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

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Ann Am Thorac Soc

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. 2024 Aug 12.

doi: 10.1513/AnnalsATS.202402-122OC. Online ahead of print.

[Chronic Airflow Limitation, Emphysema and Impaired Diffusing Capacity in Relation to Smoking Habits in a Swedish Middle-Aged Population](#)

[Anders Blomberg<sup>1</sup>](#), [Kjell Torén<sup>2,3</sup>](#), [Per Liv<sup>4</sup>](#), [Gabriel Granåsen<sup>4</sup>](#), [Anders Andersson<sup>5,6</sup>](#), [Annelie Behndig<sup>4</sup>](#), [Göran Bergström<sup>7,8</sup>](#), [John Brandberg<sup>9,10</sup>](#), [Kenneth Caidahl<sup>11,12,8</sup>](#), [Kerstin Cederlund<sup>13</sup>](#), [Arne Egesten<sup>14</sup>](#), [Magnus Ekström<sup>15</sup>](#), [Maria J Eriksson<sup>16,12</sup>](#), [Emil Hagström<sup>17,18</sup>](#), [Christer Janson<sup>19</sup>](#), [Tomas Jernberg<sup>20</sup>](#), [David Kylhammar<sup>21</sup>](#), [Lars Lind<sup>22</sup>](#), [Anne Lindberg<sup>4</sup>](#), [Eva Lindberg<sup>23</sup>](#), [Claes-Göran Löfdahl<sup>15</sup>](#), [Andrei Malinowski<sup>24</sup>](#), [Maria Mannila<sup>25</sup>](#), [Lars T Nilsson<sup>4</sup>](#), [Anna-Carin Olin<sup>2</sup>](#), [Anders Persson<sup>26,27,28</sup>](#), [Hans Lennart Persson<sup>29</sup>](#), [Annika Rosengren<sup>7,30</sup>](#), [Johan Sundström<sup>31,32</sup>](#), [Eva Swahn<sup>33</sup>](#), [Stefan Söderberg<sup>4</sup>](#), [Jenny Vikgren<sup>9,10</sup>](#), [Per Wollmer<sup>34</sup>](#), [Carl Johan Östgren<sup>35,36</sup>](#), [Jan Engvall<sup>37,36</sup>](#), [C Magnus Sköld<sup>38,39</sup>](#)

Affiliations Expand

- PMID: 39133529
- DOI: [10.1513/AnnalsATS.202402-122OC](#)

## Abstract

**Rationale:** Chronic obstructive pulmonary disease (COPD) includes respiratory symptoms and chronic airflow limitation (CAL). In some cases, emphysema and impaired diffusing capacity for carbon monoxide (DLCO) are present, but characteristics and symptoms vary with smoking exposure.

**Objectives:** To study the prevalence of CAL, emphysema and impaired DLCO in relation to smoking and respiratory symptoms in a middle-aged population.

**Methods:** We investigated 28,746 randomly invited individuals (52% women) aged 50-64 years across six Swedish sites. We performed spirometry, DLCO, high-resolution computed tomography (HRCT) and asked for smoking habits and respiratory symptoms. CAL was defined as post-bronchodilator forced expiratory volume in 1 second divided by forced expiratory volume (FEV1/FVC)<0.7.

**Results:** The overall prevalence was for CAL 8.8%, for impaired DLCO (DLCO<LLN) 5.7% and for emphysema 8.8%, with a higher prevalence in current smokers than in ex-smokers and never-smokers. The proportion of never-smokers among those with CAL, emphysema and impaired DLCO was 32%, 19% and 31% respectively. Regardless of smoking habits, the prevalence of respiratory symptoms was higher among people with CAL and impaired DLCO, compared to those with normal lung function. Asthma prevalence in never-smokers with CAL was 14%. In this group, asthma associated with lower FEV1 and more respiratory symptoms.

**Conclusions:** In this large population-based study of middle-aged people, CAL and impaired DLCO were associated with common respiratory symptoms. Self-reported asthma was not associated with CAL in never-smokers. Our findings suggest that CAL in never-smokers signifies a separate clinical phenotype that may be monitored and, possibly, treated differently from smoking-related COPD. This article is open access and distributed under the terms of the Creative Commons Attribution 4.0 International License (<https://creativecommons.org/licenses/by/4.0/>).

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## Review

## Ann Intensive Care

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. 2024 Aug 12;14(1):122.

doi: 10.1186/s13613-024-01356-5.

## [Heart-Lungs interactions: the basics and clinical implications](#)

[Mathieu Jozwiak](#)<sup>1,2</sup>, [Jean-Louis Teboul](#)<sup>3</sup>

Affiliations Expand

- PMID: 39133379
- DOI: [10.1186/s13613-024-01356-5](#)

### Abstract

Heart-lungs interactions are related to the interplay between the cardiovascular and the respiratory system. They result from the respiratory-induced changes in intrathoracic pressure, which are transmitted to the cardiac cavities and to the changes in alveolar pressure, which may impact the lung microvessels. In spontaneously breathing patients, consequences of heart-lungs interactions are during inspiration an increase in right ventricular preload and afterload, a decrease in left ventricular preload and an increase in left ventricular afterload. In mechanically ventilated patients, consequences of heart-lungs interactions are during mechanical insufflation a decrease in right ventricular preload, an increase in right ventricular afterload, an increase in left ventricular preload and a decrease in left ventricular afterload. Physiologically and during normal breathing, heart-lungs interactions do not lead to significant hemodynamic consequences. Nevertheless, in some clinical settings such as acute exacerbation of chronic obstructive pulmonary disease, acute left heart failure or acute respiratory distress syndrome, heart-lungs interactions may lead to significant hemodynamic consequences. These are linked to complex pathophysiological mechanisms, including a marked inspiratory negativity of intrathoracic pressure, a marked inspiratory increase in transpulmonary pressure and an increase in intra-abdominal pressure. The most recent application of heart-lungs interactions is the prediction of fluid responsiveness in mechanically ventilated patients. The first test to be developed using heart-lungs interactions was the respiratory variation of pulse pressure. Subsequently, many other dynamic fluid responsiveness tests using heart-lungs interactions have been developed, such as the respiratory variations of pulse contour-based stroke volume or the respiratory variations of the inferior or superior vena cava diameters. All these tests share the same limitations, the most frequent being low tidal volume ventilation, persistent spontaneous breathing activity and cardiac arrhythmia. Nevertheless, when their main limitations are properly addressed, all these tests can help intensivists in the decision-making process regarding fluid administration and fluid removal in critically ill patients.

**Keywords:** Cardiac loading conditions; Fluid responsiveness; Intrathoracic pressure; Transpulmonary pressure.

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Chronic Obstr Pulm Dis

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. 2024 Aug 5.

doi: [10.15326/jcopdf.2024.0515](https://doi.org/10.15326/jcopdf.2024.0515). Online ahead of print.

[Multimorbidities in COPD are Associated With Increased Exacerbations and Health Care Resource Utilization in Real-World Patients from a U.S. Database](#)

[Jamuna K Krishnan<sup>1</sup>, Fernando J Martinez<sup>1</sup>, Pablo Altman<sup>2</sup>, Ver Luanni F Bilano<sup>3</sup>, Edward Khokhlovich<sup>4</sup>, Raymond Przybysz<sup>2</sup>, Helene Karcher<sup>5</sup>, Matthias Schoenberger<sup>5</sup>](#)

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- PMID: 39133115
- DOI: [10.15326/jcopdf.2024.0515](https://doi.org/10.15326/jcopdf.2024.0515)

Abstract

**Background:** Patients with COPD often develop other morbidities, suggesting a systemic component to this disease. This retrospective non-interventional cohort study investigated relationships between multimorbidities in COPD and their impact on COPD exacerbations and COPD-related healthcare resource utilization (HCRU) using real-world evidence from Optum's de-identified Clinformatics® Data Mart Database.

**Methods:** Demographic and clinical characteristics were assessed. Overall comorbidity burden and proportion of individuals with gastroesophageal reflux disease (GERD), diabetes or osteoporosis/osteopenia were compared in age-matched COPD versus non-COPD cohorts using descriptive statistics. COPD exacerbations and COPD-related HCRU (hospitalizations and emergency room visits) were compared between age-matched cohorts of COPD patients with and without specific common morbidities (GERD, diabetes and osteoporosis/osteopenia). Additional weight-matching was performed for matched cohorts of COPD patients with and without diabetes, and with and without osteoporosis/osteopenia. Follow-up period was five years.

**Results:** Age-matched cohorts with and without COPD each comprised 158,106 patients. Morbidities were more common in the COPD cohort than the cohort without COPD (GERD: 44.9% vs 27.8%; diabetes: 40.8% vs 31.1%; osteoporosis/osteopenia: 18.8% vs 14.1%, respectively). Compared with matched cohorts with COPD only, cohorts of COPD patients with either GERD, diabetes or osteoporosis/osteopenia, experienced increased risk of severe exacerbations (odds ratio [OR]=1.819, OR=1.119 and OR=1.373, respectively), moderate exacerbations (OR=1.699, OR=1.102 and OR=1.322, respectively) or any exacerbations OR=1.848, OR=1.099 and OR=1.384, respectively,  $p<0.001$  for all comparisons and increased risk of COPD-related HCRU (ER visits: OR=1.983, OR=1.098 and OR=1.343, respectively; Hospitalization visits: OR=2.222, OR=1.26 and OR=1.368, respectively;  $p<0.001$  for all comparisons).

**Conclusion:** These real-world data confirm that GERD, diabetes, and osteoporosis are common morbidities in patients with COPD and, moreover, that they affect frequency of exacerbation and HCRU. Determining and addressing the mechanisms behind the systemic effects of COPD may be beneficial for COPD patients and may also help reduce COPD exacerbations.

**Keywords:** COPD; GERD; diabetes; multimorbidities; osteoporosis.

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Case Reports

Int J Chron Obstruct Pulmon Dis

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. 2024 Aug 5:19:1791-1797.

doi: 10.2147/COPD.S469214. eCollection 2024.

[The Use of Bronchial Rheoplasty in Emphysema Patients Previously Treated with Endoscopic Lung Volume Reduction: A Case Series](#)

[Kristine Jensen](#)<sup>1</sup>, [Thomas Egenod](#)<sup>2</sup>, [Daniel P Franzen](#)<sup>3,4</sup>, [Michael Perch](#)<sup>1,5</sup>

Affiliations Expand

- PMID: 39129966
- PMCID: [PMC11313571](#)
- DOI: [10.2147/COPD.S469214](#)

Abstract

Endoscopic lung volume reduction (ELVR) is an established treatment option for patients with severe emphysema. Not all patients are candidates for this type of intervention, and in the context of significant airway secretions, they may be excluded from treatment. Bronchial Rheoplasty (BR) was developed to treat mucus hypersecretion by delivering nonthermal pulsed electric fields to the airway epithelium and submucosa. The literature to date demonstrates that patients treated with BR in clinical studies have a reduction in airway goblet cell hyperplasia as well as substantive clinical improvement in the setting of chronic bronchitis (CB). In this case series, we present four patients treated at three different institutions who had previously undergone ELVR with beneficial outcome. However, over time, these patients subsequently developed worsening clinical issues, including complaints of increased and thickened mucus, along with exacerbations in the setting of a loss of some ELVR-associated benefits. These patients then underwent exploratory treatment with BR with the intent of reducing their secretion burden and potentially restoring the efficacy associated with the initial placement of the airway valves. All BR procedures were well tolerated, and three of the four patients showed substantial improvement in their symptom burden. Airway examinations during the second of the two BR procedures also revealed what appeared to be less airway mucosal inflammation and a decrease in the quantity of airway secretions. Therefore, treatment with BR may have the potential to improve and restore the initial benefits associated with ELVR, thus enhancing long-term outcomes. Further clinical studies with sufficient follow-up are warranted to assess this in a larger cohort of patients, and to determine whether treatment with BR prior to ELVR may

make more patients eligible for this treatment through reduction in their secretions and/or symptoms.

**Keywords:** bronchial rheoplasty; emphysema; endobronchial valves.

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#### Conflict of interest statement

Dr Michael Perch reports personal fees from AstraZeneca, personal fees from PulmonX, grants from PulmonX, grants from Therakos, personal fees from Takeda, personal fees from Zambon, outside the submitted work. The authors report no other conflicts of interest in this work.

#### Supplementary info

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Int J Chron Obstruct Pulmon Dis

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. 2024 Aug 7:19:1813-1818.

doi: 10.2147/COPD.S468887. eCollection 2024.

[Real-World Effectiveness of Benralizumab Among Patients with Asthma and Concomitant Chronic Obstructive Pulmonary Disease](#)

[Donna D Carstens](#)<sup>1</sup>, [Diego J Maselli](#)<sup>2</sup>, [Erin E Cook](#)<sup>3</sup>, [Fan Mu](#)<sup>3</sup>, [Jingyi Chen](#)<sup>3</sup>, [Danni Yang](#)<sup>3</sup>, [Jessica Karacz DeMartino](#)<sup>1</sup>, [Yen Chung](#)<sup>1</sup>

Affiliations Expand

- PMID: 39129964
- PMCID: [PMC11317043](#)

- DOI: [10.2147/COPD.S468887](https://doi.org/10.2147/COPD.S468887)

*No abstract available*

Conflict of interest statement

DC, JKD, and YC are employees and shareholders of AstraZeneca, which funded the development and conduct of this study and manuscript. DY, EEC, FM, and JC are employees of Analysis Group, Inc., a consulting company that has provided paid consulting services to AstraZeneca, which funded the development and conduct of this study and manuscript. DJM received consultant/speaker fees from AstraZeneca, GSK, Amgen, Sanofi/Regeneron. The authors report no other conflicts of interest in this work.

Supplementary info

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Eur J Intern Med

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. 2024 Aug 7:S0953-6205(24)00338-8.

doi: 10.1016/j.ejim.2024.07.041. Online ahead of print.

[Inhaled corticosteroids in severe COPD patients with cardiovascular diseases.](#)

[Authors' reply](#)

[Alberto Papi](#)<sup>1</sup>, [Giacomo Forini](#)<sup>2</sup>, [Mauro Maniscalco](#)<sup>3</sup>, [Elena Bargagli](#)<sup>4</sup>, [Claudia Crimi](#)<sup>5</sup>, [Pierachille Santus](#)<sup>6</sup>, [Antonio Molino](#)<sup>7</sup>, [Valeria Bandiera](#)<sup>8</sup>, [Federico Baraldi](#)<sup>9</sup>, [Silvestro Ennio D'Anna](#)<sup>10</sup>, [Mauro Carone](#)<sup>11</sup>, [Maurizio Marvisi](#)<sup>12</sup>, [Corrado Pelaia](#)<sup>13</sup>, [Giulia Scioscia](#)<sup>14</sup>, [Vincenzo Patella](#)<sup>15</sup>, [Maria Aliani](#)<sup>11</sup>, [Leonardo M Fabbri](#)<sup>16</sup>; [ICSLIFE Study Group](#)

Affiliations Expand

- PMID: 39117553

- DOI: [10.1016/j.ejim.2024.07.041](https://doi.org/10.1016/j.ejim.2024.07.041)

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J Chest Surg

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. 2024 Aug 8.

doi: 10.5090/jcs.24.010. Online ahead of print.

[Different DL<sub>co</sub> Parameters as Predictors of Postoperative Pulmonary Complications in Mild Chronic Obstructive Pulmonary Disease Patients with Lung Cancer](#)

[Mil Hoo Kim<sup>1</sup>, Joonseok Lee<sup>1</sup>, Joung Woo Son<sup>1</sup>, Beatrice Chia-Hui Shih<sup>1</sup>, Woohyun Jeong<sup>1</sup>, Jae Hyun Jeon<sup>1</sup>, Kwhanmien Kim<sup>1,2</sup>, Sanghoon Jheon<sup>1,2</sup>, Sukki Cho<sup>1,2</sup>](#)

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- PMID: 39115197

- DOI: [10.5090/jcs.24.010](https://doi.org/10.5090/jcs.24.010)

Free article

Abstract

**Background:** Numerous studies have investigated methods of predicting postoperative pulmonary complications (PPCs) in lung cancer surgery, with chronic

obstructive pulmonary disease (COPD) and low forced expiratory volume in 1 second (FEV1) being recognized as risk factors. However, predicting complications in COPD patients with preserved FEV1 poses challenges. This study considered various diffusing capacity of the lung for carbon monoxide (DL<sub>CO</sub>) parameters as predictors of pulmonary complication risks in mild COPD patients undergoing lung resection.

**Methods:** From January 2011 to December 2019, 2,798 patients undergoing segmentectomy or lobectomy for non-small cell lung cancer (NSCLC) were evaluated. Focusing on 709 mild COPD patients, excluding no COPD and moderate/severe cases, 3 models incorporating DL<sub>CO</sub>, predicted postoperative DL<sub>CO</sub> (ppoDL<sub>CO</sub>), and DL<sub>CO</sub> divided by the alveolar volume (DL<sub>CO</sub>/VA) were created for logistic regression. The Akaike information criterion and Bayes information criterion were analyzed to assess model fit, with lower values considered more consistent with actual data.

**Results:** Significantly higher proportions of men, current smokers, and patients who underwent an open approach were observed in the PPC group. In multivariable regression, male sex, an open approach, DL<sub>CO</sub> <80%, ppoDL<sub>CO</sub> <60%, and DL<sub>CO</sub>/VA <80% significantly influenced PPC occurrence. The model using DL<sub>CO</sub>/VA had the best fit.

**Conclusion:** Different DL<sub>CO</sub> parameters can predict PPCs in mild COPD patients after lung resection for NSCLC. The assessment of these factors using a multivariable logistic regression model suggested DL<sub>CO</sub>/VA as the most valuable predictor.

**Keywords:** Chronic obstructive pulmonary disease; Lung resection; Non-small cell lung carcinoma; Postoperative complications; Pulmonary diffusing capacity.

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Respir Med

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. 2024 Aug 5:232:107762.

doi: 10.1016/j.rmed.2024.107762. Online ahead of print.

## [Nasal high flow or noninvasive ventilation? navigating hypercapnic COPD exacerbation treatment: A randomized noninferiority clinical trial](#)

[Ioannis Pantazopoulos<sup>1</sup>](#), [Stylianos Boutlas<sup>2</sup>](#), [Georgios Mavrovounis<sup>3</sup>](#), [Athanasia Papalampidou<sup>4</sup>](#), [Nikolaos Papagiannakis<sup>5</sup>](#), [Marina Kontou<sup>6</sup>](#), [Eleni Bibaki<sup>7</sup>](#), [Nikolaos Athanasiou<sup>8</sup>](#), [Georgios Meletis<sup>7</sup>](#), [Konstantinos Gourgoulialis<sup>2</sup>](#), [Spyros Zakynthinos<sup>4</sup>](#), [Eleni Ischaki<sup>4</sup>](#)

### Affiliations Expand

- PMID: 39111544
- DOI: [10.1016/j.rmed.2024.107762](#)

### Abstract

**Background:** Noninvasive ventilation (NIV) has been the cornerstone for managing acute exacerbations of COPD (AECOPD) with hypercapnic respiratory failure. Nasal high flow (NHF) oxygen therapy has emerged as a potential alternative, offering a more tolerable modality with promising outcomes. The aim of the present study was to evaluate whether NHF respiratory support is noninferior to NIV with respect to treatment failure, in patients with mild-to-moderate hypercapnic AECOPD.

**Methods:** In this multi-center, randomized, noninferiority trial, 105 patients with AECOPD and respiratory failure type II were enrolled. Participants were randomly assigned to receive either NHF therapy or NIV. The primary endpoint was the frequency of treatment failure, defined as the need for intubation and invasive mechanical ventilation or a switch to the alternative treatment group. Secondary endpoints included changes in respiratory parameters, patient comfort indicators, and the occurrence of complications.

**Results:** The findings revealed no significant difference in the primary outcome between the groups, with a treatment failure rate of 19.6 % (10 out of 51) in the NHF group and 14.8 % (8 out of 54) in the NIV group. Interestingly, NHF users reported significantly lower levels of dyspnea and discomfort at multiple follow-up points. Despite the differences in patient comfort, respiratory parameters such as respiratory rate, arterial blood gases, and use of accessory muscles of respiration showed no significant disparities between the groups throughout the study period.

**Conclusions:** NHF therapy was similar to NIV in preventing treatment failure among patients with hypercapnic AECOPD, offering a viable alternative with enhanced comfort.

**Trial registration:** The study was prospectively registered in ClinicalTrials.gov (Identifier: [NCT03466385](#)) on March 15, 2018.

**Keywords:** COPD; Hypercapnia; Nasal high flow; Noninvasive ventilation; Respiratory failure type II.

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Conflict of interest statement

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

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**Ann Am Thorac Soc**

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. 2024 Aug 7.

doi: 10.1513/AnnalsATS.202405-478PS. Online ahead of print.

[Is Smoked Marijuana a Risk Factor for COPD? An Enduring Controversy](#)

[Donald P Tashkin](#)<sup>1</sup>

**Affiliations** [Expand](#)

- PMID: 39110420
- DOI: [10.1513/AnnalsATS.202405-478PS](#)

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Clinical Trial

Respirol Case Rep

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. 2024 Aug 6;12(8):e01449.

doi: 10.1002/rcr2.1449. eCollection 2024 Aug.

[A double-blind randomized controlled trial of N-acetylcysteine \(NAC\) for the treatment of acute exacerbation of chronic obstructive pulmonary disease](#)

[Wang Chung Kwok<sup>1</sup>](#), [Shung Kay Samuel Chan<sup>1</sup>](#), [Ka Yan Chiang<sup>1</sup>](#), [Chung Man James Ho<sup>1</sup>](#)

Affiliations Expand

- PMID: 39108325
- PMCID: [PMC11301653](#)
- DOI: [10.1002/rcr2.1449](#)

Abstract

**Background:** Chronic obstructive pulmonary disease (COPD) is a common respiratory disease with acute exacerbation (AECOPD) being a common sequelae which negatively impact health status, rates of hospitalization and readmission, and disease progression. N-acetylcysteine (NAC) has been studied in COPD in both stable state and acute exacerbations, which has been shown to have small beneficial effects in stable COPD, as well as AECOPD. Yet, there has been lack of study with well-designed protocol to assess the role of NAC in more objective outcomes in AECOPD.

**Methods:** This is a double-blind randomized controlled trial. Patients will be randomized in 1:1 ratio to receive oral NAC at 600 mg twice daily or placebo twice daily with standard of care. Partial pressure of oxygen (PaO<sub>2</sub>), partial pressure of carbon dioxide (PaCO<sub>2</sub>) and the ratio of partial pressure arterial oxygen and fraction of inspired oxygen (PaO<sub>2</sub>/FiO<sub>2</sub>) will be measured on days 1 and 7. The following will be measure at baseline and on day 4 and 7: Forced expiratory volume in one second (FEV<sub>1</sub>), 24-hour sputum volume, oxygen saturation (SaO<sub>2</sub>), end-tidal CO<sub>2</sub>, Leicester Cough Questionnaire (LCQ) score, COPD Assessment Test (CAT) score, grading of

wheeze and grade of dyspnoea; blood inflammatory markers (leucocyte count, neutrophil count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and high sensitivity CRP (hs-CRP)). Patients will be randomized to oral NAC at 600 mg twice daily or placebo for 7 days. The main outcome measures include: The difference in PaO<sub>2</sub> on day 7. Secondary outcome: Change in following parameters on day 4/7 from baseline: FEV<sub>1</sub>, sputum volume, CAT score, LCQ score, SaO<sub>2</sub>, grade of wheeze; mMRC Dyspnoea Scale, end-tidal CO<sub>2</sub>, blood inflammatory marker, change in PaO<sub>2</sub>/FiO<sub>2</sub> ratio from baseline to day 7, PaCO<sub>2</sub> on day 7, 28 and 90 days' mortality, time to wean off supplemental oxygen, length of stay. Primary and secondary outcomes will be compared among the two treatment groups with two-sample *t*-test.

**Discussion:** We hypothesize that NAC use in COPD exacerbation can provide benefits in clinical and laboratory parameters.

**Trial registration:** *Name of the registry* : ClinicalTrials.gov *Trial registration number* : [NCT05706402](https://clinicaltrials.gov/ct2/show/NCT05706402). *URL of the trial registry record for this trial* : <https://classic.clinicaltrials.gov/ct2/show/NCT05706402> *Date of registration* : Registered on 11th January 2023 *Funding of the trial* : The Health and Medical Research Fund (HMRF). *Name and contact information for the trial sponsor* : Wang Chung Kwok, Clinical Assistant Professor, Honorary Associate Consultant, Queen Mary Hospital, The University of Hong Kong, Hong Kong. *Role of sponsor* : The funder is not involved in the planning of the study, gathering, analysing, and interpreting the data, or in preparing the manuscript.

**Keywords:** COPD, COPD exacerbation; N-acetylcysteine; RCT.

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#### Conflict of interest statement

There will be no conflict of interests from both the department and any of the investigators involved. Ka Yan Chiang and Chung Man James Ho are Editorial Board members of *Respirology Case Reports* and co-authors of this article. They were excluded from all editorial decision-making related to the acceptance of this article for publication.

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#### Supplementary info

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. 2024 Aug 6:S0953-6205(24)00336-4.

doi: 10.1016/j.ejim.2024.07.039. Online ahead of print.

[Atrial fibrillation-related mortality trends among adults with comorbid chronic obstructive pulmonary disease in the United States from 1999 to 2020](#)

[Usama Qamar](#)<sup>1</sup>, [Waleed Qamar](#)<sup>1</sup>, [Siddharth Agarwal](#)<sup>2</sup>

Affiliations Expand

- PMID: 39107209
- DOI: [10.1016/j.ejim.2024.07.039](#)

*No abstract available*

**Keywords:** Atrial fibrillation; Chronic obstructive pulmonary disease; Disparities; Mortality; Trends.

**Conflict of interest statement**

**Declaration of competing interest** The authors declare they have no conflict of interest.

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Expert Rev Respir Med

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. 2024 Aug 8:1-10.

doi: 10.1080/17476348.2024.2389960. Online ahead of print.

**[Effect of ensifentrine on dyspnea in patients with moderate-to-severe chronic obstructive pulmonary disease: pooled analysis of the ENHANCE trials](#)**

**[Donald A Mahler](#)<sup>1,2</sup>, [Surya P Bhatt](#)<sup>3</sup>, [Tara Rheault](#)<sup>4</sup>, [Daniel Reyner](#)<sup>4</sup>, [Thomas Bengtsson](#)<sup>5</sup>, [Amy Dixon](#)<sup>4</sup>, [Kathleen Rickard](#)<sup>4</sup>, [Dave Singh](#)<sup>6</sup>**

Affiliations Expand

- PMID: 39106052
- DOI: [10.1080/17476348.2024.2389960](https://doi.org/10.1080/17476348.2024.2389960)

Abstract

**Background:** Dyspnea is a critical component of chronic obstructive pulmonary disease (COPD). We report the effect of ensifentrine, a novel PDE3/PDE4 inhibitor, on dyspnea using pooled data from the Phase 3 ENHANCE-1/2 trials.

**Methods:** The pooled population (ensifentrine,  $n = 975$ ; placebo,  $n = 574$ ) included patients aged 40-80 years with post-bronchodilator  $FEV_1/FVC < 0.7$ ,  $FEV_1$  30-70% predicted, mMRC Dyspnea Scale score  $\geq 2$ , and a smoking history  $\geq 10$  pack-years. Patients taking dual LAMA/LABA or LAMA/LABA/ICS triple therapy were excluded. Dyspnea measures included the Transition Dyspnea Index (TDI), Evaluating Respiratory Symptoms (E-RS), and rescue medication use.

**Results:** After 24 weeks, ensifentrine significantly improved TDI scores (least-squares mean difference, 0.97; 95% CI, 0.64, 1.30;  $p < 0.001$ ) and across all TDI subdomains. Ensicentrine-treated patients were more likely to be TDI responders at week 24 ( $p < 0.001$ ), which was consistent across clinically relevant subgroups. Ensicentrine-treated patients had improved E-RS breathlessness subdomain scores ( $p = 0.053$ ) and reduced rescue medication use ( $p = 0.002$ ).

**Conclusion:** Ensicentrine produced clinically meaningful improvements in multiple dyspnea measures in patients with symptomatic, moderate-to-severe COPD. A limitation of this study was the exclusion of patients taking dual LAMA/LABA and LAMA/LABA/ICS triple therapy.

**Clinical trial registration:** www.clinicaltrials.gov identifiers are ENHANCE-1: [NCT04535986](https://clinicaltrials.gov/ct2/show/study/NCT04535986); ENHANCE-2: [NCT04542057](https://clinicaltrials.gov/ct2/show/study/NCT04542057).

**Keywords:** Dyspnea; PDE3 inhibitor; PDE4 inhibitor; chronic obstructive pulmonary disease; ensifentrine.

Supplementary info

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. 2024 Aug 5;10(4):00061-2024.

doi: 10.1183/23120541.00061-2024. eCollection 2024 Jul.

[Transcriptomics using lung resection material to advance our understanding of COPD and idiopathic pulmonary fibrosis pathogenesis](#)

[Kamini Rakkar](#)<sup>1</sup>, [Dhruma Thakker](#)<sup>1</sup>, [Michael A Portelli](#)<sup>1</sup>, [Ian Hall](#)<sup>1</sup>, [Holger Schlüter](#)<sup>2</sup>, [Ian Sayers](#)<sup>1</sup>

## Affiliations Expand

- PMID: 39104962
- PMCID: [PMC11299008](#)
- DOI: [10.1183/23120541.00061-2024](#)

## Abstract

Genes involved in cell death, inflammation and viral infection are common to both COPD and IPF. A link to rheumatic disease is unique to COPD, and IPF-specific analyses showed increases in gene expression of keratins, collagens, mucins and MMPs. <https://bit.ly/3JoW73H>.

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## Conflict of interest statement

Conflict of interest: D. Thakker has nothing to disclose. Conflict of interest: K. Rakkar reports support for the present manuscript from Boehringer Ingelheim. Conflict of interest: M.A. Portelli reports support for the present manuscript from

Boehringer Ingelheim; funding from the University of Nottingham UNICAS fund, outside the submitted work; and payment for lectures, presentations, speakers' bureaus, manuscript writing or educational events from the University of Malta, outside the submitted work. Conflict of interest: I. Hall reports support for the present manuscript from Boehringer Ingelheim; grants or contracts from the NIHR and Wellcome Trust, outside the submitted work; and is vice chair of the Trustees of Asthma+Lung UK (unpaid), disclosure made outside the submitted work. Conflict of interest: H. Schlüter reports support for the present manuscript from Boehringer Ingelheim and is employed by Boehringer Ingelheim. Conflict of interest: I. Sayers reports support for the present manuscript from Boehringer Ingelheim; and research grants received from GlaxoSmithKline, the Biotechnology and Biological Sciences Research Council, a Wellcome Trust Discovery Award and the Nottingham NIHR Biomedical Research Centre, outside the submitted work.

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

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. 2024 Aug 5;10(4):01052-2023.

doi: 10.1183/23120541.01052-2023. eCollection 2024 Jul.

[Symptom burden and its associations with clinical characteristics in patients with COPD: a clustering approach](#)

[Sarah Houben-Wilke<sup>1</sup>](#), [Qichen Deng<sup>1</sup>](#), [Daisy J A Janssen<sup>1,2</sup>](#), [Frits M E Franssen<sup>1,3,4</sup>](#), [Martijn A Spruit<sup>1,3,4</sup>](#)

Affiliations Expand

- PMID: 39104954

- PMID: [PMC11299006](#)
- DOI: [10.1183/23120541.01052-2023](#)

## Abstract

**Background:** Symptom burden in patients with COPD is often under-recognised. In this cross-sectional analysis, we aimed to study the severity of a variety of (non-)respiratory symptoms in patients with and without COPD and to explore the associations between clusters based on symptom severity and other clinical characteristics.

**Methods:** Characteristics were assessed in 538 patients with COPD from primary, secondary and tertiary care and 116 non-COPD participants. The severity of 20 symptoms was measured using a visual analogue scale (VAS), ranging from 0 mm (no symptom) to 100 mm (maximum severity). K-means cluster analysis was applied to symptom severity in the patient sample only.

**Results:** People with COPD were comparable with non-COPD participants in terms of gender (58% *versus* 55% male,  $p=0.132$ ) and age ( $64\pm 9$  years *versus*  $63\pm 6$  years,  $p=0.552$ ) and had a reduced forced expiratory volume in 1 s ( $57\pm 23\%$  predicted *versus*  $111\pm 17\%$  predicted,  $p<0.001$ ). The COPD group had higher VAS scores for most symptoms ( $p<0.05$ ). The most severe symptoms in patients with COPD were dyspnoea, fatigue and muscle weakness while non-COPD participants mainly experienced insomnia and micturition. Three clusters were identified in the patient sample. Health status and care dependency differed between all clusters, while functional mobility, exacerbation history and lung function differed between cluster 1 and the other two clusters ( $p<0.05$ ).

**Conclusions:** People with COPD report a high burden of respiratory as well as non-respiratory symptoms. Cluster analysis demonstrated a co-occurrence of different levels of symptom severity, highlighting the heterogeneity of symptoms experience. Identifying clusters of patients with shared symptom experiences will help us to understand the impact of the disease and define integrated, multidimensional treatment strategies.

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## Conflict of interest statement

**Conflict of interest:** D.J.A. Janssen has received lectures fees from Boehringer Ingelheim, and nonpersonal lecture fees from Chiesi, AstraZeneca and Abbott within the previous 3 years, outside the submitted work. **Conflict of interest:** F.M.E. Franssen reports grants and personal fees from AstraZeneca; personal fees from Boehringer Ingelheim, Chiesi and GlaxoSmithKline; grants and personal fees from Novartis; and personal fees from TEVA, outside the submitted work. **Conflict of interest:** M.A. Spruit reports grants and/or fees from the Netherlands Lung Foundation, Stichting Astma Bestrijding, Boehringer Ingelheim, AstraZeneca, Chiesi, GlaxoSmithKline and TEVA, all paid to the institution and all outside the submitted work. **Conflict of interest:** The remaining authors have nothing to disclose.

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. 2024 Aug 5;10(4):00984-2023.

doi: 10.1183/23120541.00984-2023. eCollection 2024 Jul.

#### [Hybrid compared to conventional pulmonary rehabilitation: an equivalence analysis](#)

[Marieke Wuyts](#)<sup>1,2</sup>, [Iris Coosemans](#)<sup>3</sup>, [Stephanie Everaerts](#)<sup>3</sup>, [Astrid Blondeel](#)<sup>1</sup>, [Sofie Breuls](#)<sup>1</sup>, [Heleen Demeyer](#)<sup>1,2</sup>, [Wim Janssens](#)<sup>3,4</sup>, [Thierry Troosters](#)<sup>1</sup>

#### Affiliations Expand

- PMID: 39104952
- PMCID: [PMC11298995](#)
- DOI: [10.1183/23120541.00984-2023](#)

#### Abstract

**Background:** Pulmonary rehabilitation (PR) is a well-established intervention for patients with COPD, but access, uptake and completion are low. This retrospective propensity-matched study aimed to analyse equivalence from a hybrid PR modality against conventional PR.

**Methods:** Between 2013 and 2019, 214 patients with COPD with valid baseline physical activity assessments enrolled in conventional PR for three times per week for 3 months. In 2021-2022, 44 patients with COPD enrolled in 3 months of hybrid PR, introducing two providers: once per week in the outpatient centre and two times

per week in a primary care setting near the patient's home. All sessions were supervised. Propensity score matching (1:1) was performed. Equivalence between both programmes was analysed for exercise capacity with the equivalence margins of  $\pm 30$  m on the 6-min walk distance (6MWD). Clinical outcomes, accessibility and adherence were compared using t-tests.

**Results:** 44 patients (mean $\pm$ sd age 67 $\pm$ 8 years; forced expiratory volume in 1 s (FEV<sub>1</sub>) 47 $\pm$ 15% predicted; 6MWD 355 $\pm$ 122 m) in the hybrid PR group were matched to 44 patients (mean $\pm$ sd age 66 $\pm$ 8 years; FEV<sub>1</sub> 46 $\pm$ 17% predicted; 6MWD 354 $\pm$ 103 m) in the conventional PR group. Equivalence on the increase in 6MWD could not be confirmed; nevertheless, both groups improved their 6MWD clinically significantly (hybrid PR change 63 m (90% CI 43-83 m); conventional PR change 39 m (90% CI 26-52 m)). Changes in quality of life and symptoms were similar. Dropout in hybrid PR (23%) was comparable to conventional PR (27%) (p=0.24). Adherence in both groups was high and accessibility was better for patients following hybrid PR.

**Conclusion:** Hybrid PR can be offered as an effective alternative to conventional PR, if patients are willing to take up the offer.

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Conflict of interest statement

Conflicts of interest: The authors declare that they have no conflicts of interest.

- [31 references](#)
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. 2024 Aug 5;28(1):264.

doi: 10.1186/s13054-024-05050-7.

[Probing the efficacy of high-flow nasal cannula in the treatment of acute exacerbations of COPD with acute-moderate hypercapnic respiratory failure](#)

[Ioannis Pantazopoulos](#)<sup>1</sup>, [Georgios Mavrovouni](#)<sup>2</sup>

Affiliations Expand

- PMID: 39103951
- PMCID: [PMC11302174](#)
- DOI: [10.1186/s13054-024-05050-7](#)

*No abstract available*

Conflict of interest statement

The authors declare no competing interests.

Comment on

- [High flow nasal cannula oxygen therapy versus non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease with acute-moderate hypercapnic respiratory failure: a randomized controlled non-inferiority trial.](#)

Tan D, Wang B, Cao P, Wang Y, Sun J, Geng P, Walline JH, Wang Y, Wang C. Crit Care. 2024 Jul 18;28(1):250. doi: 10.1186/s13054-024-05040-9. PMID: 39026242 Free PMC article. Clinical Trial.

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Supplementary info

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Randomized Controlled Trial

Respir Res

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. 2024 Aug 5;25(1):297.

doi: 10.1186/s12931-024-02918-8.

[Benefits of budesonide/glycopyrronium/formoterol fumarate dihydrate on lung function and exacerbations of COPD: a post-hoc analysis of the KRONOS study by blood eosinophil level and exacerbation history](#)

[Shigeo Muro](#)<sup>1</sup>, [Tomotaka Kawayama](#)<sup>2</sup>, [Hisatoshi Sugiura](#)<sup>3</sup>, [Munehiro Seki](#)<sup>4</sup>, [Elizabeth A Duncan](#)<sup>5</sup>, [Karin Bowen](#)<sup>6</sup>, [Jonathan Marshall](#)<sup>7</sup>, [Ayman Megally](#)<sup>8</sup>, [Mehul Patel](#)<sup>9</sup>

Affiliations Expand

- PMID: 39103901
- PMCID: [PMC11302094](#)
- DOI: [10.1186/s12931-024-02918-8](#)

Abstract

**Background:** Japanese guidelines recommend triple inhaled corticosteroid (ICS)/long-acting muscarinic antagonist (LAMA)/long-acting  $\beta_2$ -agonist (LABA) therapy in patients with chronic obstructive pulmonary disease (COPD) and no concurrent asthma diagnosis who experience frequent exacerbations and have blood eosinophil (EOS) count  $\geq 300$  cells/mm<sup>3</sup>, and in patients with COPD and asthma with continuing/worsening symptoms despite receiving dual ICS/LABA therapy. These post-hoc analyses of the KRONOS study in patients with COPD and without an asthma diagnosis, examine the effects of fixed-dose triple therapy with budesonide/glycopyrronium/formoterol fumarate dihydrate (BGF) versus dual therapies on lung function and exacerbations based on blood EOS count - focusing on blood EOS count 100 to  $< 300$  cells/mm<sup>3</sup> - as a function of exacerbation history and COPD severity.

**Methods:** In KRONOS, patients were randomized to receive treatments that included BGF 320/14.4/10  $\mu\text{g}$ , glycopyrronium/formoterol fumarate dihydrate (GFF) 14.4/10  $\mu\text{g}$ , or budesonide/formoterol fumarate dihydrate (BFF) 320/10  $\mu\text{g}$  via metered dose inhaler (two inhalations twice-daily for 24 weeks). These post-hoc analyses assessed changes from baseline in morning pre-dose trough forced expiratory volume in 1 s (FEV<sub>1</sub>) over 12-24 weeks and moderate or severe COPD exacerbations

rates over 24 weeks. The KRONOS study was not prospectively powered for these subgroup analyses.

**Results:** Among patients with blood EOS count 100 to < 300 cells/mm<sup>3</sup>, least squares mean treatment differences for lung function improvement favored BGF over BFF in patients without an exacerbation history in the past year and in patients with moderate and severe COPD, with observed differences ranging from 62 ml to 73 ml across populations. In this same blood EOS population, moderate or severe exacerbation rates were reduced for BGF relative to GFF by 56% in patients without an exacerbation history in the past year, by 47% in patients with moderate COPD, and by 50% in patients with severe COPD.

**Conclusions:** These post-hoc analyses of patients with moderate-to-very severe COPD from the KRONOS study seem to indicate clinicians may want to consider a step-up to triple therapy in patients with persistent/worsening symptoms with blood EOS count > 100 cells/mm<sup>3</sup>, even if disease severity is moderate and there is no recent history of exacerbations.

**Trial registration:** ClinicalTrials.gov registry number [NCT02497001](https://clinicaltrials.gov/ct2/show/study/NCT02497001) (registration date, 13 July 2015).

**Keywords:** Blood eosinophils; Budesonide/glycopyrronium/formoterol fumarate dihydrate (BGF); Chronic obstructive pulmonary disease (COPD); Disease severity; Exacerbation rates; Fixed-dose triple therapy; Lung function.

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#### Conflict of interest statement

SM has received lecture fees from AstraZeneca, GlaxoSmithKline, Nippon Boehringer Ingelheim, and Novartis Pharma. TK has received grants from Helios co. Ltd. and lecture fees from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Kyorin, Novartis, Sanofi, and Teijin healthcare. HS has received lecture fees from AstraZeneca, GlaxoSmithKline, Nippon Boehringer Ingelheim, Novartis Pharma, and Sanofi. MS is an employee of AstraZeneca K.K. Kita-ku and owns stock and/or stock options in the company. EAD is a former employee of AstraZeneca and owns stock and/or stock options in the company. KB, JM, AM, and MP are employees of AstraZeneca and own stock and/or stock options in the company.

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

#### Supplementary info

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J Clin Nurs

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. 2024 Aug 5.

doi: 10.1111/jocn.17397. Online ahead of print.

[Generic and disease-specific self-care instruments in older patients affected by multiple chronic conditions: A descriptive study](#)

[Maddalena De Maria<sup>1</sup>, Manuela Saurini<sup>2</sup>, Ilaria Erba<sup>3</sup>, Ercole Vellone<sup>2,4</sup>, Barbara Riegel<sup>5</sup>, Davide Ausili<sup>6</sup>, Maria Matarese<sup>7</sup>](#)

Affiliations Expand

- PMID: 39101399
- DOI: [10.1111/jocn.17397](https://doi.org/10.1111/jocn.17397)

Abstract

**Aims:** To describe and compare generic and disease-specific self-care measures in patients with multiple chronic conditions (MCCs) in the three dimensions of self-care maintenance, monitoring, and management.

**Design:** Multicentre cross-sectional study.

**Methods:** Patients aged 65 and over with MCCs. We used Self-Care of Chronic Illness Inventory to measure generic self-care, Self-care of Diabetes Inventory to measure self-care in diabetes mellitus, Self-Care of Heart Failure (HF) Index to measure self-care in HF, and Self-Care of Chronic Obstructive Pulmonary Disease Inventory to measure self-care in chronic lung diseases.

**Results:** We recruited 896 patients. Multimorbid patients with diabetes had lower scores on the self-care maintenance scale, and diabetic patients in insulin treatment on the generic management scale than on the disease-specific instrument. Multimorbid patients with HF or chronic lung diseases scored higher on generic self-care maintenance and monitoring scales than disease-specific ones. There was a partial consistency between the generic and disease-specific self-care maintenance and management. Inadequate behaviours were recorded in disease-specific self-care monitoring rather than generic ones.

**Conclusions:** Older patients affected by MCCs scored differently in the generic and disease-specific instruments, showing inadequate self-care in some of the three self-care dimensions.

**Implications for the profession and/or patient care:** The choice between generic and disease-specific instruments to use in clinical practice and research should be made considering the specific aims, settings, patients characteristics, and knowledge of the different performance of the instruments by users.

**Impact:** No study has described and compared generic and specific self-care measures in patients affected by MCCs. Knowing these differences can help nurses choose the most suitable measure for their aims, context, and patients and plan generic and disease-specific self-care educational interventions for those behaviours in which MCCs patients perform poorly.

**Patient contribution:** Patients were informed about the study, provided informed consent, and answered questionnaires through interviews.

**Keywords:** chronic illness; chronic obstructive pulmonary disease; diabetes; heart failure; instruments; self-care.

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- [55 references](#)

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J Asthma

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. 2024 Aug 12:1-14.

doi: 10.1080/02770903.2024.2388781. Online ahead of print.

[A novel approach to investigate severe asthma and COPD: the 3d ex vivo respiratory mucosa model](#)

[Alberto Fucarino](#)<sup>1</sup>, [Alessandro Pitruzzella](#)<sup>2</sup>, [Stefano Burgio](#)<sup>3,4</sup>, [Giorgia Intili](#)<sup>2</sup>, [Olga Maria Manna](#)<sup>2</sup>, [Michele Domenico Modica](#)<sup>2,5</sup>, [Salvatore Poma](#)<sup>5</sup>, [Alida Benfante](#)<sup>6</sup>, [Alessandra Tomasello](#)<sup>6</sup>, [Nicola Scichilone](#)<sup>6</sup>, [Fabio Bucchieri](#)<sup>2</sup>

#### Affiliations Expand

- PMID: 39096201
- DOI: [10.1080/02770903.2024.2388781](https://doi.org/10.1080/02770903.2024.2388781)

#### Abstract

**Purpose:** This article illustrates the replication of asthma and COPD conditions in a laboratory setting and the potential applications of this methodology.

**Introduction:** Biologic drugs have been shown to enhance the treatment of severe asthma and COPD. Monoclonal antibodies against specific targets have dramatically changed the management of these conditions. Although the inflammatory pathways of asthma and COPD have already been clearly outlined, alternative mechanisms of action remain mostly unexplored. They could provide additional insights into these diseases and their clinical management.

**Aims:** *In vivo* or *in vitro* models have thus been developed to test alternative hypotheses. This study describes sophisticated *ex vivo* models that mimic the response of human respiratory mucosa to disease triggers, aiming to narrow the gap between laboratory studies and clinical practice.

**Results:** These models successfully replicate crucial aspects of these diseases, such as inflammatory cell presence, cytokine production, and changes in tissue structure, offering a dynamic platform for investigating disease processes and evaluating potential treatments, such as monoclonal antibodies. The proposed models have the potential to enhance personalized medicine approaches and patient-specific treatments, helping to advance the understanding and management of respiratory diseases.

**Keywords:** Chronic obstructive pulmonary disease (COPD); air-liquid interface (ALI) cultures; asthma; drug efficacy evaluation; *ex vivo* respiratory mucosa model; inflammatory lung diseases; tissue remodeling.

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. 2024 Aug 8:1-14.

doi: 10.1080/17476348.2024.2388293. Online ahead of print.

**[Efficacy and safety of bronchoscopic lung volume reduction for chronic obstructive pulmonary disease: a systematic review and network meta-analysis](#)**

**[Ranran Zhang](#)<sup>1,2</sup>, [Ziwen Zheng](#)<sup>1</sup>, [Yiding Bian](#)<sup>1,3</sup>, [Mingming Deng](#)<sup>1</sup>, [Felix F J Herth](#)<sup>4</sup>, [Gang Hou](#)<sup>1,2</sup>**

Affiliations Expand

- PMID: 39095948
- DOI: [10.1080/17476348.2024.2388293](https://doi.org/10.1080/17476348.2024.2388293)

**Abstract**

**Background:** Various bronchoscopic lung volume reduction (BLVR) methods have been developed to treat chronic obstructive pulmonary disease (COPD). The efficacy and safety of these interventions remain unclear. This study assessed the efficacy and safety of various BLVR interventions in COPD patients.

**Methods:** PubMed and Embase were searched from inception to 21 October 2023. The primary outcomes assessed included the 6-min walking distance (6MWD), St. George Respiratory Questionnaire (SGRQ) score, lung function, and adverse events (AE). A frequentist approach with a random-effects model was used for a network meta-analysis.

**Results:** Twelve randomized controlled trials (RCTs) with 1646 patients were included in this meta-analysis. Patients treated with an endobronchial valve (EBV) achieved a minimum clinically important difference (MCID) in 6MWD and SGRQ at 6 months. Patients treated with coils achieved MCID in the SGRQ score at 12 months. Patients with aspiration valve system and bronchoscopic thermal vapor ablation (BTVA) achieved MCID in the SGRQ score at 6 months.

**Conclusions:** In COPD patients, EBV should be considered first, while being wary of pneumothorax. Coil and BTVA are potential therapeutic alternatives. Although BTVA demonstrates a safer procedural profile than coils, additional studies are imperative to clarify its efficacy.

**Keywords:** Bronchoscopic lung volume reduction; chronic obstructive pulmonary disease; emphysema; endobronchial valve; network meta-analysis.

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. 2024 Aug 8;64(2):2301960.

doi: 10.1183/13993003.01960-2023. Print 2024 Aug.

[The 2022 ERS/ATS z-score classification to grade airflow obstruction: relationship with exercise outcomes across the spectrum of COPD severity](#)

[Lamyaa Al Sa'idi](#)<sup>1</sup>, [Danilo C Berton](#)<sup>2</sup>, [J Alberto Neder](#)<sup>3</sup>

Affiliations Expand

- PMID: 38936965
- DOI: [10.1183/13993003.01960-2023](#)

*No abstract available*

Conflict of interest statement

Conflict of interest: The authors have no potential conflicts of interest to disclose.

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. 2024 Aug 8;64(2):2400462.

doi: 10.1183/13993003.00462-2024. Print 2024 Aug.

[Global herpes zoster burden in adults with asthma: a systematic review and meta-analysis](#)

[Kevin J Mortimer](#)<sup>1,2,3</sup>, [Alvaro A Cruz](#)<sup>4</sup>, [Ingrid T Sepúlveda-Pachón](#)<sup>5</sup>, [Anamaria Jorga](#)<sup>6</sup>, [Hilde Vroliing](#)<sup>7</sup>, [Charles Williams](#)<sup>8</sup>

Affiliations Expand

- PMID: 38901886
- PMCID: [PMC11306804](#)
- DOI: [10.1183/13993003.00462-2024](#)

Abstract

**Background:** Asthma is a common respiratory disease, which may be associated with an increased risk of herpes zoster (HZ), often a debilitating disease associated with severe pain. This is the first systematic review with the objective of summarising evidence on HZ burden in adults with asthma.

**Methods:** A global systematic literature review and meta-analysis was conducted (MEDLINE and Embase, 2003-2024) on HZ burden (incidence, risk and complications) in adults (≥18 years) with asthma.

**Results:** There were 19 studies included on HZ outcomes in adults with asthma. Pooled HZ incidence per 1000 person-years was 5.71 (95% CI 4.68-6.96) in adults aged ≥18 years (4.20 (95% CI 3.09-5.70) in those aged <60 years *versus* 10.33 (95% CI 9.17-11.64) in those aged ≥60 years). The pooled rate ratio for developing HZ was 1.23 (95% CI 1.11-1.35) in those aged ≥18 years and 1.36 (95% CI 1.15-1.61) in those

aged  $\geq 50$  years. The risk of HZ was higher in people with asthma using systemic corticosteroids, long-acting  $\beta$ -agonists plus inhaled corticosteroids and "add-on therapy". Asthma was also associated with an increased risk of post-herpetic neuralgia (OR 1.21, 95% CI 1.06-1.37) and HZ ophthalmicus (OR 1.9, 95% CI 1.1-3.2). Differences in study design, setting, case definitions and follow-up durations led to heterogeneity.

**Conclusions:** This systematic literature review and meta-analysis found that adults with asthma have an increased risk of HZ, with higher risks in older age groups and in those on certain treatments, such as oral corticosteroids. HZ vaccines are available for adults, including those with comorbidities such as asthma, and can be considered as part of integrated respiratory care.

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#### Conflict of interest statement

**Conflict of interest:** A. Jorga and C. Williams are employed by GSK. A. Jorga holds shares in Pfizer and GSK. H. Vroling and I.T. Sepúlveda-Pachón are employees of P95/Pallas. P95/Pallas received funding from GSK for the submitted work. P95/Pallas holds/held contracts with AstraZeneca, GSK, Pfizer, Sanofi, Seqirus, Merck, Takeda, Orchard, Biomarin, Daiichi, Bavarian Nordic and Bayer (work for the non-GSK companies was not related to HZ). K.J. Mortimer declares grants and sponsorship from AstraZeneca and GSK to support the Global Asthma Network, consulting fees from AstraZeneca and GSK on asthma and COPD-related advisory boards, and honorarium from GSK for lectures on improving vaccine access for people with asthma, outside the submitted work. A.A. Cruz declares grants and sponsorship from GSK to support the ProAR Foundation, and consulting or lecture fees from Abdi-Ibrahim, AstraZeneca, Boehringer Ingelheim, Chiesi, Crossject, Eurofarma, Farmoquimica, Glennmark, GSK, Mylan, Novartis and Sanofi on asthma-related activities. The authors declare no other financial or non-financial relationships and activities or conflicts of interest.

#### Comment in

- [The burden of zoster in asthma: what is left to learn?](#)

Bloom C. *Eur Respir J*. 2024 Aug 8;64(2):2401300. doi: 10.1183/13993003.01300-2024. Print 2024 Aug. PMID: 39117424 No abstract available.

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

#### Supplementary info

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

Nat Med

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. 2024 Aug 8.

doi: 10.1038/s41591-024-03164-7. Online ahead of print.

[Proteomic aging clock predicts mortality and risk of common age-related diseases in diverse populations](#)

[M Austin Argentieri<sup>1,2,3</sup>, Sihao Xiao<sup>4,5</sup>, Derrick Bennett<sup>4</sup>, Laura Winchester<sup>5,6</sup>, Alejo J Nevado-Holgado<sup>5,6</sup>, Upamanyu Ghose<sup>5,6</sup>, Ashwag Albukhari<sup>5,7</sup>, Pang Yao<sup>4</sup>, Mohsen Mazidi<sup>4</sup>, Jun Lv<sup>8,9,10</sup>, Iona Millwood<sup>4</sup>, Hannah Fry<sup>4</sup>, Rodosthenis S Rodosthenous<sup>11</sup>, Jukka Partanen<sup>12</sup>, Zhili Zheng<sup>13</sup>, Mitja Kurki<sup>13</sup>, Mark J Daly<sup>13,14</sup>, Aarno Palotie<sup>11</sup>, Cassandra J Adams<sup>5,15</sup>, Liming Li<sup>8,9,10</sup>, Robert Clarke<sup>4</sup>, Najaf Amin<sup>4</sup>, Zhengming Chen<sup>4</sup>, Cornelia M van Duijn<sup>16,17</sup>](#)

Affiliations Expand

- PMID: 39117878
- DOI: [10.1038/s41591-024-03164-7](#)

Abstract

Circulating plasma proteins play key roles in human health and can potentially be used to measure biological age, allowing risk prediction for age-related diseases, multimorbidity and mortality. Here we developed a proteomic age clock in the UK Biobank (n = 45,441) using a proteomic platform comprising 2,897 plasma proteins and explored its utility to predict major disease morbidity and mortality in diverse populations. We identified 204 proteins that accurately predict chronological age (Pearson r = 0.94) and found that proteomic aging was associated with the incidence of 18 major chronic diseases (including diseases of the heart, liver, kidney and lung, diabetes, neurodegeneration and cancer), as well as with multimorbidity and all-cause mortality risk. Proteomic aging was also associated with age-related measures of biological, physical and cognitive function, including telomere length, frailty index and reaction time. Proteins contributing most substantially to the proteomic age clock are involved in numerous biological functions, including extracellular matrix interactions, immune response and inflammation, hormone regulation and reproduction, neuronal structure and function and development and differentiation. In a validation study involving biobanks in China (n = 3,977) and Finland (n = 1,990), the proteomic age clock showed similar age prediction accuracy (Pearson r = 0.92 and r = 0.94, respectively)

compared to its performance in the UK Biobank. Our results demonstrate that proteomic aging involves proteins spanning multiple functional categories and can be used to predict age-related functional status, multimorbidity and mortality risk across geographically and genetically diverse populations.

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. 2024 Aug 8:13:e58296.

doi: 10.2196/58296.

[The Effectiveness of Collaborative Care Interventions for the Management of Patients With Multimorbidity: Protocol for a Systematic Review, Meta-Analysis, and Meta-Regression Analysis](#)

[Anne-Maj Knudsen](#)<sup>1,2</sup>, [Ann-Cathrine Dalgård Dunvald](#)<sup>3,4</sup>, [Stine Hangaard](#)<sup>1,2</sup>, [Ole Hejlesen](#)<sup>1</sup>, [Thomas Kronborg](#)<sup>1,2</sup>

Affiliations Expand

- PMID: 39115256
- DOI: [10.2196/58296](#)

Free article

Abstract

**Background:** Collaborative care interventions have been proposed as a promising strategy to support patients with multimorbidity. Despite this, the effectiveness of

**collaborative care interventions requires further evaluation. Existing systematic reviews describing the effectiveness of collaborative care interventions in multimorbidity management tend to focus on specific interventions, patient subgroups, and settings. This necessitates a comprehensive review that will provide an overview of the effectiveness of collaborative care interventions for adult patients with multimorbidity.**

**Objective: This systematic review aims to systematically assess the effectiveness of collaborative care interventions in comparison to usual care concerning health-related quality of life (HRQoL), mental health, and mortality among adult patients with multimorbidity.**

**Methods: Randomized controlled trials evaluating collaborative care interventions designed for adult patients (18 years and older) with multimorbidity compared with usual care will be considered for inclusion in this review. HRQoL will be the primary outcome. Mortality and mental health outcomes such as rating scales for anxiety and depression will serve as secondary outcomes. The systematic search will be conducted in the CENTRAL, PubMed, CINAHL, and Embase databases. Additional reference and citation searches will be performed in Google Scholar, Web of Science, and Scopus. Data extraction will be comprehensive and include information about participant characteristics, study design, intervention details, and main outcomes. Included studies will be assessed for limitations according to the Cochrane Risk of Bias tool. Meta-analysis will be conducted to estimate the pooled effect size. Meta-regression or subgroup analysis will be undertaken to explore if certain factors can explain the variation in effect between studies, if feasible. The certainty of evidence will be evaluated using the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) approach.**

**Results: The preliminary literature search was performed on February 16, 2024, and yielded 5255 unique records. A follow-up search will be performed across all databases before submission. The findings will be presented in forest plots, a summary of findings table, and in narrative format. This systematic review is expected to be completed by late 2024.**

**Conclusions: This review will provide an overview of pooled estimates of treatment effects across HRQoL, mental health, and mortality from randomized controlled trials evaluating collaborative care interventions for adults with multimorbidity. Furthermore, the intention is to clarify the participant, intervention, or study characteristics that may influence the effect of the interventions. This review is expected to provide valuable insights for researchers, clinicians, and other decision-makers about the effectiveness of collaborative care interventions targeting adult patients with multimorbidity.**

**Trial registration: International Prospective Register of Systematic Reviews (PROSPERO) CRD42024512554;  
[https://www.crd.york.ac.uk/PROSPERO/display\\_record.php?RecordID=512554](https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=512554).**

**International registered report identifier (irrid): DERR1-10.2196/58296.**

**Keywords: collaborative care; comorbidity; meta-analysis; multidisciplinary teams; multimorbidity; multiple chronic conditions; patient care team; quality of life; systematic review.**

©Anne-Maj Knudsen, Ann-Cathrine Dalgård Dunvald, Stine Hangaard, Ole Hejlesen, Thomas Kronborg. Originally published in JMIR Research Protocols (<https://www.researchprotocols.org>), 08.08.2024.

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Geriatr Gerontol Int

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. 2024 Aug 8.

doi: 10.1111/ggi.14956. Online ahead of print.

[Multimorbidity and risk of falls, fractures, and joint replacements over two decades: Findings from the Hertfordshire Cohort Study](#)

[Leo D Westbury](#)<sup>1</sup>, [Camille Pearse](#)<sup>1</sup>, [Roshan Rambukwella](#)<sup>1</sup>, [Kate A Ward](#)<sup>1,2</sup>, [Cyrus Cooper](#)<sup>1,2,3</sup>, [Elaine M Dennison](#)<sup>1,2,4</sup>

Affiliations Expand

- PMID: 39115113
- DOI: [10.1111/ggi.14956](https://doi.org/10.1111/ggi.14956)

Abstract

**Aim:** To examine the relationship between level of morbidity burden and long-term risk of fractures, falls, and joint replacements in the community-dwelling participants of the Hertfordshire Cohort Study.

**Methods:** Data were analyzed from 2997 individuals (age 59-73 at baseline). Outcomes (fractures, falls, and lower limb joint replacements) were identified using ICD-10 and OPCS-4 codes from Hospital Episode Statistics data, available from

baseline (1998-2004) until December 2018. Number of systems medicated (marker of morbidity level) in relation to risk of outcomes was examined using sex-stratified Cox regression.

**Results:** Among both men and women, a greater number of systems medicated was related to increased risk of falls ( $P < 0.001$ ) and lower limb joint replacements ( $P < 0.003$ ). More systems medicated was only related to increased risk of fracture among women ( $P$ -values for trend of  $<0.001$  among women and  $0.186$  among men).

**Conclusions:** Higher morbidity was associated with increased risk of adverse health outcomes related to poor musculoskeletal health, but these relationships varied according to the musculoskeletal outcome studied. Intervention strategies to reduce multimorbidity among middle-aged and older people may hence reduce the burden of musculoskeletal aging. *Geriatr Gerontol Int* 2024; **••**: ••••.

**Keywords:** fracture; joint replacement; multimorbidity; osteoarthritis; osteoporosis.

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Clin Teach

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. 2024 Aug 7:e13794.

doi: 10.1111/tct.13794. Online ahead of print.

[Teaching multimorbidity to medical students](#)

[Kristy Penner](#)<sup>1</sup>, [Sonja Wicklum](#)<sup>2</sup>, [Aaron Johnston](#)<sup>3</sup>, [Martina Ann Kelly](#)<sup>2</sup>

Affiliations [Expand](#)

- PMID: 39112096
- DOI: [10.1111/tct.13794](https://doi.org/10.1111/tct.13794)

## Abstract

**Background:** Multimorbidity is a rising health care phenomenon and doctors require specific skill sets to effectively care for patients with multiple illnesses. Despite this, most medical education is taught using a single-disease, systems-based approach. Consequently, students can struggle to manage patients with multimorbidity. To help final year medical students manage patients with multimorbidity in clinical practice, we devised, taught, and evaluated a heuristic: collect, cluster and co-ordinate.

**Approach:** Students attended a 1-hour online workshop during their family medicine clerkship. Using a flipped classroom design, students watched a podcast, followed by facilitated small-group work.

**Evaluation:** Out of 132 final-year medical students, 102 participated in the evaluation. Students rated their confidence managing patients with multimorbidity, pre and post teaching on a Likert scale. Prior to teaching, 36% (n = 37) students rated their ability to manage a patient with multimorbidity as slightly confident. After teaching, 74.5% (76) students rated their ability to manage the same patient as fairly or completely confident. Prior to graduation students were surveyed to determine if they had applied the framework during clinical placements. Sixty-one students responded; 32 applied the heuristic during family medicine and in other clinical rotations such as paediatrics, obstetrics, emergency medicine and anaesthesia.

**Implications:** Specific instruction on managing consultations with patients experiencing multimorbidity during undergraduate medical education increased learner confidence caring for these patients. The heuristic was relevant and applied in disciplines outside family medicine. Students indicated that earlier teaching on this topic would have prepared them better for clinical placements.

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## Review

### BMC Health Serv Res

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. 2024 Aug 5;24(1):895.

doi: 10.1186/s12913-024-11351-y.

[Care models for individuals with chronic multimorbidity: lessons for low- and middle-income countries](#)

[Aklilu Endalamaw](#)<sup>1,2</sup>, [Anteneh Zewdie](#)<sup>3</sup>, [Eskinder Wolka](#)<sup>3</sup>, [Yibeltal Assefa](#)<sup>4</sup>

### Affiliations Expand

- PMID: 39103802
- PMCID: [PMC11302242](#)
- DOI: [10.1186/s12913-024-11351-y](#)

### Abstract

**Background:** Patients with multiple long-term conditions requires understanding the existing care models to address their complex and multifaceted health needs. However, current literature lacks a comprehensive overview of the essential components, impacts, challenges, and facilitators of these care models, prompting this scoping review.

**Methods:** A scoping review was conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-analysis Extension for Scoping Reviews guideline. Our search encompassed articles from PubMed, Web of Science, EMBASE, SCOPUS, and Google Scholar. The World Health Organization's health system framework was utilized to synthesis the findings. This framework comprises six building blocks (service delivery, health workforce, health information systems, access to essential medicines, financing, and leadership/governance) and eight key characteristics of good service delivery models (access, coverage, quality, safety, improved health, responsiveness, social and financial risk protection, and improved efficiency). Findings were synthesized qualitatively to identify components, impacts, barriers, and facilitators of care models.

**Results:** A care model represents various collective interventions in the healthcare delivery aimed at achieving desired outcomes. The names of these care models are derived from core activities or major responsibilities, involved healthcare teams,

diseases conditions, eligible clients, purposes, and care settings. Notable care models include the Integrated, Collaborative, Integrated-Collaborative, Guided, Nurse-led, Geriatric, and Chronic care models, as well as All-inclusive Care Model for the Elderly, IMPACT clinic, and Geriatric Patient-Aligned Care Teams (GeriPACT). Other care models (include Care Management Plus, Value Stream Mapping, Preventive Home Visits, Transition Care, Self-Management, and Care Coordination) have supplemented the main ones. Care models improved quality of care (such as access, patient-centeredness, timeliness, safety, efficiency), cost of care, and quality of life for patients that were facilitated by presence of shared mission, system and function integration, availability of resources, and supportive tools.

**Conclusions:** Care models were implemented for the purpose of enhancing quality of care, health outcomes, cost efficiency, and patient satisfaction by considering careful recruitment of eligible clients, appropriate selection of service delivery settings, and robust organizational arrangements involving leadership roles, healthcare teams, financial support, and health information systems. The distinct team compositions and their roles in service provision processes differentiate care models.

**Keywords:** Care models; Multimorbidity; Review.

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**Conflict of interest statement**

The authors declare no competing interests.

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- [1 figure](#)

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**Review**

**Geriatr Gerontol Int**

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. 2024 Aug 4.

doi: 10.1111/ggi.14949. Online ahead of print.

### [Senotherapy preserves resilience in aging](#)

[Takumi Mikawa](#)<sup>1,2</sup>, [Kazumichi Yoshida](#)<sup>3</sup>, [Hiroshi Kondoh](#)<sup>1</sup>

Affiliations Expand

- PMID: 39098000
- DOI: [10.1111/ggi.14949](#)

### Abstract

In aging societies, social and economic burdens of aging-related diseases are increasing significantly. Senotherapy, which targets aging by eliminating senescent cells (senolytics) or removing sources of chronic inflammation (senostatics), are proposed as novel strategies for aging-related diseases. Aged or frail people suffer a decline of tissue reserve capacity during aging. Resilience, which is much reduced in older people, is essential for recovery from diseases, stresses or crises. Impaired resilience is one of the reasons why aged people experience a gradual waning of their daily activity and an increase of multimorbidity. Calorie restriction results in senostatic alleviation of chronic inflammation, whereas senolytic drugs induce apoptosis of senescent cells, which exacerbate aging by excreting inflammatory factors. Thus, both senolytics and senostatics are expected to reduce sterile inflammation, originating from senescent cells. *Geriatr Gerontol Int* 2024; ••: •••••.

**Keywords:** resilience; senescence-associated secretor phenotype; senolysis; senostatics; senotherapy.

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BMJ Open

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. 2024 Aug 3;14(8):e082585.

doi: 10.1136/bmjopen-2023-082585.

[Association between maternal multimorbidity and neurodevelopment of offspring: a prospective birth cohort study from the Japan Environment and Children's Study](#)

[Takanobu Akagi<sup>1</sup>, Yasuaki Saijo<sup>2</sup>, Eiji Yoshioka<sup>1</sup>, Yukihiro Sato<sup>1</sup>, Kentaro Nakanishi<sup>3</sup>, Yasuhito Kato<sup>3</sup>, Ken Nagaya<sup>4</sup>, Satoru Takahashi<sup>5</sup>, Yoshiya Ito<sup>6</sup>, Hiroyoshi Iwata<sup>7</sup>, Takeshi Yamaguchi<sup>7</sup>, Chihiro Miyashita<sup>7</sup>, Sachiko Ito<sup>7</sup>, Reiko Kishi<sup>7</sup>; Japan Environment and Children's Study group; JECS](#)

Collaborators, Affiliations Expand

- PMID: 39097305
- DOI: [10.1136/bmjopen-2023-082585](https://doi.org/10.1136/bmjopen-2023-082585)

Free article

Abstract

**Objectives:** To investigate the association between multimorbidity during pregnancy and neurodevelopmental delay in offspring using data from a Japanese nationwide birth cohort study.

**Design:** This study was a prospective birth cohort study.

**Setting:** This study population included 104 059 fetal records who participated in The Japan Environment and Children's Study from 2011 to 2014.

**Participants:** Pregnant women whose children had undergone developmental testing were included in this analysis.

**Primary and secondary outcome measures:** Neurodevelopment of offspring was assessed using the Japanese version of the Ages and Stages Questionnaire, third edition, comprising five developmental domains. The number of comorbidities among the pregnant women was categorised as zero, single disease or multimorbidity (two or more diseases). Maternal chronic conditions included in

multimorbidity were defined as conditions with high prevalence among women of reproductive age. A multivariate logistic regression analysis was conducted to examine the association between multimorbidity in pregnant women and offspring development.

**Results:** Pregnant women with multimorbidity, single disease and no disease accounted for 3.6%, 30.6% and 65.8%, respectively. The ORs for neurodevelopmental impairment during the follow-up period were similar for infants of mothers with no disease comorbidity and those with a single disease comorbidity. However, the ORs for neurodevelopmental impairment were significantly higher for children born to mothers with multimorbidity compared with those born to healthy mothers.

**Conclusion:** An association was observed between the number of comorbidities in pregnant women and developmental delay in offspring. Multimorbidity in pregnant women may be associated with neurodevelopmental delay in their offspring. Further research is required in this regard in many other regions of the world.

**Keywords:** Maternal medicine; Multimorbidity; PUBLIC HEALTH; Paediatric neurology; Pregnant Women.

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**Conflict of interest statement**

**Competing interests:** None declared.

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**Comparative Study**

**Am J Epidemiol**

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. 2024 Aug 5;193(8):1146-1154.

doi: 10.1093/aje/kwae031.

## [Characterizing multimorbidity in ALIVE: comparing single and ensemble clustering methods](#)

[Jacqueline E Rudolph](#)<sup>1</sup>, [Bryan Lau](#)<sup>1</sup>, [Becky L Genberg](#)<sup>1</sup>, [Jing Sun](#)<sup>1</sup>, [Gregory D Kirk](#)<sup>1,2</sup>, [Shruti H Mehta](#)<sup>1</sup>

### Affiliations Expand

- PMID: 38576181
- PMCID: PMC11299029 (available on 2025-04-03)
- DOI: [10.1093/aje/kwae031](#)

### Abstract

Multimorbidity, defined as having 2 or more chronic conditions, is a growing public health concern, but research in this area is complicated by the fact that multimorbidity is a highly heterogeneous outcome. Individuals in a sample may have a differing number and varied combinations of conditions. Clustering methods, such as unsupervised machine learning algorithms, may allow us to tease out the unique multimorbidity phenotypes. However, many clustering methods exist, and choosing which to use is challenging because we do not know the true underlying clusters. Here, we demonstrate the use of 3 individual algorithms (partition around medoids, hierarchical clustering, and probabilistic clustering) and a clustering ensemble approach (which pools different clustering approaches) to identify multimorbidity clusters in the AIDS Linked to the Intravenous Experience cohort study. We show how the clusters can be compared based on cluster quality, interpretability, and predictive ability. In practice, it is critical to compare the clustering results from multiple algorithms and to choose the approach that performs best in the domain(s) that aligns with plans to use the clusters in future analyses.

**Keywords:** clustering; ensemble clustering; hierarchical clustering; multimorbidity; partition around medoids; probabilistic clustering; unsupervised machine learning.

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### Conflict of interest statement

The authors declare no conflicts of interest.

- [35 references](#)

## Supplementary info

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

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Ann Am Thorac Soc

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. 2024 Aug 12.

doi: 10.1513/AnnalsATS.202402-122OC. Online ahead of print.

## [Chronic Airflow Limitation, Emphysema and Impaired Diffusing Capacity in Relation to Smoking Habits in a Swedish Middle-Aged Population](#)

[Anders Blomberg](#)<sup>1</sup>, [Kjell Torén](#)<sup>2,3</sup>, [Per Liv](#)<sup>4</sup>, [Gabriel Granåsen](#)<sup>4</sup>, [Anders Andersson](#)<sup>5,6</sup>, [Annelie Behndig](#)<sup>4</sup>, [Göran Bergström](#)<sup>7,8</sup>, [John Brandberg](#)<sup>9,10</sup>, [Kenneth Caidahl](#)<sup>11,12,8</sup>, [Kerstin Cederlund](#)<sup>13</sup>, [Arne Egesten](#)<sup>14</sup>, [Magnus Ekström](#)<sup>15</sup>, [Maria J Eriksson](#)<sup>16,12</sup>, [Emil Hagström](#)<sup>17,18</sup>, [Christer Janson](#)<sup>19</sup>, [Tomas Jernberg](#)<sup>20</sup>, [David Kylhammar](#)<sup>21</sup>, [Lars Lind](#)<sup>22</sup>, [Anne Lindberg](#)<sup>4</sup>, [Eva Lindberg](#)<sup>23</sup>, [Claes-Göran Löfdahl](#)<sup>15</sup>, [Andrei Malinowski](#)<sup>24</sup>, [Maria Mannila](#)<sup>25</sup>, [Lars T Nilsson](#)<sup>4</sup>, [Anna-Carin Olin](#)<sup>2</sup>, [Anders Persson](#)<sup>26,27,28</sup>, [Hans Lennart Persson](#)<sup>29</sup>, [Annika Rosengren](#)<sup>7,30</sup>, [Johan Sundström](#)<sup>31,32</sup>, [Eva Swahn](#)<sup>33</sup>, [Stefan Söderberg](#)<sup>4</sup>, [Jenny Vikgren](#)<sup>9,10</sup>, [Per Wollmer](#)<sup>34</sup>, [Carl Johan Östgren](#)<sup>35,36</sup>, [Jan Engvall](#)<sup>37,36</sup>, [C Magnus Sköld](#)<sup>38,39</sup>

Affiliations Expand

- PMID: 39133529
- DOI: [10.1513/AnnalsATS.202402-122OC](https://doi.org/10.1513/AnnalsATS.202402-122OC)

Abstract

**Rationale:** Chronic obstructive pulmonary disease (COPD) includes respiratory symptoms and chronic airflow limitation (CAL). In some cases, emphysema and impaired diffusing capacity for carbon monoxide (DLCO) are present, but characteristics and symptoms vary with smoking exposure.

**Objectives:** To study the prevalence of CAL, emphysema and impaired DLCO in relation to smoking and respiratory symptoms in a middle-aged population.

**Methods:** We investigated 28,746 randomly invited individuals (52% women) aged 50-64 years across six Swedish sites. We performed spirometry, DLCO, high-resolution computed tomography (HRCT) and asked for smoking habits and respiratory symptoms. CAL was defined as post-bronchodilator forced expiratory volume in 1 second divided by forced expiratory volume (FEV1/FVC)<0.7.

**Results:** The overall prevalence was for CAL 8.8%, for impaired DLCO (DLCO<LLN) 5.7% and for emphysema 8.8%, with a higher prevalence in current smokers than in ex-smokers and never-smokers. The proportion of never-smokers among those with CAL, emphysema and impaired DLCO was 32%, 19% and 31% respectively. Regardless of smoking habits, the prevalence of respiratory symptoms was higher among people with CAL and impaired DLCO, compared to those with normal lung function. Asthma prevalence in never-smokers with CAL was 14%. In this group, asthma associated with lower FEV1 and more respiratory symptoms.

**Conclusions:** In this large population-based study of middle-aged people, CAL and impaired DLCO were associated with common respiratory symptoms. Self-reported asthma was not associated with CAL in never-smokers. Our findings suggest that CAL in never-smokers signifies a separate clinical phenotype that may be monitored and, possibly, treated differently from smoking-related COPD. This article is open access and distributed under the terms of the Creative Commons Attribution 4.0 International License (<https://creativecommons.org/licenses/by/4.0/>).

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J Asthma

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. 2024 Aug 12:1-12.

doi: 10.1080/02770903.2024.2391441. Online ahead of print.

[Efficacy and Safety of Subcutaneous and Sublingual Allergen Immunotherapy in the Treatment of Asthma in Children: A Systematic Review and Meta-Analysis](#)

[Wenwen Yang<sup>1</sup>, Weijie Wang<sup>1</sup>, Yishu Ji<sup>1</sup>, Huisong Pan<sup>1</sup>](#)

## Affiliations Expand

- PMID: 39132908
- DOI: [10.1080/02770903.2024.2391441](https://doi.org/10.1080/02770903.2024.2391441)

## Abstract

**Objective:** Asthma is a common chronic condition in children globally. Allergen-specific immunotherapy, such as subcutaneous (SCIT) and sublingual (SLIT) therapies, are promising by increasing allergen tolerance. This meta-analysis compares the efficacy and safety of SLIT and SCIT in pediatric asthma.

**Methods:** We searched PubMed, Cochrane Library, and Embase for randomized controlled trials and case-control studies comparing SLIT and SCIT in asthmatic children. Meta-analysis was conducted using random-effects models with calculations via R software version 4.3.2 and RevMan version 5.4. Study quality and bias risk were assessed using the NOS and Cochrane Risk of Bias Tool.

**Results:** The literature search yielded a total of 1787 records, with 7 studies meeting the inclusion criteria after screening and assessments. There was no significant difference in the Total Asthma Symptoms Score (TASS) between SLIT and SCIT (mean difference -0.05 [95% CI: -0.21; 0.10]). However, asthma improvement rates were higher in the SLIT group (risk ratio 0.77 [95% CI: 0.64; 0.93]). FEV1 improvement showed no significant difference (mean difference -1.60 [95% CI: -6.27; 3.08]). Adverse events were similar between the treatments (risk ratio 0.56 [95% CI: 0.11; 2.82]).

**Conclusions:** SLIT and SCIT were generally similarly effective and safe for treating pediatric asthma. SLIT may be preferred due to its non-invasive administration. More research is needed on long-term effects and tailored treatment approaches.

**Keywords:** Allergen-Specific Immunotherapy; Childhood Asthma; Meta-Analysis; Subcutaneous Immunotherapy; Sublingual Immunotherapy.

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Int J Chron Obstruct Pulmon Dis

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. 2024 Aug 7:19:1813-1818.

doi: 10.2147/COPD.S468887. eCollection 2024.

## [Real-World Effectiveness of Benralizumab Among Patients with Asthma and Concomitant Chronic Obstructive Pulmonary Disease](#)

[Donna D Carstens](#)<sup>1</sup>, [Diego J Maselli](#)<sup>2</sup>, [Erin E Cook](#)<sup>3</sup>, [Fan Mu](#)<sup>3</sup>, [Jingyi Chen](#)<sup>3</sup>, [Danni Yang](#)<sup>3</sup>, [Jessica Karacz DeMartino](#)<sup>1</sup>, [Yen Chung](#)<sup>1</sup>

### Affiliations Expand

- PMID: 39129964
- PMCID: [PMC11317043](#)
- DOI: [10.2147/COPD.S468887](#)

*No abstract available*

### Conflict of interest statement

DC, JKD, and YC are employees and shareholders of AstraZeneca, which funded the development and conduct of this study and manuscript. DY, EEC, FM, and JC are employees of Analysis Group, Inc., a consulting company that has provided paid consulting services to AstraZeneca, which funded the development and conduct of this study and manuscript. DJM received consultant/speaker fees from AstraZeneca, GSK, Amgen, Sanofi/Regeneron. The authors report no other conflicts of interest in this work.

### Supplementary info

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Respirology

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. 2024 Aug 11.

doi: 10.1111/resp.14815. Online ahead of print.

[A snapshot of SABA co-prescribing with ICS-formoterol maintenance and reliever therapy](#)

[Rebekah Lamb](#)<sup>1</sup>, [Kyley Kerse](#)<sup>1</sup>, [Heidi Kristono](#)<sup>1</sup>, [Karen Oldfield](#)<sup>1</sup>, [Richard Beasley](#)<sup>1,2</sup>

Affiliations Expand

- PMID: 39129181

- DOI: [10.1111/resp.14815](#)

*No abstract available*

Keywords: anti-inflammatory reliever; asthma; budesonide/formoterol; guideline; implementation.

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. 2024 Aug 11.

doi: 10.1111/cga.12581. Online ahead of print.

## [Montelukast use in pregnancy: A systematic review and meta-analysis of maternal and fetal outcomes in asthma treatment](#)

[Areeba Fareed](#)<sup>1</sup>, [Dima Siblini](#)<sup>2</sup>, [Rayyan Vaid](#)<sup>1</sup>, [Hadi Farhat](#)<sup>2</sup>, [Ahmad Rida](#)<sup>2</sup>, [Abdulrahmon Moradeyo](#)<sup>3</sup>, [Muhammad Ahsan Khan](#)<sup>4</sup>

Affiliations Expand

- PMID: 39129058
- DOI: [10.1111/cga.12581](#)

Abstract

This systematic review and meta-analysis evaluated the safety of montelukast in treating asthma during pregnancy, focusing on maternal and fetal outcomes such as congenital anomalies (CA), preterm delivery, low birthweight, spontaneous abortion, gestational diabetes mellitus, and preeclampsia. A comprehensive literature search was conducted in Google Scholar, PubMed, and the Cochrane Library databases from inception until April 30, 2024. The eligible studies assessed the safety of montelukast for asthma treatment during pregnancy. The review suggests that montelukast use during pregnancy may not significantly increase the risk of major CA. The pooled results yielded risk ratio (RR) for CA was 1.13 [95% CI (0.74, 1.73),  $p = 0.56$ ,  $I^2 = 0\%$ ]. Montelukast may be associated with preterm delivery and a low birthweight odds ratio (OR) of 1.82 [95% CI (1.35, 2.45),  $p < 0.001$ ,  $I^2 = 0\%$ ]. No significant risks were found concerning neurodevelopmental outcomes. The associations with spontaneous abortion were inconclusive [OR = 1.03, 95% CI (0.72, 1.5),  $p = 0.86$ ,  $I^2 = 73\%$ ], highlighting the need for further research. This comprehensive review underscores the importance of further investigating the safety profile of montelukast during pregnancy. While the overall findings indicate a relatively favorable safety profile, especially regarding major CA, careful consideration is needed for the potential risks of preterm delivery and low birthweight.

**Keywords:** asthma; congenital anomalies; fetal outcomes; maternal outcomes; montelukast.

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- [31 references](#)

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Lancet Respir Med

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. 2024 Aug 8:S2213-2600(24)00242-X.

doi: 10.1016/S2213-2600(24)00242-X. Online ahead of print.

[Patient-reported outcomes: missing in asthma remission](#)

[Amy Hai Yan Chan](#)<sup>1</sup>, [Paul Leong](#)<sup>2</sup>, [John Politis](#)<sup>2</sup>, [Vanessa M McDonald](#)<sup>3</sup>, [Philip Bardin](#)<sup>2</sup>

Affiliations Expand

- PMID: 39128472
- DOI: [10.1016/S2213-2600\(24\)00242-X](#)

*No abstract available*

Conflict of interest statement

AHYC receives research grants from the Health Research Council of New Zealand, Asthma UK, the University of Auckland, WHO, Life AI, the MedTech CMDT fund, and Trudell Medical International, all paid to her institution. She previously held the Robert Irwin Postdoctoral Fellowship and is the current recipient of the Auckland Medical Research Foundation Senior Research Fellowship. AHYC receives consultancy fees from AcademyeX, Spoonful of Sugar, and Active Healthcare; receives travel support from AstraZeneca and the Asthma and Respiratory Foundation of New Zealand; and was previously on the Board of Asthma New Zealand. She has received speaker honoraria from the American Academy of Allergy, Asthma, and Immunology; the Asian Pacific Society of Respiriology; and the European Respiratory Society. She is a member of Pharmacy Council New Zealand Respiratory Effectiveness Group, the scientific advisory board for Asthma Respiratory Foundation New Zealand, the Auckland Medical Research Foundation medical committee; she is the global lead for the International Pharmaceutical Federation; is research lead for the Commonwealth Pharmacists Association; is an international member of the Pharmacy Respiratory Task Force; and is working group lead for the European Respiratory Society Clinical Research Collaboration CONNECT. PL has received honoraria from GSK, AstraZeneca, and Chiesi. VMM has received honoraria for advisory boards and educational lectures from GSK,

AstraZeneca, Menarini, and Boehringer Ingelheim; has received research funds from the Australian National Health and Medical Research Council, the Medical Research Futures Fund, and GSK; and is board director of the Thoracic Society of Australia and New Zealand. PB has been on advisory boards and provided educational lectures for GSK, AstraZeneca, Sanofi, and Chiesi. JP declares no competing interests.

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J Allergy Clin Immunol Pract

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. 2024 Aug 8:S2213-2198(24)00827-4.

doi: 10.1016/j.jaip.2024.08.011. Online ahead of print.

[Severe Eosinophilic Asthma or Eosinophilic Granulomatosis with Polyangitis: potential biomarkers for novel diagnostic strategies](#)

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Affiliations Expand

- PMID: 39127105
- DOI: [10.1016/j.jaip.2024.08.011](https://doi.org/10.1016/j.jaip.2024.08.011)

Abstract

**Background:** Severe Eosinophilic Asthma (SEA) may be the prodromal phase of Eosinophilic Granulomatosis with Polyangiitis (EGPA). Nevertheless, few studies have tried to recognize EGPA in the early stages of the disease.

**Objectives:** To identify a panel of clinical and biological markers to detect which severe asthmatic patient might be considered in a prodromal phase of EGPA and crafting a strategy for diagnostic decision-making.

**Methods:** 30 patients with EGPA and 49 with SEA were enrolled. A complete pulmonary, ear, nose and Throat (ENT) and rheumatologic assessment were made. Blood (eosinophil count, eosinophilic cationic protein-ECP, IL5, IL4, total-IgE, IgG4, anti-neutrophil cytoplasmic antibody (ANCA), sputum (eosinophils count, periostin, IL8 and GMCSF) and nasal smear (eosinophilia) biomarkers were assessed. Asthma Control Test, Short Form-36, SinoNasalOutcome Test-22, and Asthma Quality of Life Questionnaire were also used.

**Results:** SEA patients had poorer asthma control ( $p<0.001$ ) and higher level of sputum eosinophils ( $p<0.002$ ) while EGPA patients reported higher levels of blood eosinophils in the past. Sputum GMCSF was the only biomarker significantly increased in EGPA patients compared with SEA ( $p<0.0001$ ). Among SEA patients, those with some suggestive but not diagnostic criteria of EGPA, particularly tissue eosinophilic infiltrates, presented higher levels of sputum GMCSF ( $p<0.0005$ ), blood and sputum eosinophils ( $p<0.0006$ ,  $p<0.011$ ) in comparison with the other patients.

**Conclusion:** Sputum GMCSF and eosinophils might be useful biomarkers to support early diagnosis and treatment choices in SEA patients, suspected of having EGPA.

**Keywords:** Asthma; Biologics; Biomarkers; Cytology; EGPA; Eosinophils; FeNO; GMCSF; Polyposis; Sputum.

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. 2024 Aug 8:S2213-2198(24)00824-9.

doi: 10.1016/j.jaip.2024.08.008. Online ahead of print.

[Oral and Inhaled Corticosteroid Dose Reductions With Tezepelumab Versus Placebo in Patients With Severe, Uncontrolled Asthma From DESTINATION](#)

[Michael E Wechsler](#)<sup>1</sup>, [Daiana Stolz](#)<sup>2</sup>, [Njira L Lugogo](#)<sup>3</sup>, [Scott Caveney](#)<sup>4</sup>, [Gun Almqvist](#)<sup>5</sup>, [Artur Bednarczyk](#)<sup>6</sup>, [Ales Kotalik](#)<sup>7</sup>, [Shradha Chandarana](#)<sup>8</sup>, [Christopher S Ambrose](#)<sup>9</sup>

#### Affiliations Expand

- PMID: 39127103
- DOI: [10.1016/j.jaip.2024.08.008](https://doi.org/10.1016/j.jaip.2024.08.008)

#### Abstract

The Global Initiative for Asthma recommends gradually stepping down treatments to the lowest oral/inhaled corticosteroid doses that control symptoms and exacerbations. Tezepelumab treatment enabled reductions in oral/inhaled corticosteroid doses versus placebo, while preserving asthma symptom control and lung function.

Keywords: ICS; OCS; OCS sparing; TSLP; asthma; thymic stromal lymphopoietin.

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#### J Allergy Clin Immunol Pract

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. 2024 Aug 8:S2213-2198(24)00826-2.

doi: 10.1016/j.jaip.2024.08.010. Online ahead of print.

#### [Dupilumab improves pediatric type 2 asthma outcomes independent of patient baseline characteristics](#)

[Jorge F Maspero](#)<sup>1</sup>, [Alessandro G Fiocchi](#)<sup>2</sup>, [Antoine Deschildre](#)<sup>3</sup>, [Leonard B Bacharier](#)<sup>4</sup>, [Arman Altincatal](#)<sup>5</sup>, [Elizabeth Laws](#)<sup>6</sup>, [David J Lederer](#)<sup>7</sup>, [Bolanle Akinlade](#)<sup>7</sup>, [Megan Hardin](#)<sup>5</sup>

## Affiliations Expand

- PMID: 39127101
- DOI: [10.1016/j.jaip.2024.08.010](https://doi.org/10.1016/j.jaip.2024.08.010)

## Abstract

Dupilumab, a biological therapy that blocks the shared receptor component for interleukins-4/13, reduced exacerbations and improved lung function in children with uncontrolled moderate-to-severe type 2 asthma independent of most baseline patient and asthma characteristics.

**Keywords:** Dupilumab; anti–interleukin-13; anti–interleukin-4; asthma exacerbation; demographics; disease characteristics; lung function; pediatric asthma; type 2 inflammation.

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## Review

## J Clin Med

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. 2024 Aug 5;13(15):4558.

doi: 10.3390/jcm13154558.

## [Exercise-Induced Bronchoconstriction in Children: State of the Art from Diagnosis to Treatment](#)

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## Affiliations Expand

- PMID: 39124824
- PMCID: [PMC11312884](#)
- DOI: [10.3390/jcm13154558](#)

## Abstract

Exercise-induced bronchoconstriction (EIB) is a common clinical entity in people with asthma. EIB is characterized by postexercise airway obstruction that results in symptoms such as coughing, dyspnea, wheezing, chest tightness, and increased fatigue. The underlying mechanism of EIB is not completely understood. "Osmotic theory" and "thermal or vascular theory" have been proposed. Initial assessment must include a specific work-up to exclude alternative diagnoses like exercise-induced laryngeal obstruction (EILO), cardiac disease, or physical deconditioning. Detailed medical history and clinical examination must be followed by basal spirometry and exercise challenge test. The standardized treadmill running (TR) test, a controlled and standardized method to assess bronchial response to exercise, is the most adopted exercise challenge test for children aged at least 8 years. In the TR test, the goal is to reach the target heart rate in a short period and maintain it for at least 6 min. The test is then followed by spirometry at specific time points (5, 10, 15, and 30 min after exercise). In addition, bronchoprovocation tests like dry air hyperpnea (exercise and eucapnic voluntary hyperpnea) or osmotic aerosols (inhaled mannitol) can be considered when the diagnosis is uncertain. Treatment options include both pharmacological and behavioral approaches. Considering medications, the use of short-acting beta-agonists (SABA) just before exercise is the commonest option strategy, but daily inhaled corticosteroids (ICS) can also be considered, especially when EIB is not controlled with SABA only or when the patients practice physical activity very often. Among the behavioral approaches, warm-up before exercise, breathing through the nose or face mask, and avoiding polluted environments are all recommended strategies to reduce EIB risk. This review summarizes the latest evidence published over the last 10 years on the pathogenesis, diagnosis using spirometry and indirect bronchoprovocation tests, and treatment strategies, including SABA and ICS, of EIB. A specific focus has been placed on EIB management in young athletes, since this condition can not only prevent them from practicing regular physical activity but also competitive sports.

**Keywords:** EIB; EILO; asthma; athletes; children; deconditioning; exercise induced asthma; exercise induced bronchoconstriction; vocal cord dysfunction.

## Conflict of interest statement

The authors declare no conflicts of interest.

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

## Supplementary info

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Expert Rev Respir Med

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. 2024 Aug 9.

doi: 10.1080/17476348.2024.2390987. Online ahead of print.

[Imagining the severe asthma decision trees of the future](#)

[Arnaud Bourdin](#)<sup>1</sup>, [Phil Bardin](#)<sup>2</sup>, [Pascal Chanez](#)<sup>3 4</sup>

Affiliations Expand

- PMID: 39120156
- DOI: [10.1080/17476348.2024.2390987](https://doi.org/10.1080/17476348.2024.2390987)

Abstract

**Introduction:** There are no validated decision-making algorithms concerning severe asthma (SA) management. Future risks are crucial factors and can be derived from SA trajectories.

**Areas covered:** The future severe asthma-decision trees should revisit current knowledges and gaps. A focused literature search has been conducted.

**Expert opinion:** Asthma severity is currently defined *a priori* thereby precluding a role for early interventions aiming to prevent outcomes such as exacerbations (systemic corticosteroids exposure) and lung function decline. Asthma 'at-risk' might represent the ultimate paradigm but merits longitudinal studies considering modern interventions. Real exacerbations, severe airway hyperresponsiveness, excessive T2 related biomarkers, noxious environments and patient behaviors,

harms of OCS and high doses inhaled corticosteroids (ICS) and low adherence-to-effectiveness ratios of ICS-containing inhalers are predictors of future risks. New tools such as imaging, genetic and epigenetic signatures should be used. Logical and numerical artificial intelligence may be used to generate a consistent risk score. A pragmatic definition of response to treatments will allow development of a validated and applicable algorithm. Biologics have the best potential to minimize the risks, but cost remains an issue. We propose a simplified six-step algorithm for decision making that is ultimately aiming to achieve asthma remission.

Keywords: Severe asthma; biomarkers; imaging; prediction.

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Allergy Asthma Clin Immunol

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. 2024 Aug 8;20(1):45.

doi: 10.1186/s13223-024-00899-3.

[Focused allergic rhinitis practice parameter for Canada](#)

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Affiliations Expand

- PMID: 39118164
- PMCID: [PMC11311964](#)
- DOI: [10.1186/s13223-024-00899-3](#)

Abstract

Allergic rhinitis (AR) is a prevalent disease in Canada that affects both children and adults. Several guidelines for the management of AR have been published by professional allergy societies worldwide. However, there are regional differences in the clinical management of AR, and regulatory approval of some AR pharmacotherapies varies among countries. Thus, six research questions specific to the treatment of AR in Canada were identified for this focused practice parameter. Reviews of the literature published since 2016 were conducted to obtain evidence-based support for the responses of the Work Group to each research question. In response to research question 1 "In patients with symptoms indicative of AR, is serum-specific IgE sufficient to identify candidates for immunotherapy or is a skin prick test mandatory?" the Work Group concluded that either sIgE testing or skin prick test are acceptable for diagnosing AR and guiding immunotherapy. In response to research question 2 "When taking into account the preferences of the patient and the prescriber (stakeholder engagement) should second-generation oral antihistamine (OAH) or intranasal corticosteroid (INCS) be first line?" the Work Group concluded that existing guidelines generally agree on the use of INCS as a first-line therapy used for AR, however, patient and provider preferences and considerations can easily shift the first choice to a second-generation OAH. In response to research question 3 "Is a combination intranasal antihistamine (INAH)/INCS formulation superior to INCS plus OAH? Do they become equivalent after prolonged use?" the Work Group concluded that that the combination INAH/INCS is superior to an INCS plus OAH. However, there was insufficient evidence to answer the second question. In response to research question 4 "Do leukotriene receptor antagonists (LTRA) have a greater benefit than OAH in AR for some symptoms to justify a therapeutic trial in those who cannot tolerate INCS?" the Work Group concluded that LTRAs have inferior, or at best equivalent, daytime or overall symptom control compared with OAH, but LTRAs may improve nighttime symptom control and provide benefits in patients with AR and concomitant asthma. In response to research question 5 "Should sublingual immunotherapy (SLIT) tablets be considered first-line immunotherapeutic options over subcutaneous immunotherapy (SCIT) based on the evidence of efficacy?" the Work Group concluded that the choice of SLIT or SCIT cannot be made on efficacy alone, and differences in other factors outweigh any differences in efficacy. In response to research question 6 "Based on efficacy data, should ALL patients seen by an allergist be offered SLIT or SCIT as a treatment option?" the Work Group concluded that the efficacy data suggests that SLIT or SCIT should be used broadly in patients with AR, but other clinical concerns also need to be taken into consideration.

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#### Conflict of interest statement

A.K. Ellis has participated in advisory boards for ALK-Abello, AstraZeneca, Bausch Health, LEO Pharma, Miravo, Merck, Novartis, has been a speaker for ALK-Abello, AstraZeneca, Bausch, Miravo, Medexus, Mylan, Novartis, Pfizer, Sanofi, StallergenesGreer and Regeneron. Her institution has received research grants from ALK Abello, Aralez, AstraZeneca, Bayer LLC, Medexus, Novartis, Sanofi and Regeneron. She has also served as an independent consultant to Bayer LLC, Pharming, and Regeneron. V. Cook has received honoraria for speaking engagements for Miravo/Aralez, Pfizer, and ALK and served on advisory boards or speakers' bureaus for Sanofi and ALK. P. Keith Paul has participated in advisory boards for ALK-Abello, AstraZeneca, Bausch Health, CSL Behring,

GlaxoSmithKline, LEO Pharma, Miravo, Merck, Novartis, Sanofi, Takeda and Valeo. He has been a speaker for ALK-Abello, Bausch, GlaxoSmithKline, Medexus, Novartis, and Sanofi. His institution has received research grants from CSL Behring and Takeda. He has also served as a consultant to Bayer LLC, CADTH, and the Canadian Pharmacists Association. S.R. Mace has served on a speakers' bureau for Miravo. W. Moote has nothing to disclose. A. O'Keefe reports research funding from Sanofi, has served as a speaker for Novartis, ALK, Innomar, Medexus, GlaxoSmithKline, Sanofi, and has served as a consultant for ALK, Sanofi, Takeda and Astra Zeneca. J. Quirt has participated in advisory boards for Aralez and Sanofi. L. Rosenfield has nothing to disclose. P. Small has nothing to disclose. W. Watson has nothing to disclose.

All recommendations in this document are evidence based and concluded on by all authors equally as consensus-based recommendations.

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

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Editorial

Eur Respir J

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. 2024 Aug 8;64(2):2401300.

doi: 10.1183/13993003.01300-2024. Print 2024 Aug.

[The burden of zoster in asthma: what is left to learn?](#)

[Chloe Bloom<sup>1</sup>](#)

Affiliations Expand

- PMID: 39117424

- DOI: [10.1183/13993003.01300-2024](https://doi.org/10.1183/13993003.01300-2024)

*No abstract available*

Conflict of interest statement

Conflict of interest: C. Bloom reports grants from NIHR (advanced fellowship) and Asthma + Lung UK.

Comment on

- [Global herpes zoster burden in adults with asthma: a systematic review and meta-analysis.](#)

Mortimer KJ, Cruz AA, Sepúlveda-Pachón IT, Jorga A, Vroiling H, Williams C. *Eur Respir J*. 2024 Aug 8;64(2):2400462. doi: 10.1183/13993003.00462-2024. Print 2024 Aug. PMID: 38901886 Free PMC article. Review.

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Allergy

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. 2024 Aug 8.

doi: 10.1111/all.16267. Online ahead of print.

[Mepolizumab depletes inflammatory but preserves homeostatic eosinophils in severe asthma](#)

[Michael Fricker](#)<sup>1,2</sup>, [John Harrington](#)<sup>2,3</sup>, [Sarah A Hiles](#)<sup>2,4</sup>, [Peter G Gibson](#)<sup>1,2,3</sup>

Affiliations [Expand](#)

- PMID: 39115364

- DOI: [10.1111/all.16267](https://doi.org/10.1111/all.16267)

## Abstract

**Background:** Eosinophils are key therapeutic targets in severe asthma that are suppressed by IL5 (mepolizumab) and IL5 receptor (benralizumab) blockade. The effect of IL5 pathway biologics on recently described homeostatic (hEOs) and inflammatory (iEOs) eosinophil subsets is unknown. We aimed to determine the relative impact of mepolizumab and benralizumab treatment on eosinophil subset and phenotype, and explore clinical associations of eosinophil subsets with severe asthma characteristics and treatment response.

**Methods:** We performed a cross-sectional observational study of severe asthma (eosinophilic n = 32, non-eosinophilic n = 23, mepolizumab-treated n = 25), with longitudinal follow-up of 30 eosinophilic participants at two timepoints (4-24 weeks, >24 weeks) post-commencement of mepolizumab (n = 20) or benralizumab (n = 10). Blood hEOs and iEOs were measured by flow cytometry assessment of surface CD62L protein.

**Results:** iEO proportion was significantly lower in mepolizumab-treated participants in both the cross-sectional and longitudinal study. Mepolizumab and benralizumab depleted iEOs to a similar extent, however a significantly greater number of hEOs remained in mepolizumab participants at follow-up. Greater iEO proportion correlated with poorer asthma control in eosinophilic but not non-eosinophilic asthma. Higher residual iEO proportion correlated with poorer asthma control in mepolizumab-treated individuals. Reduced blood eosinophil viability was observed in around half of mepolizumab-treated participants, which was associated with significantly better asthma control and spirometry.

**Conclusions:** Mepolizumab depletes iEOs and reduces circulating eosinophil viability in severe asthma but preserves a residual population of circulatory hEOs. In contrast benralizumab depleted both iEOs and hEOs. Higher iEO abundance and eosinophil viability are associated with poorer clinical outcomes following mepolizumab-treatment. Monitoring circulating eosinophil phenotype and viability may be useful to predict biologic treatment response in severe asthma.

**Keywords:** asthma; benralizumab; eosinophil; mepolizumab; subset.

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. 2024 Aug 7;25(1):300.

doi: 10.1186/s12931-024-02921-z.

[Therapeutic effect of long-acting muscarinic antagonist for treating uncontrolled asthma assessed using impulse oscillometry](#)

[Hiroyuki Sugawara](#)<sup>1,2</sup>, [Atsushi Saito](#)<sup>3</sup>, [Saori Yokoyama](#)<sup>1,2</sup>, [Hirofumi Chiba](#)<sup>1</sup>

Affiliations Expand

- PMID: 39113044
- PMCID: [PMC11308707](#)
- DOI: [10.1186/s12931-024-02921-z](#)

Abstract

**Background:** In recent years, the incorporation of LAMAs into asthma therapy has been expected to enhance symptom control. However, a significant number of patients with asthma continue to experience poorly managed symptoms. There have been limited investigations on LAMA-induced airway alterations in asthma treatment employing IOS. In this study, we administered a LAMA to patients with poorly controlled asthma, evaluated clinical responses and respiratory function, and investigated airway changes facilitated by LAMA treatments using the IOS.

**Methods:** Of a total of 1282 consecutive patients with asthma, 118 exhibited uncontrolled symptoms. Among them, 42 switched their treatment to high-dose fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) (ICS/LABA/LAMA). The patients were then assessed using AHQ-33 or LCQ and ACT. Spirometry parameters (such as FEV<sub>1</sub> or MMEF) and IOS parameters (such as R20 or AX) were measured and compared before and after exacerbations and the addition of LAMA.

**Results:** Of the 42 patients, 17 who switched to FF/UMEC/VI caused by dyspnea exhibited decreased pulmonary function between period 1 and baseline, followed by an increase in pulmonary function between baseline and period 2. Significant

differences were observed in IOS parameters such as R20, R5-R20, Fres, or AX between period 1 and baseline as well as between baseline and period 2. Among the patients who switched to inhaler due to cough, 25 were classified as responders (n = 17) and nonresponders (n = 8) based on treatment outcomes. Among nonresponders, there were no significant differences in spirometry parameters such as FEV<sub>1</sub> or PEF and IOS parameters such as R20 or AX between period 1 and baseline. However, among responders, significant differences were observed in all IOS parameters, though not in most spirometry parameters, between period 1 and baseline. Furthermore, significant differences were noted between baseline and period 2 in terms of FEV<sub>1</sub>, %MMEF, %PEF, and all IOS parameters.

**Conclusion:** ICS/LABA/LAMA demonstrates superiority over ICS/LABA in improving symptoms and lung function, which is primarily attributed to the addition of LAMA. Additionally, IOS revealed the effectiveness of LAMA across all airway segments, particularly in the periphery. Hence, LAMA can be effective against various asthma phenotypes characterized by airway inflammation, even in real-world cases.

**Keywords:** Bronchial asthma; Impulse oscillometry system (IOS); Long-acting muscarinic antagonist (LAMA); Pulmonary function test.

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**Conflict of interest statement**

The authors declare no competing interests.

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- [5 figures](#)

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**Int Forum Allergy Rhinol**

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. 2024 Aug 7.

doi: 10.1002/alr.23426. Online ahead of print.

[Nasal virus infection induces asthma exacerbation through B-cell-dependent recruitment of inflammatory monocytes](#)

[Kody A Waldstein](#)<sup>1</sup>, [Arman Issimov](#)<sup>1</sup>, [Maria Ganama](#)<sup>1</sup>, [Valerie Jinge](#)<sup>1,2</sup>, [Stephen Tilley](#)<sup>3</sup>, [Xiaoyang Hua](#)<sup>1,2</sup>

Affiliations Expand

- PMID: 39110115
- DOI: [10.1002/alr.23426](#)

Abstract

**Background:** Upper respiratory viral infections (URVIs) are responsible for 80% of asthma exacerbation episodes. However, the underlying mechanisms remain poorly understood.

**Methods:** In this study, we used a mouse model of URVI and examined the impact of URVI on asthma phenotypes and the underlying mechanisms.

**Results:** Previously, we have reported that nasal-restricted infection with respiratory syncytial virus (RSV) only produces mild sino-nasal inflammation and mucus production, without causing direct lung infection. However, such nasal-restricted infection dramatically enhanced T<sub>H</sub>2 and T<sub>H</sub>17 inflammatory responses in the lungs and increased airway hyperresponsiveness (AHR) in mice with house dust mite (HDM)-induced asthma. Additionally, nasal-restricted infection with RSV recruited Ly6C<sup>+</sup> inflammatory monocytes (IMs) into the lungs of mice with and without HDM-induced asthma. The expression of monocyte chemokines, including CCL2 and CCL7, also increased. Interestingly, nasal virus infection-induced AHR was abolished in mice depleted of IMs and in CCR2<sup>-/-</sup> mice, indicating that the recruited IMs play a key role in nasal virus infection-induced asthma exacerbations in mice. Lastly, we observed that recruitment of Ly6C<sup>+</sup> IMs following URVI was abolished in mice lacking B cells and that nasal-restricted infection with RSV increased numbers of CCL2<sup>+</sup>CCL7<sup>+</sup> B cells in the lungs of mice as compared to controls.

**Conclusions:** Taken together, our data have shown that URVI enhances the allergic inflammatory response and AHR through a B cell–monocyte regulatory axis.

**Keywords:** allergen; allergy; asthma; inflammation; viral rhinosinusitis.

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- [45 references](#)

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J Asthma

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. 2024 Aug 10:1-3.

doi: 10.1080/02770903.2024.2390030. Online ahead of print.

[Introducing the concept of loss of corticosteroid credit in asthma](#)

[Luis J Nannini](#)<sup>1</sup>

Affiliations Expand

- PMID: 39109837
- DOI: [10.1080/02770903.2024.2390030](https://doi.org/10.1080/02770903.2024.2390030)

Abstract

The widespread use of systemic corticosteroids (SCS) in asthma is associated with significant comorbidities and mortality. A dose-response relationship for cumulative SCS exposure with most adverse outcomes began at cumulative exposures of 1.0- <2.5 g, equivalent to four lifetime SCS courses. The purpose of creating the SCS credit concept was to increase awareness of the risks of SCS exposure and to promote better therapeutic alternatives. Consuming the lifetime SCS credit of 1.5 g/yr significantly increased morbidity and mortality.

Keywords: Systemic corticosteroids; asthma pharmacology; comorbidities.

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18

Int J Nurs Pract

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. 2024 Aug 6:e13290.

doi: 10.1111/ijn.13290. Online ahead of print.

[Virtual care for paediatric asthma: A randomized controlled trial](#)

[Merve Gümüş<sup>1</sup>](#), [Figen Yardimci<sup>1</sup>](#), [Handan Duman Şenol<sup>2</sup>](#), [Esen Demir<sup>2</sup>](#)

Affiliations Expand

- PMID: 39107823
- DOI: [10.1111/ijn.13290](#)

Abstract

**Aims:** This work aims to investigate whether virtual care can improve clinical outcomes for children with asthma, similar to face-to-face specialty care.

**Design:** The study used a randomized controlled trial design, with participants allocated to either a virtual care group (n = 47) or a control group (n = 50) using simple randomization.

**Methods:** The study was conducted from March to August 2021, and a sample of 97 children with asthma was recruited. Children in the virtual care group received online training in four modules within the first month and support through virtual meetings and phone or video calls, while the control group received standard care. The primary outcome of the study was the Asthma Control Test and Child Asthma Control Test.

**Results:** The virtual care group had significantly better outcomes than the control group in terms of C-ACT scores for children aged 7-11 years, fewer days under 80% of the optimum level of peak expiratory flow, lower peak expiratory flow variability, fewer rescue medication uses, and more symptom-free days. The virtual care group also had a lower number of unscheduled hospital visits and a greater improvement in quality of life compared with the control group.

**Conclusion:** This study demonstrated that virtual care can improve disease management and quality of life for children with asthma.

**Keywords:** asthma; child; nursing; quality of life; telemedicine.

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- [29 references](#)

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19

#### Respir Care

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. 2024 Aug 6:respcare.11934.

doi: 10.4187/respcare.11934. Online ahead of print.

#### [Class III Obesity as a Risk Factor for Persistent Asthma](#)

[Yonsu Kim](#)<sup>1</sup>, [Sheniz Moonie](#)<sup>2</sup>, [Ji Won Yoo](#)<sup>3</sup>, [Tae-Ha Chung](#)<sup>4</sup>

#### Affiliations Expand

- PMID: 39107060
- DOI: [10.4187/respcare.11934](#)

#### Abstract

**Background:** The burden of asthma remains steady with no decline observed in the past few decades. Obesity prevalence has been steadily increasing with a rate of 41.9% in the United States between 2017-2020. Obesity is an inflammatory chronic condition that may partially contribute to the burden and severity of asthma. This study aimed to examine whether the association between obesity and asthma varies with the categories of obesity (class I, II, and III) and persistent asthma (mild, moderate, and severe asthma). We hypothesized that subjects with elevated body mass index (BMI) are more likely to be diagnosed with persistent asthma than subjects without obesity with asthma.

**Methods:** As a retrospective and cross-sectional study, this study used a total of 1,977 records of subjects with asthma (age  $\geq 19$  y) hospitalized in Nevada between 2016-2021. BMI and persistent asthma were evaluated as the main exposure and outcome of interest. Logistic regression was used to estimate the magnitude of the association between obesity and persistent asthma.

**Results:** Among the selected subject records, subjects with obesity were more likely to be diagnosed with persistent asthma compared to subjects without obesity (odds ratio 1.50 [CI 1.10-2.05]). Subgroup analyses revealed that subjects with class III obesity (BMI  $\geq$  40) were more likely than subjects without obesity to be diagnosed with mild persistent asthma (odds ratio 2.21 [CI 1.18-4.16]) and severe persistent asthma (odds ratio 1.74 [CI 1.12-2.70]).

**Conclusions:** Obesity was identified as a risk factor for persistent asthma, particularly class III obesity. This in turn increases the potential for greater health care utilization and economic burden. Public health and clinical interventions are necessary among those with comorbid asthma and obesity.

**Keywords:** asthma; class III obesity; comorbidities; morbid obesity; obesity; severe asthma; severity.

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. 2024 Aug 6.

doi: 10.1159/000540298. Online ahead of print.

[Role of long-acting bronchodilators in patients with clinical asthma remission](#)

[Katrin Milger](#)

- PMID: 39106840
- DOI: [10.1159/000540298](https://doi.org/10.1159/000540298)

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Ann Am Thorac Soc

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. 2024 Aug 6.

doi: 10.1513/AnnalsATS.202402-130OC. Online ahead of print.

[The Impact of Eliminating Out-of-Pocket Payments on Asthma Medication Use](#)[Kate M Johnson](#)<sup>1,2</sup>, [Lucy Cheng](#)<sup>3</sup>, [Yiwei Yin](#)<sup>1</sup>, [Rachel Carter](#)<sup>4</sup>, [Santa Chow](#)<sup>4</sup>, [Emily Brigham](#)<sup>5</sup>, [Michael R Law](#)<sup>3</sup>

Affiliations Expand

- PMID: 39106523
- DOI: [10.1513/AnnalsATS.202402-130OC](#)

Abstract

**Background:** High costs of controller therapies may be a barrier to guideline-recommended asthma treatment. We determined whether eliminating out-of-pocket (OOP) payments among low-income patients with asthma impacted controller medication use.

**Methods:** We applied a controlled interrupted time series design to administrative claims data in British Columbia, Canada from 2017-2020. Cases were individuals with an annual household income <\$13,750 in whom copays were eliminated on January 2019; there was no change in public coverage for the control group with annual income >\$45,000. We evaluated trends in asthma medication costs, use, the ratio of inhaled corticosteroid (ICS)-containing medications to all asthma medications, excessive use of short-acting  $\beta$ -agonists (SABA) (>1 canister/month), and the proportion of days (PDC) covered by controller therapies.

**Results:** There were 12,940 cases (62% female, mean age 30.3 years, SD 14.9), and 71,331 controls (55% female, mean age of 31.3 years, SD 16.3). Removal of OOP payments increased monthly mean medication costs by \$3.32 (95% CI \$0.08 - \$6.56,

2020 Canadian dollars), days supply of controller medications by 1.50 days (95% CI 0.61 - 2.40), and the ratio of ICS-containing medications to total medications by 4.20% (95% CI 0.73% - 7.66%) compared to the control group. The policy had no effect on PDC by controller therapies (0.01, 95% CI -0.01 - 0.04), but non-significantly decreased the percentage of patients with excessive SABA use (-6.37%; 95% CI -12.90% - 0.16%).

Interpretation: Removal of OOP payments increased the dispensation of controller therapies, suggesting cost-related non-adherence could impair optimal asthma management.

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22

J Asthma

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. 2024 Aug 6:1-12.

doi: 10.1080/02770903.2024.2388774. Online ahead of print.

[Association Between Cardiometabolic Index and Asthma in Adults: Evidence from NHANES 2005-2018](#)

[Chengjia Li](#)<sup>1</sup>, [Tianwei Meng](#)<sup>1</sup>, [Boyu Wang](#)<sup>1</sup>, [Changxing Liu](#)<sup>1</sup>, [Nan Jiang](#)<sup>2</sup>, [Jiarui Li](#)<sup>1</sup>, [Huijun Chen](#)<sup>3</sup>

Affiliations Expand

- PMID: 39105683
- DOI: [10.1080/02770903.2024.2388774](https://doi.org/10.1080/02770903.2024.2388774)

Abstract

Objectives: Cardiometabolic Index (CMI) is a surrogate marker for metabolic disorders. It is associated with various chronic diseases. This study aims to investigate the relationship between CMI and asthma.

**Methods:** Data from seven consecutive National Health and Nutrition Examination Survey cycles between 2005 and 2018 were used. The study included adults with self-reported asthma diagnoses and complete information for CMI calculation. The formula for CMI is  $CMI = [WC (cm)/height (cm)] \times [TG (mg/dL)/HDL-C (mg/dL)]$ . A multivariate logistic regression model was employed to examine the linear relationship between CMI and asthma. Subgroup analyses were conducted to explore potential influencing factors. Additionally, smooth curve fitting and threshold effect analysis were used to describe the non-linear relationship.

**Results:** A higher CMI was possibly associated with an increased prevalence of asthma. After adjusting for various covariates including marital status, Poverty Income Ratio, Body Mass Index, hypertension, diabetes, smoking, alcohol consumption, heart attack, and stroke, the results remained significant (OR = 1.03; 95%CI, 1.00-1.05,  $P = 0.0178$ ,  $R^2 = 0.52$ ). Participants with the highest CMI had a 38% increased risk of asthma prevalence compared to those with the lowest CMI. (OR = 1.38; 95%CI, 1.19-1.60,  $P < 0.0001$ ).

**Conclusion:** The findings reveal that elevated CMI levels correlate with an increased risk of asthma, highlighting CMI's potential as a predictive marker for asthma, particularly in populations with a CMI below 1.97. These results suggest that interventions aimed at improving metabolic health may prove effective in managing or preventing asthma.

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23

ERJ Open Res

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. 2024 Aug 5;10(4):00931-2023.

doi: 10.1183/23120541.00931-2023. eCollection 2024 Jul.

[Untargeted metabolomic analysis reveals different metabolites associated with response to mepolizumab and omalizumab in asthma](#)

[Tanawin Nopsopon](#)<sup>1</sup>, [Yulu Chen](#)<sup>2</sup>, [Qingwen Chen](#)<sup>2</sup>, [Craig E Wheelock](#)<sup>3,4</sup>, [Scott T Weiss](#)<sup>2</sup>, [Michael McGeachie](#)<sup>2</sup>, [Jessica Lasky-Su](#)<sup>2,5</sup>, [Ayobami Akenroye](#)<sup>1,2,5</sup>

Affiliations Expand

- PMID: 39104961
- PMCID: [PMC11298997](#)
- DOI: [10.1183/23120541.00931-2023](#)

## Abstract

**Background:** There is limited evidence on biomarkers associated with response to the monoclonal antibodies currently approved for asthma treatment. We sought to identify circulatory metabolites associated with response to treatment with mepolizumab or omalizumab.

**Methods:** We conducted global metabolomic profiling of pre-treatment plasma samples from 100 patients with moderate-to-severe asthma who initiated mepolizumab (n=31) or omalizumab (n=69). The primary outcome was the change in exacerbations within 12 months of therapy. Negative binomial models were used to assess the association between each metabolite and exacerbations, adjusting for age, sex, body mass index, baseline exacerbations and inhaled corticosteroid use. Chemical similarity enrichment analysis (ChemRICH) was conducted to identify chemical subclasses associated with treatment response.

**Results:** The mean age of the mepolizumab group was 58.7 years with on average 2.9 exacerbations over the year prior to initiation of biologic therapy. The mean age in the omalizumab group was 48.8 years with 1.5 exacerbations in the preceding year. Patients with higher levels of two tocopherol metabolites were associated with more exacerbations on mepolizumab ( $\delta$ -carboxyethyl hydroxychroman (CEHC) ( $p=2.65E-05$ , false discovery rate (FDR)=0.01) and  $\delta$ -CEHC glucuronide ( $p=2.47E-06$ , FDR=0.003)). Higher levels of six androgenic steroids, three carnitine metabolites and two bile acid metabolites were associated with decreased exacerbations in the omalizumab group. In enrichment analyses, xanthine metabolites (cluster FDR=0.0006) and tocopherol metabolites (cluster FDR=0.02) were associated with worse mepolizumab response, while androgenic steroids (cluster FDR=1.9E-18), pregnenolone steroids (cluster  $p=3.2E-07$ , FDR=1.4E-05) and secondary bile acid metabolites (cluster  $p=0.0003$ , FDR=0.006) were the top subclasses associated with better omalizumab response.

**Conclusion:** This study identifies distinct metabolites associated with response to mepolizumab and omalizumab, with androgenic steroids associated with response to both mepolizumab and omalizumab.

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Conflict of interest statement

Conflict of interest: All authors have no relevant conflicts of interest to disclose. S.T. Weiss receives royalties from UpToDate and is on the Board of Histolix, a digital pathology company.

- [54 references](#)

- [5 figures](#)

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. 2024 Aug 5;10(4):00912-2023.

doi: 10.1183/23120541.00912-2023. eCollection 2024 Jul.

[Burden of eosinophilic granulomatosis with polyangiitis in Europe](#)

[Rupert W Jakes](#)<sup>1</sup>, [Namhee Kwon](#)<sup>2</sup>, [Lynn Huynh](#)<sup>3</sup>, [Jeremiah Hwee](#)<sup>4</sup>, [Lee Baylis](#)<sup>5</sup>, [Rafael Alfonso-Cristancho](#)<sup>6</sup>, [Shawn Du](#)<sup>3</sup>, [Anamika Khanal](#)<sup>3</sup>, [Mei Sheng Duh](#)<sup>3</sup>, [Benjamin Terrier](#)<sup>7</sup>

Affiliations Expand

- PMID: 39104949
- PMCID: [PMC11299011](#)
- DOI: [10.1183/23120541.00912-2023](#)

Abstract

**Background and aims:** Real-world evidence characterising the burden of eosinophilic granulomatosis with polyangiitis (EGPA) in Europe is limited. The aim of this study was to characterise patients in a large European EGPA cohort.

**Methods:** This retrospective, non-interventional, longitudinal study (GSK ID: 214661) recruited cross-specialty physicians from France, Germany, Italy, Spain and the UK to conduct medical chart reviews for patients with a physician-confirmed diagnosis of EGPA. Patients were  $\geq 12$  years of age at diagnosis with  $\geq 1$  year of follow-up data from the first clinical visit with the physician (index date). Outcome measures

collected from index date to end of follow-up included clinical manifestations and healthcare resource utilisation (HCRU).

**Results:** In total, 407 patient medical charts were reviewed by 204 physicians; median (interquartile range) duration of follow-up from index date was 2.2 (1.7-3.5) years. Most patients (73.5%) had asthma. Patients underwent multiple diagnostic assessments, and 74.9% received  $\geq 3$  different therapies between diagnosis and end of follow-up (98.8% oral corticosteroids, 63.9% immunosuppressive therapies, 45.5% biologics). During follow-up, 84.5% of patients experienced EGPA clinical manifestations; most were considered moderate or severe and commonly affected the lungs (55.8%; including lung infiltrates 25.8% and severe asthma 24.8%), ear, nose and throat (53.3%), and skin (41.8%). HCRU was substantial: 26.0% of patients made emergency department visits, 36.6% were hospitalised and 84.8% had outpatient visits.

**Conclusions:** These real-world data show that EGPA presents a substantial burden to patients and the healthcare system. Earlier and better differential diagnosis and appropriate treatment may help reduce incidence of clinical manifestations and HCRU.

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Conflict of interest statement

Conflict of interest: R.W. Jakes, N. Kwon, J. Hwee, L. Baylis and R. Alfonso-Cristancho are employed by GSK, or were at the time of the study, and hold financial equities in GSK. Conflict of interest: L. Huynh, S. Du, A. Khanal and M. Sheng Duh are employees of Analysis Group, Inc., or were at the time of the study. Analysis Group, Inc. received research funds from GSK to conduct the study and have received research funds for previous studies from GSK, AbbVie, Apellis, AstraZeneca, Ayala Pharmaceuticals, Bayer, Blueprint Medicines, Humacyte, Janssen, Merck, Novartis, Pfizer, Sanofi and Takeda. Conflict of interest: B. Terrier reports consulting fees from AstraZeneca, Vifor, and GSK; payment or honoraria for lectures, presentations, speaker bureaus, manuscript writing or educational events from AstraZeneca, Vifor, GSK, and Boehringer Ingelheim and support for attending meetings and/or travel from Vifor and GSK.

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## Randomized Controlled Trial

### Respir Res

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. 2024 Aug 5;25(1):297.

doi: [10.1186/s12931-024-02918-8](https://doi.org/10.1186/s12931-024-02918-8).

[Benefits of budesonide/glycopyrronium/formoterol fumarate dihydrate on lung function and exacerbations of COPD: a post-hoc analysis of the KRONOS study by blood eosinophil level and exacerbation history](#)

[Shigeo Muro](#)<sup>1</sup>, [Tomotaka Kawayama](#)<sup>2</sup>, [Hisatoshi Sugiura](#)<sup>3</sup>, [Munehiro Seki](#)<sup>4</sup>, [Elizabeth A Duncan](#)<sup>5</sup>, [Karin Bowen](#)<sup>6</sup>, [Jonathan Marshall](#)<sup>7</sup>, [Ayman Megally](#)<sup>8</sup>, [Mehul Patel](#)<sup>9</sup>

### Affiliations Expand

- PMID: 39103901
- PMCID: [PMC11302094](#)
- DOI: [10.1186/s12931-024-02918-8](https://doi.org/10.1186/s12931-024-02918-8)

### Abstract

**Background:** Japanese guidelines recommend triple inhaled corticosteroid (ICS)/long-acting muscarinic antagonist (LAMA)/long-acting  $\beta_2$ -agonist (LABA) therapy in patients with chronic obstructive pulmonary disease (COPD) and no concurrent asthma diagnosis who experience frequent exacerbations and have blood eosinophil (EOS) count  $\geq 300$  cells/mm<sup>3</sup>, and in patients with COPD and asthma with continuing/worsening symptoms despite receiving dual ICS/LABA therapy. These post-hoc analyses of the KRONOS study in patients with COPD and without an asthma diagnosis, examine the effects of fixed-dose triple therapy with budesonide/glycopyrronium/formoterol fumarate dihydrate (BGF) versus dual therapies on lung function and exacerbations based on blood EOS count - focusing on blood EOS count 100 to  $< 300$  cells/mm<sup>3</sup> - as a function of exacerbation history and COPD severity.

**Methods:** In KRONOS, patients were randomized to receive treatments that included BGF 320/14.4/10  $\mu\text{g}$ , glycopyrronium/formoterol fumarate dihydrate (GFF) 14.4/10  $\mu\text{g}$ , or budesonide/formoterol fumarate dihydrate (BFF) 320/10  $\mu\text{g}$  via metered dose inhaler (two inhalations twice-daily for 24 weeks). These post-hoc analyses assessed changes from baseline in morning pre-dose trough forced expiratory

volume in 1 s (FEV<sub>1</sub>) over 12-24 weeks and moderate or severe COPD exacerbations rates over 24 weeks. The KRONOS study was not prospectively powered for these subgroup analyses.

**Results:** Among patients with blood EOS count 100 to < 300 cells/mm<sup>3</sup>, least squares mean treatment differences for lung function improvement favored BGF over BFF in patients without an exacerbation history in the past year and in patients with moderate and severe COPD, with observed differences ranging from 62 ml to 73 ml across populations. In this same blood EOS population, moderate or severe exacerbation rates were reduced for BGF relative to GFF by 56% in patients without an exacerbation history in the past year, by 47% in patients with moderate COPD, and by 50% in patients with severe COPD.

**Conclusions:** These post-hoc analyses of patients with moderate-to-very severe COPD from the KRONOS study seem to indicate clinicians may want to consider a step-up to triple therapy in patients with persistent/worsening symptoms with blood EOS count > 100 cells/mm<sup>3</sup>, even if disease severity is moderate and there is no recent history of exacerbations.

**Trial registration:** ClinicalTrials.gov registry number [NCT02497001](https://clinicaltrials.gov/ct2/show/study/NCT02497001) (registration date, 13 July 2015).

**Keywords:** Blood eosinophils; Budesonide/glycopyrronium/formoterol fumarate dihydrate (BGF); Chronic obstructive pulmonary disease (COPD); Disease severity; Exacerbation rates; Fixed-dose triple therapy; Lung function.

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#### Conflict of interest statement

SM has received lecture fees from AstraZeneca, GlaxoSmithKline, Nippon Boehringer Ingelheim, and Novartis Pharma. TK has received grants from Helios co. Ltd. and lecture fees from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Kyorin, Novartis, Sanofi, and Teijin healthcare. HS has received lecture fees from AstraZeneca, GlaxoSmithKline, Nippon Boehringer Ingelheim, Novartis Pharma, and Sanofi. MS is an employee of AstraZeneca K.K. Kita-ku and owns stock and/or stock options in the company. EAD is a former employee of AstraZeneca and owns stock and/or stock options in the company. KB, JM, AM, and MP are employees of AstraZeneca and own stock and/or stock options in the company.

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

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Review

J Transl Med

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. 2024 Aug 5;22(1):736.

doi: 10.1186/s12967-024-05534-8.

[Beyond CAR-T: The rise of CAR-NK cell therapy in asthma immunotherapy](#)

[Mohadeseh Mohammad Taheri](#)<sup>1</sup>, [Fatemeh Javan](#)<sup>1</sup>, [Mohadeseh Poudineh](#)<sup>1</sup>, [Seyed Shamseddin Athari](#)<sup>2,3</sup>

Affiliations Expand

- PMID: 39103889
- PMCID: [PMC11302387](#)
- DOI: [10.1186/s12967-024-05534-8](#)

Abstract

Asthma poses a major public health burden. While existing asthma drugs manage symptoms for many, some patients remain resistant. The lack of a cure, especially for severe asthma, compels exploration of novel therapies. Cancer immunotherapy successes with CAR-T cells suggest its potential for asthma treatment. Researchers are exploring various approaches for allergic diseases including membrane-bound IgE, IL-5, PD-L2, and CTLA-4 for asthma, and Dectin-1 for fungal asthma. NK cells offer several advantages over T cells for CAR-based immunotherapy. They offer key benefits: (1) HLA compatibility, meaning they can be used in a wider range of patients without the need for matching tissue types. (2) Minimal side effects (CRS and GVHD) due to their limited persistence and cytokine profile. (3) Scalability for "off-the-shelf" production from various sources. Several strategies have been introduced that highlight the superiority and challenges of CAR-NK cell therapy for asthma treatment including IL-10, IFN- $\gamma$ , ADCC, perforin-granzyme, FASL, KIR, NCRs (NKP46), DAP, DNAM-1, TGF- $\beta$ , TNF- $\alpha$ , CCL, NKG2A, TF, and EGFR.

Furthermore, we advocate for incorporating AI for CAR design optimization and CRISPR-Cas9 gene editing technology for precise gene manipulation to generate highly effective CAR constructs. This review will delve into the evolution and production of CAR designs, explore pre-clinical and clinical studies of CAR-based therapies in asthma, analyze strategies to optimize CAR-NK cell function, conduct a comparative analysis of CAR-T and CAR-NK cell therapy with their respective challenges, and finally present established novel CAR designs with promising potential for asthma treatment.

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#### Conflict of interest statement

The authors declare no conflict of interest.

- [524 references](#)
- [8 figures](#)

#### Supplementary info

Publication types, MeSH terms, SubstancesExpand

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#### Infect Dis Ther

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. 2024 Aug 3.

doi: 10.1007/s40121-024-01023-z. Online ahead of print.

#### [Proportion of Patients in the United States Who Fill Their Nirmatrelvir/Ritonavir Prescriptions](#)

[Abby E Rudolph](#)<sup>1</sup>, [Farid L Khan](#)<sup>2</sup>, [Tanya G Singh](#)<sup>3</sup>, [Srinivas Rao Valluri](#)<sup>2</sup>, [Laura A Puzniak](#)<sup>2</sup>, [John M McLaughlin](#)<sup>2</sup>

#### Affiliations Expand

- PMID: 39097548
- DOI: [10.1007/s40121-024-01023-z](https://doi.org/10.1007/s40121-024-01023-z)

## Abstract

**Introduction:** Although real-world studies demonstrate that those prescribed nirmatrelvir/ritonavir (and particularly within 5 days of symptom onset) are less likely to experience severe COVID-19 outcomes, prior studies show that only a small fraction of patients with COVID-19 who are eligible for nirmatrelvir/ritonavir receive a prescription. Studies calculating the proportion of nirmatrelvir/ritonavir prescriptions filled and identifying individual- and pharmacy-level correlates of filling nirmatrelvir/ritonavir are lacking.

**Methods:** This retrospective cohort study included individuals aged  $\geq 12$  years with a nirmatrelvir/ritonavir prescription ordered at a large national retail pharmacy (December 22, 2021-August 12, 2023). Those taking contraindicated medications were excluded. For those with only one nirmatrelvir/ritonavir prescription ordered, the outcome was whether the prescription was filled (yes/no). In a subanalysis of these individuals, the outcome was whether the prescription was filled within 5 days of symptom onset (yes/no). For those with multiple prescriptions ordered, the outcome was whether  $> 1$  (vs. 0 or 1) prescriptions were filled. A log-binomial regression with generalized estimating equations was used to identify individual (clinical and demographic) and pharmacy-level (percentage of trade area that is non-Hispanic white, urbanicity, US Census region, and tract-level area deprivation index) correlates.

**Results:** A total of 2,103,570 unique nirmatrelvir/ritonavir prescriptions were ordered for 1,985,990 individuals. Among the 95% of individuals prescribed only one nirmatrelvir/ritonavir course, 88% filled their prescription. Among those with  $> 1$  prescription ordered, 77% (82,993/108,411) filled one and 13% (13,662/108,411) filled  $> 1$ . Patients  $\geq 50$  years of age and those with documented high-risk conditions were slightly more likely to fill prescriptions, regardless of whether one or multiple courses were ordered. Individuals with cancer, asthma, or taking corticosteroids or immunosuppressive medications were more likely to fill multiple prescriptions.

**Conclusions:** Most patients filled their nirmatrelvir/ritonavir prescriptions. Interventions to improve uptake should focus on increasing patient and provider awareness, reducing nirmatrelvir/ritonavir prescribing disparities, and ensuring treatment initiation within 5 days.

**Keywords:** Disparities; Nirmatrelvir/ritonavir; Paxlovid; Prescriptions filled; Symptom onset date.

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- [35 references](#)

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Editorial

Thorax

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. 2024 Aug 3:thorax-2024-221939.

doi: 10.1136/thorax-2024-221939. Online ahead of print.

[Fixing lung health in the UK: accelerating respiratory research and innovation](#)

[Cheryl Routley](#)<sup>1</sup>, [Samantha Walker](#)<sup>2</sup>, [Eric Wfw Alton](#)<sup>3</sup>, [Ian P Hall](#)<sup>4</sup>

Affiliations Expand

- PMID: 39097411
- DOI: [10.1136/thorax-2024-221939](#)

*No abstract available*

**Keywords:** asthma; bronchiectasis; cystic fibrosis; idiopathic pulmonary fibrosis; interstitial fibrosis; pulmonary disease, chronic obstructive; respiratory infection; respiratory measurement.

**Conflict of interest statement**

**Competing interests:** Eric Alton Royalties or licenses: Royalties from Boehringer Ingelheim related to cystic fibrosis gene therapy programme. Consulting fees: Boehringer Ingelheim - payments made to EA and institution; AlveoGene - payments made to EA. Patents planned, issued or pending: multiple patents filed by Imperial College. Participation on a Data Safety Monitoring Board or Advisory Board: Boehringer Ingelheim Advisory Board - payments made to EA Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid. Founder Director, AlveoGeneStock or stock options AlveoGene shares - payments to EA. Sam Walker Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid co-Chair of Lung Research and Innovation Group (LRIG). Ian Hall: Grants or contracts from any entity. NIHR Senior Investigator

Award - research grant to institution. Support for attending meetings and/or travel. Travel to AUKCAR meeting in Reading, 2024 - Expenses covered by Asthma+Lung UK Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid co-Chair of Lung Research and Innovation Group (LRIG).

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J Asthma

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. 2024 Aug 3:1-11.

doi: 10.1080/02770903.2024.2386442. Online ahead of print.

[Analysis of asthma incidence and mortality rates among children aged 0-14 in 204 countries from 1990 to 2019](#)

[Fei Cheng](#)<sup>1</sup>, [Li He](#)<sup>2</sup>, [Dachuan Deng](#)<sup>3</sup>, [Jinhui Zhang](#)<sup>2</sup>, [Cheng Liu](#)<sup>2</sup>

Affiliations Expand

- PMID: 39074060
- DOI: [10.1080/02770903.2024.2386442](https://doi.org/10.1080/02770903.2024.2386442)

Abstract

**Objective:** Asthma is a common chronic respiratory disease in children. Understanding incidence and mortality trends is crucial for prevention and intervention strategies.

**Methods:** Data from the Global Burden of Disease (GBD) study were used to analyze asthma incidence and mortality trends among children aged 0-14 in 204 countries

from 1990 to 2019. The 30-year trends were calculated using the Estimated Annual Percentage Change (EAPC).

**Results:** Globally, pediatric asthma cases increased from 18,857,697 in 1990 to 20,191,786 in 2019. Incidence rates for children <5, 5-9, and 10-14 years are 1509.36, 980.25, and 586.95 per 100,000, respectively. Over 30 years, pediatric asthma mortality rates significantly decreased from 1.59 to 0.51 per 100,000, with minimal gender differences. High-income North America, Tropical Latin America, and the Caribbean show the highest incidence rates at 3203.2, 2493.83, and 2314.8 per 100,000. The USA, Puerto Rico, and Haiti have the highest national rates at 3357.17, 2695.30, and 2605.38 per 100,000. Regions with higher Sociodemographic Index levels tend to have higher incidence rates. Pediatric asthma prevalence varies by region and age group.

**Conclusion:** Our study of asthma incidence and mortality rates among children aged 0-14 across 204 countries from 1990 to 2019 reveals significant global disparities. These findings underscore the influence of socioeconomic and environmental factors on asthma prevalence and outcomes.

**Keywords:** Epidemiology; Global burden of disease; Incidence; Pediatric asthma.

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Review

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. 2024 Aug 8;64(2):2400462.

doi: 10.1183/13993003.00462-2024. Print 2024 Aug.

[Global herpes zoster burden in adults with asthma: a systematic review and meta-analysis](#)

[Kevin J Mortimer](#)<sup>1,2,3</sup>, [Alvaro A Cruz](#)<sup>4</sup>, [Ingrid T Sepúlveda-Pachón](#)<sup>5</sup>, [Anamaria Jorga](#)<sup>6</sup>, [Hilde Vroliing](#)<sup>7</sup>, [Charles Williams](#)<sup>8</sup>

## Affiliations Expand

- PMID: 38901886
- PMCID: [PMC11306804](#)
- DOI: [10.1183/13993003.00462-2024](#)

## Abstract

**Background:** Asthma is a common respiratory disease, which may be associated with an increased risk of herpes zoster (HZ), often a debilitating disease associated with severe pain. This is the first systematic review with the objective of summarising evidence on HZ burden in adults with asthma.

**Methods:** A global systematic literature review and meta-analysis was conducted (MEDLINE and Embase, 2003-2024) on HZ burden (incidence, risk and complications) in adults (≥18 years) with asthma.

**Results:** There were 19 studies included on HZ outcomes in adults with asthma. Pooled HZ incidence per 1000 person-years was 5.71 (95% CI 4.68-6.96) in adults aged ≥18 years (4.20 (95% CI 3.09-5.70) in those aged <60 years *versus* 10.33 (95% CI 9.17-11.64) in those aged ≥60 years). The pooled rate ratio for developing HZ was 1.23 (95% CI 1.11-1.35) in those aged ≥18 years and 1.36 (95% CI 1.15-1.61) in those aged ≥50 years. The risk of HZ was higher in people with asthma using systemic corticosteroids, long-acting β-agonists plus inhaled corticosteroids and "add-on therapy". Asthma was also associated with an increased risk of post-herpetic neuralgia (OR 1.21, 95% CI 1.06-1.37) and HZ ophthalmicus (OR 1.9, 95% CI 1.1-3.2). Differences in study design, setting, case definitions and follow-up durations led to heterogeneity.

**Conclusions:** This systematic literature review and meta-analysis found that adults with asthma have an increased risk of HZ, with higher risks in older age groups and in those on certain treatments, such as oral corticosteroids. HZ vaccines are available for adults, including those with comorbidities such as asthma, and can be considered as part of integrated respiratory care.

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## Conflict of interest statement

**Conflict of interest:** A. Jorga and C. Williams are employed by GSK. A. Jorga holds shares in Pfizer and GSK. H. Vroling and I.T. Sepúlveda-Pachón are employees of P95/Pallas. P95/Pallas received funding from GSK for the submitted work. P95/Pallas holds/held contracts with AstraZeneca, GSK, Pfizer, Sanofi, Seqirus, Merck, Takeda, Orchard, Biomarin, Daiichi, Bavarian Nordic and Bayer (work for the non-GSK companies was not related to HZ). K.J. Mortimer declares grants and sponsorship from AstraZeneca and GSK to support the Global Asthma Network, consulting fees from AstraZeneca and GSK on asthma and COPD-related advisory boards, and honorarium from GSK for lectures on improving vaccine access for people with asthma, outside the submitted work. A.A. Cruz declares grants and

sponsorship from GSK to support the ProAR Foundation, and consulting or lecture fees from Abdi-Ibrahim, AstraZeneca, Boehringer Ingelheim, Chiesi, Crossject, Eurofarma, Farmoquimica, Glennmark, GSK, Mylan, Novartis and Sanofi on asthma-related activities. The authors declare no other financial or non-financial relationships and activities or conflicts of interest.

Comment in

- [The burden of zoster in asthma: what is left to learn?](#)

Bloom C. *Eur Respir J*. 2024 Aug 8;64(2):2401300. doi: 10.1183/13993003.01300-2024. Print 2024 Aug. PMID: 39117424 No abstract available.

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. 2024 Aug 5;221(8):e20231827.

doi: 10.1084/jem.20231827. Epub 2024 Jun 18.

[Human CD127 negative ILC2s show immunological memory](#)

[Laura Mathä](#) <sup>#1 2</sup>, [Lisette Krabbendam](#) <sup>#3 4</sup>, [Sergio Martinez Høyer](#) <sup>#1</sup>, [Balthasar A Heesters](#) <sup>3 5</sup>, [Korneliusz Golebski](#) <sup>3 6</sup>, [Chantal Kradolfer](#) <sup>3</sup>, [Maryam Ghaedi](#) <sup>2 7</sup>, [Junjie Ma](#) <sup>1</sup>, [Ralph Stadhouders](#) <sup>4</sup>, [Claus Bachert](#) <sup>8 9 10 11 12</sup>, [Lars-Olaf Cardell](#) <sup>11</sup>, [Nan Zhang](#) <sup>10</sup>, [Gabriele Holtappels](#) <sup>10</sup>, [Sietze Reitsma](#) <sup>13</sup>, [Leanne Carijn Helgers](#) <sup>3 14</sup>, [Teunis B H Geijtenbeek](#) <sup>3 14</sup>, [Jonathan M Coquet](#) <sup>1</sup>, [Fumio Takei](#) <sup>2 15</sup>, [Hergen Spits](#) <sup>3</sup>, [Itziar Martinez-Gonzalez](#) <sup>1 3</sup>

Affiliations Expand

- PMID: 38889332
- PMCID: [PMC11187981](#)
- DOI: [10.1084/jem.20231827](#)

## Abstract

ILC2s are key players in type 2 immunity and contribute to maintaining homeostasis. ILC2s are also implicated in the development of type 2 inflammation-mediated chronic disorders like asthma. While memory ILC2s have been identified in mouse, it is unknown whether human ILC2s can acquire immunological memory. Here, we demonstrate the persistence of CD45RO, a marker previously linked to inflammatory ILC2s, in resting ILC2s that have undergone prior activation. A high proportion of these cells concurrently reduce the expression of the canonical ILC marker CD127 in a tissue-specific manner. Upon isolation and in vitro stimulation of CD127-CD45RO+ ILC2s, we observed an augmented ability to proliferate and produce cytokines. CD127-CD45RO+ ILC2s are found in both healthy and inflamed tissues and display a gene signature of cell activation. Similarly, mouse memory ILC2s show reduced expression of CD127. Our findings suggest that human ILC2s can acquire innate immune memory and warrant a revision of the current strategies to identify human ILC2s.

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## Conflict of interest statement

Disclosures: K. Golebski reported grants from GlaxoSmithKline, personal fees from ALK, grants from SANOFI, and grants from STIMAG outside the submitted work. S. Reitsma reported personal fees from Sanofi, grants from Sanofi, personal fees and grants from GSK, personal fees from Novartis, and grants from Novartis outside the submitted work. H. Spits reported being a consultant for GSK. No other disclosures were reported.

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- [13 figures](#)

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Editorial

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. 2024 Aug 8;64(2):2400242.

doi: 10.1183/13993003.00242-2024. Print 2024 Aug.

[Missing airways, ventilation defects and conductive airway physiology in asthma](#)

[Sylvia Verbanck](#)<sup>1</sup>, [Rachel L Eddy](#)<sup>2</sup>, [Marrissa J McIntosh](#)<sup>3</sup>, [Grace Parraga](#)<sup>3,4</sup>, [Brody H Foy](#)<sup>5</sup>

Affiliations Expand

- PMID: 38843912
- DOI: [10.1183/13993003.00242-2024](https://doi.org/10.1183/13993003.00242-2024)

*No abstract available*

Conflict of interest statement

**Conflict of interest:** R.L. Eddy reports grants from Michael Smith Health Research BC, Canadian Respiratory Research Network and the Natural Sciences and Engineering Research Council Canada, consulting fees from VIDA Diagnostics Inc., lecture honoraria from Thorasys Thoracic Medical Systems Inc., travel support from Canadian Institutes of Health Research – Institute of Circulatory and Respiratory Health, and a leadership role as Xenon MRI Clinical Trials Consortium Steering Committee Member, outside the submitted work. G. Parraga reports grants from the Canada Foundation for Innovation and the Natural Sciences and Engineering Research Council Canada, lecture honoraria from GSK, advisory board participation with Polarean and CIHR, and a leadership role as Xenon MRI Clinical Trials Consortium Steering Committee Member, outside the submitted work. The remaining authors have no potential conflicts of interest to disclose.

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

1

Otolaryngol Head Neck Surg

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. 2024 Aug 10.

doi: 10.1002/ohn.937. Online ahead of print.

[Unveiling the Impact of Smoking on Allergic Rhinitis: Disease Severity and Efficacy of Subcutaneous Immunotherapy](#)

[Xuan Yuan](#)<sup>1 2 3 4</sup>, [Liyuan Liu](#)<sup>5</sup>, [Benjian Zhang](#)<sup>1 2 3 4</sup>, [Shaobing Xie](#)<sup>1 2 3 4</sup>, [Lai Meng](#)<sup>1 2 3 4</sup>, [Wei Zhong](#)<sup>1 2 3 4</sup>, [Jiaxin Jia](#)<sup>1 2 3 4</sup>, [Hua Zhang](#)<sup>1 2 3 4</sup>, [Weihong Jiang](#)<sup>1 2 3 4</sup>, [Zhihai Xie](#)<sup>1 2 3 4</sup>

Affiliations Expand

. PMID: 39126287

. DOI: [10.1002/ohn.937](https://doi.org/10.1002/ohn.937)

Abstract

**Objective:** To evaluate the impact of smoking statuses on disease severity and subcutaneous

**immunotherapy (SCIT) efficacy in allergic rhinitis (AR).**

**Study design: Open observational cohort study.**

**Setting: Tertiary referral center.**

**Methods: Five hundred and five AR patients undergoing dust mite allergen SCIT were categorized into never smokers, former smokers, and current smokers. AR severity was assessed using widely employed questionnaires. The changes in questionnaire scores pre- and post-SCIT were evaluated for SCIT efficacy. The differences in disease severity and SCIT efficacy were compared for different smoking statuses among AR patients.**

**Results: Compared to never smokers, former and current smokers exhibited higher proportion of male, alcohol, and asthma ( $P < .05$ ). Current smokers had a greater prevalence of allergic conjunctivitis than former smokers ( $P < .05$ ). Before SCIT, AR severity was similar across 3 groups, even after adjusting for confounders ( $P > .05$ ). Current smokers reported lower SCIT efficacy in the first year ( $P < .05$ ). By the third year, 3 groups showed comparable long-term efficacy ( $P > .05$ ). However, current smokers experienced a significant decrease in benefits 2 years post-SCIT ( $P < .05$ ) and lower improvement rates at the end of the 3-years SCIT period and 2 years following SCIT ( $P < .05$ ).**

**Conclusion: AR patients across different smoking statuses demonstrated similar baseline disease severity and long-time SCIT efficacy. Active smoking was associated with increased asthma risk, delayed early SCIT efficacy perception, reduced improvement over 3 years, and diminished benefits 2 years after SCIT. Prompt smoking cessation is crucial to mitigate these effects.**

**Keywords: allergic rhinitis; disease severity; efficacy; smoking; subcutaneous immunotherapy.**

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**Allergy Asthma Clin Immunol**

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2024 Aug 8;20(1):45.

doi: 10.1186/s13223-024-00899-3.

## [Focused allergic rhinitis practice parameter for Canada](#)

[Anne K Ellis](#)<sup>1</sup>, [Victoria Cook](#)<sup>2</sup>, [Paul K Keith](#)<sup>3</sup>, [Sean R Mace](#)<sup>4</sup>, [William Moote](#)<sup>5</sup>, [Andrew O'Keefe](#)<sup>6</sup>, [Jaclyn Quirt](#)<sup>3</sup>, [Lana Rosenfield](#)<sup>7</sup>, [Peter Small](#)<sup>8</sup>, [Wade Watson](#)<sup>9</sup>

### Affiliations Expand

- PMID: 39118164
- PMCID: [PMC11311964](#)
- DOI: [10.1186/s13223-024-00899-3](#)

### Abstract

Allergic rhinitis (AR) is a prevalent disease in Canada that affects both children and adults. Several guidelines for the management of AR have been published by professional allergy societies worldwide. However, there are regional differences in the clinical management of AR, and regulatory approval of some AR pharmacotherapies varies among countries. Thus, six research questions specific to the treatment of

**AR in Canada were identified for this focused practice parameter. Reviews of the literature published since 2016 were conducted to obtain evidence-based support for the responses of the Work Group to each research question. In response to research question 1 "In patients with symptoms indicative of AR, is serum-specific IgE sufficient to identify candidates for immunotherapy or is a skin prick test mandatory?" the Work Group concluded that either sIgE testing or skin prick test are acceptable for diagnosing AR and guiding immunotherapy. In response to research question 2 "When taking into account the preferences of the patient and the prescriber (stakeholder engagement) should second-generation oral antihistamine (OAH) or intranasal corticosteroid (INCS) be first line?" the Work Group concluded that existing guidelines generally agree on the use of INCS as a first-line therapy used for AR, however, patient and provider preferences and considerations can easily shift the first choice to a second-generation OAH. In response to research question 3 "Is a combination intranasal antihistamine (INAH)/INCS formulation superior to INCS plus OAH? Do they become equivalent after prolonged use?" the Work Group concluded that the combination INAH/INCS is superior to an INCS plus OAH. However, there was insufficient evidence to answer the second question. In response to research question 4 "Do leukotriene**

receptor antagonists (LTRA) have a greater benefit than OAH in AR for some symptoms to justify a therapeutic trial in those who cannot tolerate INCS?" the Work Group concluded that LTRAs have inferior, or at best equivalent, daytime or overall symptom control compared with OAH, but LTRAs may improve nighttime symptom control and provide benefits in patients with AR and concomitant asthma. In response to research question 5 "Should sublingual immunotherapy (SLIT) tablets be considered first-line immunotherapeutic options over subcutaneous immunotherapy (SCIT) based on the evidence of efficacy?" the Work Group concluded that the choice of SLIT or SCIT cannot be made on efficacy alone, and differences in other factors outweigh any differences in efficacy. In response to research question 6 "Based on efficacy data, should ALL patients seen by an allergist be offered SLIT or SCIT as a treatment option?" the Work Group concluded that the efficacy data suggests that SLIT or SCIT should be used broadly in patients with AR, but other clinical concerns also need to be taken into consideration.

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### **Conflict of interest statement**

**A.K. Ellis has participated in advisory boards for ALK-Abello, AstraZeneca, Bausch Health, LEO**

Pharma, Miravo, Merck, Novartis, has been a speaker for ALK-Abello, AstraZeneca, Bausch, Miravo, Medexus, Mylan, Novartis, Pfizer, Sanofi, StallergenesGreer and Regeneron. Her institution has received research grants from ALK Abello, Aralez, AstraZeneca, Bayer LLC, Medexus, Novartis, Sanofi and Regeneron. She has also served as an independent consultant to Bayer LLC, Pharming, and Regeneron. V. Cook has received honoraria for speaking engagements for Miravo/Aralez, Pfizer, and ALK and served on advisory boards or speakers' bureaus for Sanofi and ALK. P. Keith Paul has participated in advisory boards for ALK-Abello, AstraZeneca, Bausch Health, CSL Behring, GlaxoSmithKline, LEO Pharma, Miravo, Merck, Novartis, Sanofi, Takeda and Valeo. He has been a speaker for ALK-Abello, Bausch, GlaxoSmithKline, Medexus, Novartis, and Sanofi. His institution has received research grants from CSL Behring and Takeda. He has also served as a consultant to Bayer LLC, CADTH, and the Canadian Pharmacists Association. S.R. Mace has served on a speakers' bureau for Miravo. W. Moote has nothing to disclose. A. O'Keefe reports research funding from Sanofi, has served as a speaker for Novartis, ALK, Innomar, Medexus, GlaxoSmithKline, Sanofi, and has served as a consultant for ALK, Sanofi, Takeda and Astra Zeneca. J. Quirt has participated in advisory boards for Aralez and Sanofi. L. Rosenfield has nothing to disclose. P. Small has

nothing to disclose. W. Watson has nothing to disclose.

All recommendations in this document are evidence based and concluded on by all authors equally as consensus-based recommendations.

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- [1 figure](#)

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J Allergy Clin Immunol Pract

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. 2024 Aug 5:S2213-2198(24)00776-1.

doi: 10.1016/j.jaip.2024.07.026. Online ahead of print.

# Impact of allergic rhinitis control on work productivity and costs: a real-world data MASK-air study

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Affiliations Expand

- PMID: 39111363
- DOI: [10.1016/j.jaip.2024.07.026](https://doi.org/10.1016/j.jaip.2024.07.026)

Abstract

**Background:** Allergic rhinitis (AR) has a substantial socioeconomic impact associated with impaired work productivity.

**Objective:** To study the impact of AR on work productivity and estimate the corresponding indirect costs for 40 countries.

**Methods:** We conducted a cross-sectional study using direct patient data from the MASK-air® app on users with self-reported AR. We used the Work Productivity and Activity Impairment Questionnaire: Allergy Specific to measure the impact of AR on work productivity (presenteeism and absenteeism). Weekly indirect costs were estimated per country, for each level of rhinitis control and considering patients with and without asthma.

**Results:** We assessed data from 677 weeks (364 patients), 280 of which were reported by patients with asthma. Regarding presenteeism, the median impact of AR in weeks of poor disease control was 60.7% (P25-P75=24.9-74.2%), while partial and good disease control were respectively associated with an impact of 25.0% (P25-P75=12.1-42.4%) and 4.4% (P25-75=0.8-12.9%). In poorly-controlled weeks, presenteeism was associated with indirect costs ranging from 65.7 US Dollars purchase power parity (US\$ PPPs) (P25-P75=29.2-143.2) in Brazil to 693.6 US\$ PPP (P25-P75=405.2-1094.9) in Iceland. Median absenteeism per week was of 0% for all levels of rhinitis control. Patients with AR+asthma showed higher overall work impairment than patients with AR alone, particularly in poorly-controlled weeks (median work impairment in AR alone=39.1% [P25-P75=12.5-71.9%]; median work impairment in AR+asthma=68.4% [P25-P75=54.6-80.2%]).

**Conclusion: Poor AR control was associated with decreased work productivity and increased indirect costs, particularly in patients with AR+asthma. The estimates from this study underpin the economic burden of AR.**

**Keywords: Allergic rhinitis; Asthma; Indirect costs; Presenteeism; Work productivity.**

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**. 2024 Aug 6;14(1):18266.**

**doi: 10.1038/s41598-024-69228-3.**

**[Identification of ENTPD1 as a novel biomarker linking allergic rhinitis and systemic lupus erythematosus](#)**

[Min Chen](#) <sup>#1</sup>, [Yingdi Meng](#) <sup>#1</sup>, [Xiaoqiong Shi](#) <sup>1</sup>, [Chengjing Zhu](#) <sup>1</sup>, [Minhui Zhu](#) <sup>2</sup>, [Haihong Tang](#) <sup>3</sup>, [Hongliang Zheng](#) <sup>4</sup>

Affiliations Expand

- PMID: 39107483
- PMCID: [PMC11303539](#)
- DOI: [10.1038/s41598-024-69228-3](#)

Abstract

Several studies reveal that allergic rhinitis (AR) is a significant risk factor of systemic lupus erythematosus (SLE). However, studies investigating the common pathogenesis linking AR and SLE are lacking. Our study aims to search for the shared biomarkers and mechanisms that may provide new therapeutic targets for preventing AR from developing SLE. GSE50223 for AR and GSE103760 for SLE were downloaded from the Gene Expression Omnibus (GEO) database to screen differentially expressed genes (DEGs). The Gene Ontology (GO) analysis and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis were performed to explore the functions of shared DEGs. Hub genes were screened by cytoHubba (a plugin of Cytoscape) and validated in another two

**datasets. Gene set enrichment analysis (GSEA) and single-sample Gene set enrichment analysis (ssGSEA) algorithm were applied to understand the functions of hub gene. ENTPD1 was validated as a hub gene between AR and SLE. GSEA results revealed that ENTPD1 was associated with KRAS\_SIGNALING\_UP pathway in AR and related to HYPOXIA, TGF\_BETA\_SIGNALING and TNFA\_SIGNALING\_VIA\_NFKB pathways in SLE. The expression of ENTPD1 was positively correlated with activated CD8 T cell in both diseases. Thus, ENTPD1 may be a novel therapeutic target for preventing AR from developing SLE.**

**Keywords: ENTPD1; Allergic rhinitis; Bioinformatics; CD4+T cells; Systemic lupus erythematosus.**

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**Conflict of interest statement**

**The authors declare no competing interests.**

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- [7 figures](#)**

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Int Arch Allergy Immunol

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. 2024 Aug 6:1-10.

doi: 10.1159/000540358. Online ahead of print.

[Causal Effects of Asthma on Upper Airway Diseases and Allergic Diseases: A Two-Sample Mendelian Randomization](#)

[Zengxiao Zhang<sup>1</sup>, Gongfei Li<sup>2</sup>, Shizhe Zhou<sup>3</sup>, Minghui Wang<sup>4</sup>, Longgang Yu<sup>5</sup>, Yan Jiang<sup>5</sup>](#)

Affiliations Expand

. PMID: 39106836

. DOI: [10.1159/000540358](#)

Abstract

**Introduction:** Asthma is associated with upper airway diseases and allergic diseases; however, the causal effects need to be investigated further. Thus, we performed this two-sample Mendelian randomization (MR) analysis to explore and measure the causal effects of asthma on allergic rhinitis (AR), vasomotor rhinitis (VMR), allergic conjunctivitis (AC), atopic dermatitis (AD), and allergic urticaria (AU).

**Methods:** The data for asthma, AR, VMR, AC, AD, and AU were obtained from large-scale genome-wide association studies summarized recently. We defined single-nucleotide polymorphisms satisfying the MR assumptions as instrumental variables. Inverse-variance weighted (IVW) approach under random-effects was applied as the dominant method for causal estimation. The weighted median approach, MR-Egger regression analysis, MR pleiotropy residual sum and outlier test, and leave-one-out sensitivity analysis were performed as sensitivity analysis. Horizontal pleiotropy was measured using MR-Egger regression analysis. Significant causal effects were attempted for replication and meta-analysis.

**Results:** We revealed that asthma had causal effects on AR (IVW, odds ratio [OR] = 1.93; 95% confidence interval [CI], 1.74-2.14;  $p < 0.001$ ), VMR (IVW, OR = 1.40; 95% CI, 1.15-1.71;  $p < 0.001$ ), AC (IVW, OR = 1.65; 95% CI, 1.49-1.82;  $p < 0.001$ ), and AD (IVW, OR = 2.13; 95% CI, 1.82-

2.49;  $p < 0.001$ ). No causal effect of asthma on AU was observed. Sensitivity analysis further assured the robustness of these results. The evaluation of the replication stage and meta-analysis further confirmed the causal effect of asthma on AR (IVW OR = 1.81, 95% CI 1.62-2.02,  $p < 0.001$ ), AC (IVW OR = 1.44, 95% CI 1.11-1.87,  $p < 0.001$ ), and AD (IVW OR = 1.85, 95% CI 1.42-2.41,  $p < 0.001$ ).

**Conclusions:** We revealed and quantified the causal effects of asthma on AR, VMR, AC, and AD. These findings can provide powerful causal evidence of asthma on upper airway diseases and allergic diseases, suggesting that the treatment of asthma should be a preventive and therapeutic strategy for AR, VMR, AC, and AD.

**Keywords:** Allergic disease; Asthma; Causal effect; Mendelian randomization; Upper airway disease.

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Br J Sports Med

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. 2024 Aug 7:bjsports-2024-108129.

doi: 10.1136/bjsports-2024-108129. Online ahead of print.

[Paris air quality monitoring for the 2024 Olympics and Paralympics: focus on air pollutants and pollen](#)

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Affiliations Expand

. PMID: 39054048

. DOI: [10.1136/bjsports-2024-108129](#)

Free article

Abstract

**Background:** Exposure to air pollution can affect the health of individuals with respiratory disease, but may also impede the health and performance

**of athletes. This is potentially relevant for people travelling to and competing in the Olympic and Paralympic Games (OPG) in Paris. We describe anticipated air quality in Paris based on historical monitoring data and describe the impact of the process on the development of monitoring strategies for future international sporting events.**

**Methods: Air pollutant data for July to September 2020-2023 and pollen data for 2015-2022 were provided by Airparif (particulate matter (PM<sub>2.5</sub>), nitrogen dioxide (NO<sub>2</sub>) and ozone (O<sub>3</sub>)) and RNSA stations in the Paris region. Airparif's street-level numerical modelling provided spatial data for the OPG venues.**

**Results: The maximum daily mean PM<sub>2.5</sub> was 11±6 µg/m<sup>3</sup> at traffic stations, below the WHO recommended daily air quality threshold (AQT). Daily NO<sub>2</sub> concentrations ranged from 5±3 µg/m<sup>3</sup> in rural areas to 17±14 µg/m<sup>3</sup> in urban areas. Near traffic stations, this rose to 40±24 µg/m<sup>3</sup> exceeding the WHO AQT. Both peaked around 06:00 and 20:00 UTC (coordinated universal time). The ambient O<sub>3</sub> level exceeded the AQT on 20 days per month and peaked at 14:00 UTC. The main allergenic taxa from June to September was Poaceae (ie, grass pollen variety).**

**Conclusion: Air pollutant levels are expected to be within accepted air quality thresholds at the Paris OPG. However, O<sub>3</sub> concentrations may be**

**significantly raised in very hot and clear conditions and grass pollen levels will be high, prompting a need to consider and manage this risk in susceptible individuals.**

**Keywords: Athletes; Public health; Rhinitis, Allergic, Seasonal.**

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### **Conflict of interest statement**

**Competing interests: VB, RV, RSE, DB, GO and GF declare having no conflict of interest. A few authors declared they work for a non-profit organisation: NV is resident of the RNSA (French aerobiological monitoring network), is on the Board of the French Societies ATMO (no retribution – non-profit organisation), responsible for air quality monitoring in France, and APPA (association for the prevention of atmospheric pollution, non-profit organisation). He declared receiving funds from French ANSES and ARS (National Research Agency) for projects on pollen pollution and pollinators. VG, FA and JB from Airparif are involved in a project with SOLIDEO (Société de livraison d'ouvrages olympiques) to evaluate cleaning solutions implemented in the Olympic Village.**

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## CHRONIC COUGH

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J Clin Med

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. 2024 Aug 3;13(15):4549.

doi: 10.3390/jcm13154549.

[Characteristics of US Medicare Beneficiaries with Chronic Cough vs. Non-Chronic Cough: 2011-2018](#)

[Seonkyeong Yang](#)<sup>1</sup>, [Shu Huang](#)<sup>1</sup>, [Juan M Hincapie-Castillo](#)<sup>2</sup>, [Xuehua Ke](#)<sup>3</sup>, [Helen Ding](#)<sup>3</sup>, [Mandel R Sher](#)<sup>4</sup>, [Bobby Jones](#)<sup>1</sup>, [Debbie L Wilson](#)<sup>1</sup>, [Wei-Hsuan Lo-Ciganic](#)<sup>5 6 7</sup>

Affiliations Expand

- PMID: 39124815
- PMCID: [PMC11312945](#)
- DOI: [10.3390/jcm13154549](#)

Abstract

**Background:** Chronic cough (CC), characterized as a cough lasting >8 weeks, is a common multi-factorial syndrome in the community, especially in older adults. **Methods:** Using a pre-existing algorithm to identify patients with CC within the 2011-2018 Medicare beneficiaries, we examined trends in gabapentinoid use through repeated cross-sectional analyses and identified distinct utilization

trajectories using group-based trajectory modeling (GBTM) in a retrospective cohort study. Individuals without CC but with any respiratory conditions related to cough served as a comparator group. Results: Among patients with CC, gabapentinoid use increased from 18.6% in 2011 to 24.1% in 2018 ( $p = 0.002$ ), with a similar upward trend observed in the non-CC cohort but with overall lower usage (14.7% to 18.4%;  $p < 0.001$ ). Patients with CC had significantly higher burdens of respiratory and non-respiratory comorbidities, as well as greater healthcare service and medication use compared to the non-CC cohort. The GBTM analyses identified three distinct gabapentinoid utilization trajectories for CC and non-CC patients: no use (77.3% vs. 84.5%), low use (13.9% vs. 10.3%), and high use (8.8% vs. 5.2%). Conclusions: Future studies are needed to evaluate the safety and effectiveness of gabapentinoid use in patients with refractory or unexplained CC in real-world settings.

**Keywords:** Medicare; antitussive; chronic cough; cough medication; drug utilization; gabapentinoid; group-based trajectory model.

#### Conflict of interest statement

Xuehua Ke and Helen Ding are employees of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA and own stock in Merck & Co., Inc., Rahway, NJ, USA. Mandel R. Sher has received consulting fees from Merck & Co., Inc., Rahway, NJ, USA for this study, research funding from Bayer, NeRRe, Bellus, and Shionogi unrelated to this study, and consulting fees from Bayer, Bellus, Merck, NeRRe, Nocion, Shionogi and Soundable Health unrelated to this study. Wei-Hsuan Lo-Ciganic has received research funding from Bristol Myers Squibb unrelated to this study and has a patent pending for U1195.70174US00. Debbie Wilson reported grants from Bristol Myers Squibb outside the submitted work and serves as an editorial board member for the Journal of Pharmacy Technology.

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Am J Respir Crit Care Med

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. 2024 Aug 7.

doi: 10.1164/rccm.202405-0887RL. Online ahead of print.

### [Cough Reflex Hypersensitivity in CANVAS-associated Chronic Cough](#)

[Barnaby Hirons](#)<sup>1,2</sup>, [Peter S P Cho](#)<sup>3,1</sup>, [Riccardo Curro](#)<sup>4,5</sup>, [Bianca Rugginini](#)<sup>4,5</sup>, [Richard D Turner](#)<sup>6,7</sup>, [James H Hull](#)<sup>8</sup>, [Caroline J Jolley](#)<sup>2,1</sup>, [Robert D Hadden](#)<sup>9,10</sup>, [Andrea Cortese](#)<sup>4,5</sup>, [Surinder S Birring](#)<sup>2,11</sup>

#### Affiliations Expand

- PMID: 39110429
- DOI: [10.1164/rccm.202405-0887RL](https://doi.org/10.1164/rccm.202405-0887RL)

*No abstract available*

Keywords: CANVAS; capsaicin tussive challenge; chronic cough; cough hypersensitivity; genetic.

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#### Clinical Trial

#### Respirol Case Rep

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. 2024 Aug 6;12(8):e01449.

doi: 10.1002/rcr2.1449. eCollection 2024 Aug.

[A double-blind randomized controlled trial of N-acetylcysteine \(NAC\) for the treatment of acute exacerbation of chronic obstructive pulmonary disease](#)

[Wang Chung Kwok<sup>1</sup>](#), [Shung Kay Samuel Chan<sup>1</sup>](#), [Ka Yan Chiang<sup>1</sup>](#), [Chung Man James Ho<sup>1</sup>](#)

Affiliations Expand

- PMID: 39108325
- PMCID: [PMC11301653](#)
- DOI: [10.1002/rcr2.1449](#)

Abstract

**Background:** Chronic obstructive pulmonary disease (COPD) is a common respiratory disease with acute exacerbation (AECOPD) being a common sequelae which negatively impact health status, rates of hospitalization and readmission, and disease progression. N-acetylcysteine (NAC) has been studied in COPD in both stable state and acute exacerbations, which has been shown to have small beneficial effects in stable COPD, as well as AECOPD. Yet, there has been lack of study with well-designed protocol to assess the role of NAC in more objective outcomes in AECOPD.

**Methods:** This is a double-blind randomized controlled trial. Patients will be randomized in 1:1 ratio to receive oral NAC at 600 mg twice daily or placebo twice daily with standard of care. Partial pressure of oxygen (PaO<sub>2</sub>), partial pressure of carbon dioxide (PaCO<sub>2</sub>) and the ratio of partial pressure arterial oxygen and fraction of inspired oxygen (PaO<sub>2</sub>/FiO<sub>2</sub>) will be measured on days 1 and 7. The following will be measure at baseline and on day 4 and 7: Forced expiratory volume in one second (FEV<sub>1</sub>), 24-hour sputum volume, oxygen saturation (SaO<sub>2</sub>), end-tidal CO<sub>2</sub>, Leicester Cough Questionnaire (LCQ) score, COPD Assessment Test (CAT) score, grading of wheeze and grade of dyspnoea; blood inflammatory markers (leucocyte count, neutrophil count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and high sensitivity CRP (hs-CRP)). Patients will be randomized to oral NAC at 600 mg twice daily or placebo for 7 days. The main outcome measures include: The difference in PaO<sub>2</sub> on day 7. Secondary outcome: Change in following parameters on day 4/7 from baseline: FEV<sub>1</sub>, sputum volume, CAT score, LCQ score, SaO<sub>2</sub>, grade of wheeze; mMRC Dyspnoea Scale, end-tidal CO<sub>2</sub>, blood inflammatory marker, change in PaO<sub>2</sub>/FiO<sub>2</sub> ratio from baseline to day 7, PaCO<sub>2</sub> on day 7, 28 and 90 days' mortality, time to wean off supplemental oxygen, length of stay. Primary and secondary outcomes will be compared among the two treatment groups with two-sample *t*-test.

**Discussion:** We hypothesize that NAC use in COPD exacerbation can provide benefits in clinical and laboratory parameters.

**Trial registration:** *Name of the registry* : ClinicalTrials.gov *Trial registration number* : [NCT05706402](#). *URL of the trial registry record for this trial* : <https://classic.clinicaltrials.gov/ct2/show/NCT05706402> *Date of registration* :

Registered on 11th January 2023 *Funding of the trial* : The Health and Medical Research Fund (HMRF). *Name and contact information for the trial sponsor* : Wang Chung Kwok, Clinical Assistant Professor, Honorary Associate Consultant, Queen Mary Hospital, The University of Hong Kong, Hong Kong. *Role of sponsor* : The funder is not involved in the planning of the study, gathering, analysing, and interpreting the data, or in preparing the manuscript.

Keywords: COPD, COPD exacerbation; N-acetylcysteine; RCT.

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#### Conflict of interest statement

There will be no conflict of interests from both the department and any of the investigators involved. Ka Yan Chiang and Chung Man James Ho are Editorial Board members of *Respirology Case Reports* and co-authors of this article. They were excluded from all editorial decision-making related to the acceptance of this article for publication.

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#### J Voice

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. 2024 Aug 5:S0892-1997(24)00232-7.

doi: 10.1016/j.jvoice.2024.07.020. Online ahead of print.

[Temporary Vocal Fold Augmentation Outcomes for Refractory Chronic Cough with Concurrent Nonparalytic Glottic Insufficiency due to Vocal Fold Atrophy](#)

[Christopher D Dwyer](#)<sup>1</sup>, [Mira Fein](#)<sup>1</sup>, [Lindsey Gordon](#)<sup>1</sup>, [Samantha Kridgen](#)<sup>1</sup>, [Douglas Roth](#)<sup>1</sup>, [Jennifer Winston](#)<sup>1</sup>, [Thomas L Carroll](#)<sup>2</sup>

## Affiliations Expand

- PMID: 39107214
- DOI: [10.1016/j.jvoice.2024.07.020](https://doi.org/10.1016/j.jvoice.2024.07.020)

## Abstract

**Objective:** Determine the effect of temporary vocal fold augmentation on refractory chronic cough (RCC) in patients with glottic insufficiency (GI) due to vocal fold atrophy.

**Methods:** Retrospective electronic chart review was conducted for patients with a diagnosis of bilateral vocal fold atrophy and RCC undergoing vocal fold augmentation with carboxymethylcellulose (CMC). Patients with vocal fold immobility were excluded, and cough must have been present for at minimum 8 weeks. VHI-10, CSI, and RSI scores along with subjective overall patient report of chronic cough improvement were collected.

**Results:** A total of 28 patients underwent 30 vocal fold augmentation procedures with CMC. All had undergone extensive cough work-up and treatment trials prior to their augmentation procedure. From chart review, 13 overall subjectively reported satisfactory improvement in their cough, 5 reported partial improvement, and 7 reported no improvement in their cough. An uncertain effect on cough was documented in 5 (either patient was uncertain or no mention of cough symptom in the interval chart history note). For those subjects with both pre- and post-augmentation data, mean preaugmentation CSI:  $22.08 \pm 6.8$  ( $n = 13$ ); VHI-10:  $13.6 \pm 8.9$  ( $n = 18$ ); RSI:  $22.4 \pm 7.5$  ( $n = 17$ ). Mean postaugmentation CSI was  $20.7 \pm 9.2$  ( $n = 13$ ); VHI-10:  $15.2 \pm 8.2$  ( $n = 18$ ); RSI:  $21.1 \pm 5.8$  ( $n = 17$ ). Mean pre-post change in CSI was  $-1.4 \pm 5.1$  ( $P = 0.175$ ,  $n = 13$ , range  $-10$  to  $+6$ ).

**Conclusions:** Vocal fold augmentation seems to provide subjective cough improvement in some patients with concurrent GI due to vocal fold atrophy and RCC. It can be offered as a diagnostic trial, on which further augmentation may be offered, for patients with persistent cough despite prior work-up and treatment trials. Further controlled prospective studies are needed to identify factors that are predictive of successful cough improvement following vocal fold augmentation, as well as the effect of durable augmentation in those patients who had improvement with a diagnostic trial.

**Keywords:** Chronic cough; Glottic insufficiency; Injection laryngoplasty; Trial vocal fold injection; Vocal fold augmentation.

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## Conflict of interest statement

**Declaration of Competing Interest** The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Thomas L. Carroll reports a relationship with Pentax Medical, GSK, Ambu that includes: consulting or advisory. Thomas L. Carroll reports a relationship with Sofregen Medical Inc. that includes: board membership. Thomas L. Carroll reports a

relationship with N-Zyme Biomedical that includes: consulting or advisory and equity or stocks. Thomas L. Carroll reports a relationship with Plural Publishing that includes: equity or stocks. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Editorial

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. 2024 Aug 5;10(4):00449-2024.

doi: 10.1183/23120541.00449-2024. eCollection 2024 Jul.

[Chronic cough: symptom, sign or disease?](#)

[Alyn Morice<sup>1</sup>](#)

Affiliations Expand

- PMID: 39104960
- PMCID: [PMC11298998](#)
- DOI: [10.1183/23120541.00449-2024](#)

Abstract

Heritability can be added to the characteristics of chronic cough, making it a disease in its own right <https://bit.ly/3ykD6gB>.

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## Conflict of interest statement

Conflict of interest: A. Morice has received consulting fees from Bayer, Bellus, Merck, NeRRi, Shionogi and Trevi; lecture fees from Boehringer Ingelheim, Merck and Chiesi; and grant support from Bayer, Bellus, Merck, Noción, Philips, NeRRi, Shionogi and Trevi. He is an associate editor of this journal.

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. 2024 Aug 5;10(4):00071-2024.

doi: 10.1183/23120541.00071-2024. eCollection 2024 Jul.

[Heritability of cough across two generations: the RHINESSA study](#)

[Össur Ingi Emilsson](#)<sup>1,2</sup>, [Henrik Johansson](#)<sup>3</sup>, [Ane Johannessen](#)<sup>4</sup>, [Christer Janson](#)<sup>1</sup>, [Andreas Palm](#)<sup>1</sup>, [Karl A Franklin](#)<sup>5</sup>, [Anna Oudin](#)<sup>6</sup>, [Francisco Gómez Real](#)<sup>7,8</sup>, [Mathias Holm](#)<sup>9</sup>, [Thorarinn Gislason](#)<sup>2,10</sup>, [Eva Lindberg](#)<sup>1</sup>, [Rain Jõgi](#)<sup>11</sup>, [Vivi Schlünssen](#)<sup>12</sup>, [Francisco Javier Callejas-González](#)<sup>13</sup>, [Jingwen Zhang](#)<sup>14</sup>, [Andrei Malinowski](#)<sup>15</sup>, [Cecilie Svanes](#)<sup>16,17</sup>, [Magnus Ekström](#)<sup>18</sup>

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- PMID: 39104957
- PMCID: [PMC11299003](#)
- DOI: [10.1183/23120541.00071-2024](#)

## Abstract

**Aim:** Heritability of cough has not yet been studied. We aimed to evaluate if individuals with cough are more likely to have offspring who develop cough, and if these associations differ by type of cough (productive/nonproductive).

**Methods:** The RHINESSA Generation Study (Respiratory Health In Northern Europe, Spain and Australia) includes 7155 parents (initially aged 30-54) answering detailed questionnaires in 2000 and 2010, and 8176 offspring  $\geq 20$  years answering similar questionnaires in 2012-2019. Chronic cough was categorised as productive or nonproductive (dry) cough. Associations between parental and offspring cough were analysed using mixed-effects logistic regression, adjusting for offspring age, sex, body mass index, smoking history, education level, current asthma, rhinitis, nocturnal gastroesophageal reflux; parent sex and smoking history; centre and family.

**Results:** Among parents with nonproductive cough, 11% of their offspring reported nonproductive cough, compared with 7% of offspring to parents without nonproductive cough, adjusted odds ratio (aOR) 1.59 (95% confidence interval 1.20-2.10). Among parents with productive cough, 14% of their offspring reported productive cough, compared with 11% of offspring to parents without productive cough, aOR 1.34 (1.07-1.67). No associations were found between parent productive cough-offspring nonproductive cough, nor between parent nonproductive cough-offspring productive cough.

**Conclusions:** Parents with chronic cough are more likely to have offspring with chronic cough independent of parental asthma, suggesting cough to be a separate heritable trait. The type of cough is important, as the nonproductive cough in parent associates only with nonproductive cough in offspring, and the same applied for productive cough.

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### Conflict of interest statement

**Conflict of interest:** Ö.I. Emilsson has participated in advisory boards with MSD Sweden, not related to this manuscript. The other authors have no other competing interests to declare.

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## Qual Life Res

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. 2024 Aug 3.

doi: 10.1007/s11136-024-03694-0. Online ahead of print.

[The validity of single-item measures of health-related quality of life across groups differing in acute respiratory symptom severity](#)

[Adam B Smith](#)<sup>1</sup>, [John E Ware Jr](#)<sup>2</sup>, [Patricia Aluko](#)<sup>3</sup>, [Anuradha Kulasekaran](#)<sup>4</sup>

## Affiliations Expand

- PMID: 39096424
- DOI: [10.1007/s11136-024-03694-0](#)

## Abstract

**Purpose:** Practical considerations precluding health-related quality of life (HRQOL) monitoring in population and clinical research have spawned development of improved items for more brief surveys of frequently measured HRQOL outcomes. The aim of this study was to validate the use of the Quality of Life General (QGEN-8), a shorter 8-item alternative to the longer 36-item short form (SF)-36 Health Survey for measuring the same eight HRQOL domains across groups of adults with varying severity of acute respiratory symptoms, such as cough and sore throat.

**Methods:** National Opinion Research Center (NORC) representative probability (N = 1,648) and supplemental opt-in (N = 5,915) U.S. adult samples were surveyed cross-sectionally online in 2020. Parallel analyses compared QGEN-8 and SF-36 estimates of group means for each of eight matching profile domains and summary physical and mental scores across groups differing in severity of acute symptoms and chronic respiratory conditions using analysis of covariance (ANCOVAs) controlling for socio-demographics and presence of chronic respiratory conditions.

**Results:** In support of discriminant validity, ANCOVA estimates of QGEN-8 means with SF-36 estimates revealed the same patterns of declining HRQOL with the presence and increasing severity of symptoms and chronic condition severity.

**Conclusion:** QGEN-8<sup>®</sup> shows satisfactory validity and warrants further testing in cross-sectional and longitudinal population and clinical survey research as a more practical method for estimating group differences in SF-36 profile and summary component HRQOL scores.

**Keywords:** Acute respiratory; Chronic co-morbid conditions; Cough; HRQOL; QGEN-8; SF-36; Sore throat.

## Plain language summary

Upper respiratory tract infections (URTI) with symptoms such as cough and sore throat are highly prevalent and negatively impact on health-related quality of life (HRQOL). Existing instruments that comprehensively measure HRQOL are lengthy, potentially increasing respondent burden and restricting their use in clinical studies and research. The aim of this study was to evaluate whether eight newly constructed survey items, the QGEN-8®, measure the same HRQOL outcomes as the 36-item SF-36 Health Survey well enough to serve as a more practical alternative for purposes of detecting the physical and mental HRQOL effects on differing severity of acute URTI symptoms, specifically cough and sore throat. The results showed that the QGEN-8® was psychometrically sound and able to differentiate between different levels of URTI symptoms, even in cases where respondents had chronic respiratory conditions. This indicates that the briefer QGEN-8® with 75% shorter response time is able to provide HRQOL measurements comparable to those derived from lengthier instruments thereby lending itself more readily to use in clinical studies and research of URTI symptoms, such as cough and sore throat.

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- [26 references](#)

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

1

Eur J Med Res

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. 2024 Aug 10;29(1):413.

doi: 10.1186/s40001-024-01994-2.

[Construction of a panoramic mRNA map of adult noncystic fibrosis bronchiectasis and a preliminary study of the underlying molecular mechanisms](#)

[Wan-Ying Huang](#) <sup>#1</sup>, [Kang-Kang Hong](#) <sup>#2</sup>, [Jing Luo](#) <sup>2</sup>, [Rong-Quan He](#) <sup>3</sup>, [Zhi-Guang Huang](#) <sup>1</sup>, [Yang Xu](#) <sup>2</sup>, [Chu-Yue Zhang](#) <sup>2</sup>, [Chong-Xi Bao](#) <sup>2</sup>, [Liang-Ming Zhang](#) <sup>3</sup>, [Gang Chen](#) <sup>4</sup>, [Jin-Liang Kong](#) <sup>5</sup>

#### Affiliations Expand

- PMID: 39127654
- PMCID: [PMC11316334](#)
- DOI: [10.1186/s40001-024-01994-2](#)

#### Abstract

**Background:** The pathogenesis of noncystic fibrosis bronchiectasis in adults is complex, and the relevant molecular mechanisms remain unclear. In this study, we constructed a panoramic map of bronchiectasis mRNA, explored the potential molecular mechanisms, and identified potential therapeutic targets, thus providing a new clinical perspective for the preventive management of bronchiectasis and its acute exacerbation.

**Methods:** The mRNA profiles of peripheral blood and bronchiectasis tissues were obtained through transcriptome sequencing and public databases, and bioinformatics methods were used to screen for differentially expressed genes (DEGs). The DEGs were then subjected to biological function and pathway analyses. Some DEGs were validated using a real-time quantitative polymerase chain reaction (RT-qPCR) in peripheral blood. Spearman's correlation analysis was used to analyse the correlation between DEGs and clinical indicators.

**Results:** Based on transcriptome sequencing and public databases, the mRNA profile of bronchiectasis was determined. DEGs were obtained from the peripheral blood sequencing dataset (985 DEGs), tissue sequencing dataset (2919 DEGs), and GSE97258 dataset (1083 DEGs). Bioinformatics analysis showed that upregulated DEGs had enriched neutrophil-related pathways, and downregulated DEGs had enriched ribosome-related pathways. RT-qPCR testing confirmed the upregulated expression of VCAN, SESTD1, SLC12A1, CD177, IFI44L, SIGLEC1, and RSAD2 in bronchiectasis. These genes were related to many clinical parameters, such as neutrophils, C-reactive protein, and procalcitonin ( $P < 0.05$ ).

**Conclusions:** Transcriptomic methods were used to construct a panoramic map of bronchiectasis mRNA expression. The findings showed that neutrophil activation, chronic inflammation, immune regulation, impaired ribosomal function, oxidative phosphorylation, and energy metabolism disorders are important factors in the development of bronchiectasis. VCAN, SESTD1, SLC12A1, CD177, IFI44L, SIGLEC1, and RSAD2 may play important roles in the pathogenesis of bronchiectasis and are potential therapeutic targets.

**Keywords:** Bronchiectasis; DEGs; Pathogenesis; mRNA.

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## Conflict of interest statement

The authors declare no competing interests.

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## Review

## Insights Imaging

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. 2024 Aug 7;15(1):197.

doi: 10.1186/s13244-024-01742-4.

## [Imaging findings of thoracic manifestations of Crohn's disease and ulcerative colitis](#)

[Quentin Cassius De Linval](#)<sup>1</sup>, [Maxime Barat](#)<sup>1,2</sup>, [Mathilde Aissaoui](#)<sup>1,2</sup>, [Marie-Pauline Talabard](#)<sup>1</sup>, [Clémence Martin](#)<sup>2,3</sup>, [Georgia Malamut](#)<sup>2,4</sup>, [Emma Canniff](#)<sup>1,2</sup>, [Philippe Soyer](#)<sup>1,2</sup>, [Marie-Pierre Revel](#)<sup>1,2</sup>, [Guillaume Chassagnon](#)<sup>5,6</sup>

## Affiliations [Expand](#)

- PMID: 39112694
- PMCID: [PMC11306860](#)

- DOI: [10.1186/s13244-024-01742-4](https://doi.org/10.1186/s13244-024-01742-4)

## Abstract

Thoracic manifestations of inflammatory bowel disease (IBD) are rare, occurring in less than 1% of patients. Unlike most other extra-intestinal manifestations, they predominate in patients with ulcerative colitis rather than in Crohn's disease. In most patients, thoracic involvement follows the onset of IBD by several years. However, thoracic involvement may also occur synchronously or even precede the onset of digestive symptoms. The thoracic manifestations of IBD include airway involvement and parenchymal lung abnormalities. Airways are the most frequent anatomical site for thoracic involvement in IBD. Airway manifestations usually develop several years after the onset of intestinal manifestations, preferentially when the latter are stable or in remission. Airway manifestations include bronchial wall thickening, bronchiectasis, small airway disease, and tracheal wall thickening. Parenchymal lung abnormalities are less prevalent in IBD and include organizing pneumonia, necrobiotic nodules, noncaseating granulomatous nodules, drug-induced pneumonia, and rarely interstitial lung diseases. The differential diagnosis between organizing pneumonia, necrobiotic nodules, and noncaseating granulomatous nodules is difficult and usually requires histopathological analysis for a definite diagnosis. Radiologists play a key role in the detection of thoracic manifestations of Crohn's disease and ulcerative colitis and, therefore, need to be familiar with their imaging findings. This article aims to offer an overview of the imaging findings of thoracic manifestations in patients with Crohn's disease or ulcerative colitis. **CRITICAL RELEVANCE STATEMENT:** Thoracic manifestations of Crohn's disease and ulcerative colitis include tracheal involvement, bronchiectasis, small airway disease, and parenchymal lung abnormalities such as organizing pneumonia and necrobiotic nodules. These rare manifestations (< 1% of patients) more often affect patients with ulcerative colitis. **KEY POINTS:** Thoracic manifestations of inflammatory bowel disease are rare, occurring in less than 1% of patients. Thoracic manifestations are more frequent in patients with ulcerative colitis than Crohn's disease. Bronchial disease is the most frequent thoracic manifestation of Crohn's disease and ulcerative colitis.

**Keywords:** Bronchial diseases; Inflammatory bowel diseases; Multidetector computed tomography; Pneumonia; Tracheal diseases.

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## Conflict of interest statement

The authors declare that they have no competing interests.

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[Associations between chronic rhinosinusitis and the development of non-cystic fibrosis bronchiectasis](#)

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Abstract

**Background:** Studies have shown an association between chronic rhinosinusitis (CRS) and non-cystic fibrosis (CF) bronchiectasis.

**Objective:** We aimed to determine if CRS increases the risk of developing non-CF bronchiectasis.

**Methods:** A retrospective analysis was conducted utilizing electronic medical records from an academic center. Patients with CRS without bronchiectasis, with at least one chest computed tomography (CT) performed after the diagnosis of CRS, were identified between January 2006 and December 2015. Charts were reviewed until May 2022. The control group was age, sex, and race matched, and included patients without CRS, asthma, or chronic obstructive pulmonary disease (COPD) who had at least one chest CT. Bronchiectasis was identified by chest CT radiology reports. The odds of developing bronchiectasis were analyzed in patients with CRS without asthma or COPD (Cohort 1) and patients with CRS with asthma or COPD (Cohort 2).

**Results:** The odds of developing bronchiectasis were significantly higher in patients with CRS (139/1594, 8.7%) compared to patients in the control group (443/7992 [5.5%], OR 1.63 [1.34-1.99]). Furthermore, the odds of developing bronchiectasis were higher in Cohort 1 (63/863 [7.3%], OR 1.34 [1.02-1.76]) and Cohort 2 (76/731 [10.4%], OR 1.98 [1.53-2.55]) versus the control group. After adjusting for confounding diseases, the association was attenuated in Cohort 1 (OR 1.22 [0.92-1.61]) but remained significant in Cohort 2 (OR 1.78 [1.37-2.31]).

**Conclusions:** CRS is associated with the future development of non-CF bronchiectasis. Patients with CRS, especially those with asthma or COPD, have a higher likelihood of developing bronchiectasis than patients without CRS.

**Keywords:** chronic rhinosinusitis; non-cystic fibrosis bronchiectasis.

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Excerpt

**Clinical characteristics:** Cystic fibrosis (CF) is a multisystem disease affecting epithelia of the respiratory tract, exocrine pancreas, intestine, hepatobiliary system, and exocrine sweat glands. Morbidities include recurrent sinusitis and bronchitis, progressive obstructive pulmonary disease with bronchiectasis, exocrine pancreatic deficiency and malnutrition, pancreatitis, gastrointestinal manifestations (meconium ileus, rectal prolapse, distal intestinal obstructive syndrome), liver disease, diabetes, male infertility due to hypoplasia or aplasia of the vas deferens, and reduced fertility or infertility in some women. Pulmonary disease is the major cause of morbidity and mortality in CF.

**Diagnosis/testing:** The diagnosis of CF is established in a proband with (1) elevated immunoreactive trypsinogen on newborn screen, signs and/or symptoms suggestive of CF, or family history of CF; AND (2) evidence of an abnormality in cystic fibrosis transmembrane conductance regulator (CFTR) function: sweat chloride  $\geq 60$  mmol/L on sweat chloride testing, biallelic *CFTR* CF-causing pathogenic variants, or nasal transmembrane epithelial potential difference measurement consistent with CF.

**Management:** *Targeted therapies:* CFTR modulator therapy is available for individuals with responsive *CFTR* variants.

**Supportive care:** Newborns: management by a CF specialist or CF care center; airway clearance instruction; encouraging feeding with breast milk; routine vaccinations; contact precautions with every encounter; antibiotics for bacterial suppression and treatment; nutrition management; pancreatic enzyme replacement; nutrient-dense food and supplements; fat-soluble vitamin supplements; laxative treatment as needed with surgical management for bowel obstruction; and salt and water supplementation.

After the newborn period: airway clearance; pulmonary treatment (bronchodilator, hypertonic saline, dornase alfa, airway clearance, inhaled corticosteroids and/or long-acting beta agonist, and aerosolized antibiotic); standard treatments for pneumothorax or hemoptysis; double lung transplant for those with advanced lung disease; routine vaccinations including influenza; contact precautions; antibiotics for bacterial suppression and treatment; antibiotics and/or surgical intervention for nasal/sinus symptoms; nutrition management; pancreatic enzyme replacement; nutrient-dense food and supplements; fat-soluble vitamin supplements; laxative treatment as needed with surgical management for bowel obstruction; standard treatments for gastroesophageal reflux disease; oral ursodiol for biliary sludging/obstruction; liver transplant when indicated; management of CF-related diabetes mellitus by an endocrinologist; assisted reproductive technologies (ART) for infertility; salt and water supplementation; standard treatments for associated mental health issues.

**Surveillance:** Frequent assessment by a CF specialist to monitor for new or worsening manifestations; pulmonary function testing frequently after age five years; chest radiograph or chest CT examination to assess for bronchiectasis every two years or as needed; cultures of respiratory tract secretions at least every three months; non-tuberculosis mycobacterium culture and serum IgE annually or as indicated; annual CBC with differential; annual ENT assessment; monitoring growth and GI manifestations at each visit; fecal elastase as needed; annual serum vitamin A, D, E, and PT (as a marker of vitamin K); annual liver function tests; annual random glucose, annual two-hour glucose tolerance test beginning at age ten years;

**DXA scan as needed in adolescence; infertility assessment as needed; annual electrolytes, BUN, and creatinine; annual assessment of depression and anxiety.**

***Agents/circumstances to avoid:*** Environmental smoke, exposure to respiratory infections, dehydration.

***Evaluation of relatives at risk:*** Molecular genetic testing of at-risk sibs (if the pathogenic variants in the family are known) or sweat chloride testing of at-risk sibs (if the pathogenic variants in the family are not known) to identify as early as possible those who should be referred to a CF center for initiation of early treatment.

**Genetic counseling:** CF is inherited in an autosomal recessive manner. If both parents are known to be heterozygous for a *CFTR* pathogenic variant, each sib of an affected individual has at conception a 25% chance of being affected, a 50% chance of being heterozygous, and a 25% chance of inheriting neither of the familial pathogenic variants. Once the *CFTR* pathogenic variants have been identified in an affected family member, targeted heterozygote testing for at-risk relatives and prenatal/preimplantation genetic testing for CF are possible.

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## [Fixing lung health in the UK: accelerating respiratory research and innovation](#)

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**Keywords:** asthma; bronchiectasis; cystic fibrosis; idiopathic pulmonary fibrosis; interstitial fibrosis; pulmonary disease, chronic obstructive; respiratory infection; respiratory measurement.

Conflict of interest statement

**Competing interests:** Eric Alton Royalties or licenses: Royalties from Boehringer Ingelheim related to cystic fibrosis gene therapy programme. Consulting fees: Boehringer Ingelheim - payments made to EA and institution; AlveoGene - payments made to EA. Patents planned, issued or pending: multiple patents filed by Imperial College. Participation on a Data Safety Monitoring Board or Advisory Board: Boehringer Ingelheim Advisory Board - payments made to EA Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid. Founder Director, AlveoGeneStock or stock options AlveoGene shares - payments to EA. Sam Walker Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid co-Chair of Lung Research and Innovation Group (LRIG). Ian Hall: Grants or contracts from any entity. NIHR Senior Investigator Award - research grant to institution. Support for attending meetings and/or travel. Travel to AUKCAR meeting in Reading, 2024 - Expenses covered by Asthma+Lung UK Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid co-Chair of Lung Research and Innovation Group (LRIG).

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