED.2022.18.797.1792](https://doi.org/10.53738/REVMED.2022.18.797.1792)

Abstract

in [English](#), [French](#)

Chronic obstructive pulmonary disease (COPD) is common and should be suspected in any patient with chronic dyspnea, cough, or sputum with a history of exposure to tobacco or harmful particles. Spirometry is

used for diagnosis. Full evaluation includes the severity of obstruction and clinical data, following the Global Initiative for Chronic Obstructive Lung Disease guidelines. Although the only treatments that have an impact on mortality are tobacco cessation, pulmonary rehabilitation and, for advanced disease, oxygen therapy, new symptomatic treatment have recently been made available. The duration of antibiotic and corticosteroid treatment for exacerbations has been shortened. The new diagnostic and management recommendations are summarized in this article.

Conflict of interest statement

Les auteurs n'ont déclaré aucun conflit d'intérêts en relation avec cet article.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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Thorax

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. 2022 Sep 27;thorax-2022-219451.

doi: 10.1136/thorax-2022-219451. Online ahead of print.

[Changing practice by changing pressures: a role for oscillating positive expiratory pressure in chronic obstructive pulmonary disease](#)

[Adam Lewis](#)¹, [Christian Robert Osadnik](#)²

Affiliations expand

- PMID: 36167723
- DOI: [10.1136/thorax-2022-219451](https://doi.org/10.1136/thorax-2022-219451)

No abstract available

Keywords: COPD Exacerbations; Cough/Mechanisms/Pharmacology.

Conflict of interest statement

Competing interests: AL declares working on lung volume reduction, remote vital sign monitoring, and singing for lung health clinical studies with Professor Nicholas Hopkinson, Dr Keir Philip, Dr Winston Banya, Mrs Sara Buttery and Professor Michael Polkey. CRO declares no conflict of interest.

FULL TEXT LINKS



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J Am Vet Med Assoc

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. 2022 Sep 27;1-7.

doi: 10.2460/javma.22.03.0108. Online ahead of print.

[Specialists' approach to tracheal collapse: survey-based opinions on diagnostics, medical management, and comorbid diseases](#)

[Carr Susan V](#)¹, [Reinero Carol](#)², [Rishniw Mark](#)³, [Pritchard Jessica C](#)⁴

Affiliations expand

- PMID: 36166502
- DOI: [10.2460/javma.22.03.0108](https://doi.org/10.2460/javma.22.03.0108)

Abstract

Objective: To describe the current standard of care among specialists for the routine diagnostic evaluation and medical management of stable tracheal collapse in dogs, identifying gaps between practice and scientific evidence to facilitate the development of future prospective studies. A secondary objective was to describe the perceived incidence of selected comorbid disorders in dogs with tracheal collapse and the diagnostic tests performed to evaluate for those disorders.

Sample: 180 veterinary specialists in 22 countries.

Procedures: An electronic survey was sent to 4 specialty listservs to target diplomates. Respondents completed multiple-choice and free-response questions related to the diagnostic evaluation and treatment of a theoretical stable dog with suspected tracheal collapse.

Results: Most respondents routinely utilized radiography, tracheobronchoscopy, and fluoroscopy to diagnose tracheal collapse and performed airway sampling, sedated airway examination, and echocardiograms to rule out comorbidities. The most frequently perceived comorbid disorders included chronic bronchitis, bronchomalacia, and myxomatous mitral valve disease. Respondents most often prescribed opioid antitussives, glucocorticoids, anxiolytics, and antibiotics as treatments. Less frequently, they utilized bronchodilators and nonopioid medications for cough.

Clinical relevance: Despite a lack of published guidelines, specialists have similar approaches in their diagnostic and therapeutic approach to a stable dog with suspected tracheal collapse and believe evaluating for comorbid disorders is important. A description of a typical diagnostic approach and knowledge of realistic treatment goals will assist the general practitioner managing dogs with stable tracheal collapse. Additionally, gaps between current practices established via this survey and data supporting those practices exist, specifically concerning the use of antibiotics and nonopioid medications for cough, representing areas for further study.

FULL TEXT LINKS



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Pediatr Pulmonol

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. 2022 Oct;57(10):2562-2564.

doi: 10.1002/ppul.26048. Epub 2022 Jul 12.

[A child with chronic cough and eosinophilia secondary to Strongyloides stercoralis infection](#)

[Guy Hazan](#)¹, [Rachel C Orscheln](#)², [Lila Kertz](#)¹, [Katherine Rivera-Spoljaric](#)¹

Affiliations expand

- PMID: 35778783
- DOI: [10.1002/ppul.26048](https://doi.org/10.1002/ppul.26048)

No abstract available

Keywords: TB; asthma and early wheeze; infections: pneumonia; viral.

- [5 references](#)

SUPPLEMENTARY INFO

MeSH termsexpand

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Clinical Trial

Br J Clin Pharmacol

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. 2022 Oct;88(10):4552-4564.

doi: 10.1111/bcp.15358. Epub 2022 May 22.

[First-in-human study of eliapixant \(BAY 1817080\), a highly selective P2X3 receptor antagonist: Tolerability, safety and pharmacokinetics](#)

[Stefan Klein](#)¹, [Isabella Gashaw](#)¹, [Sybille Baumann](#)², [Xinying Chang](#)¹, [Thomas Hummel](#)³, [Uwe Thuß](#)⁴, [Christian Friedrich](#)¹

Affiliations expand

- PMID: 35437837
- DOI: [10.1111/bcp.15358](https://doi.org/10.1111/bcp.15358)

Abstract

Aims: Neuronal hypersensitisation due to adenosine triphosphate-dependent P2X3 receptor signalling plays a significant role in several disorders including chronic cough and endometriosis. This first-in-human study of eliapixant (BAY 1817080) investigated the tolerability, safety and pharmacokinetics (PK) of single doses of eliapixant, including the effect of food and coadministration with a CYP3A inhibitor on eliapixant relative bioavailability.

Methods: In this randomised, double-blind phase I study ([NCT02817100](#)), 88 healthy male subjects received single ascending doses of immediate-release eliapixant (10-800 mg) tablets or placebo under fasted conditions, with food (low-fat continental or high-fat American breakfast) or with itraconazole (fasted state). PK parameters, dose proportionality, adverse events and taste assessments (taste strips; dysgeusia questionnaire) were evaluated.

Results: Eliapixant had a long half-life (23.5-58.9 h [fasted state]; 32.8-43.8 h [high-fat breakfast]; 38.9-46.0 h [low-fat breakfast]). Less than dose-proportional increases in maximum plasma concentrations (C_{\max}) and area under the concentration-time curve from time 0 to infinity ($AUC_{[0-\infty]}$) were observed with ascending eliapixant doses. We observed a pronounced food effect with the high-fat breakfast (4.1-fold increased C_{\max} ; 2.7-fold increased $AUC_{[0-\infty]}$), a smaller food effect with the low-fat breakfast and a mild-to-moderate effect of itraconazole coadministration on eliapixant (1.1-1.2-fold increased C_{\max} ; 1.7-fold increased AUC from 0 to 72 h). Eliapixant was well tolerated with minimal impact on taste perception.

Conclusion: The PK profile, particularly the long half-life, and favourable tolerability with no taste-related adverse events, supports the further development of eliapixant in disorders with underlying P2X3 receptor-mediated neuronal hypersensitisation.

Keywords: P2X3 receptor antagonists; dysgeusia; pharmacokinetics; taste perception.

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- [26 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Physiol Rev

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[Physiology and pathophysiology of human airway mucus](#)

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Abstract

The mucus clearance system is the dominant mechanical host defense system of the human lung. Mucus is cleared from the lung by cilia and airflow, including both two-phase gas-liquid pumping and cough-dependent mechanisms, and mucus transport rates are heavily dependent on mucus concentration. Importantly, mucus transport rates are accurately predicted by the gel-on-brush model of the mucociliary apparatus from the relative osmotic moduli of the mucus and periciliary-glycocalyxal (PCL-G) layers. The fluid available to hydrate mucus is generated by transepithelial fluid transport. Feedback interactions between mucus concentrations and cilia beating, via purinergic signaling, coordinate Na^+ absorptive vs Cl^- secretory rates to maintain mucus hydration in health. In disease, mucus becomes hyperconcentrated (dehydrated). Multiple mechanisms derange the ion transport pathways that normally hydrate mucus in muco-obstructive lung diseases, e.g., cystic fibrosis (CF), chronic obstructive pulmonary disease (COPD), non-CF bronchiectasis (NCFB), and primary ciliary dyskinesia (PCD). A key step in muco-obstructive disease pathogenesis is the osmotic compression of the mucus layer onto the airway surface with the formation of adherent mucus plaques and plugs, particularly in distal airways. Mucus plaques create locally hypoxic conditions and produce airflow obstruction, inflammation, infection, and, ultimately, airway wall damage. Therapies to clear adherent mucus with hydrating and mucolytic agents are rational, and strategies to develop these agents are reviewed.

Keywords: airway ion transport; gel-on-brush model; mucins; muco-obstructive diseases; mucus.

- [Cited by 5 articles](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

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