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THIS TIME NEW FORMAT, LESS ELEGANT FORMAT BUT SIMPLER AND INCLUDES ABSTRACT AND INFO RE OPEN ACCESS ARTICLES.

## COPD

PLoS One

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. 2022 Jul 8;17(7):e0270468.

doi: 10.1371/journal.pone.0270468. eCollection 2022.

## [Evaluation of risk adjustment performance of diagnosis-based and medication-based comorbidity indices in patients with chronic obstructive pulmonary disease](#)

[Huei Guo Ie](#)<sup>1</sup>, [Chao-Hsiun Tang](#)<sup>2</sup>, [Mei-Ling Sheu](#)<sup>2</sup>, [Hung-Yi Liu](#)<sup>3</sup>, [Ning Lu](#)<sup>4</sup>, [Tuan-Ya Tsai](#)<sup>5</sup>, [Bi-Li Chen](#)<sup>6</sup>, [Kuo-Cherh Huang](#)<sup>2</sup>

Affiliations expand

- PMID: 35802678
- DOI: [10.1371/journal.pone.0270468](https://doi.org/10.1371/journal.pone.0270468)

# Abstract

**Objectives:** This study assessed risk adjustment performance of six comorbidity indices in two categories of comorbidity measures: diagnosis-based comorbidity indices and medication-based ones in patients with chronic obstructive pulmonary disease (COPD).

**Methods:** This was a population-based retrospective cohort study. Data used in this study were sourced from the Taiwan National Health Insurance Research Database. The study population comprised all patients who were hospitalized due to COPD for the first time in the target year of 2012. Each qualified patient was individually followed for one year starting from the index date to assess two outcomes of interest, medical expenditures within one year after discharge and in-hospital mortality of patients. To assess how well the added comorbidity measures would improve the fitted model, we calculated the log-likelihood ratio statistic G<sub>2</sub>. Subsequently, we compared risk adjustment performance of the comorbidity indices by using the Harrell c-statistic measure derived from multiple logistic regression models.

**Results:** Analytical results demonstrated that that comorbidity measures were significant predictors of medical expenditures and mortality of COPD patients. Specifically, in the category of diagnosis-based comorbidity indices the Elixhauser index was superior to other indices, while the RxRisk-V index was a stronger predictor in the framework of medication-based codes, for gauging both medical expenditures and in-hospital mortality by utilizing information from the index hospitalization only as well as the index and prior hospitalizations.

**Conclusions:** In conclusion, this work has ascertained that comorbidity indices are significant predictors of medical expenditures and mortality of COPD patients. Based on the study findings, we propose that when designing the payment schemes for patients with chronic diseases, the health authority should make adjustments in accordance with the burden of health care caused by comorbid conditions.

## Conflict of interest statement

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Chronic Obstr Pulm Dis

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. 2022 Jul 7.

doi: 10.15326/jcopdf.2022.0293. Online ahead of print.

# Effect of Two Interventional Strategies on Improving Continuous Positive Airway Pressure Adherence in Existing COPD and Obstructive Sleep Apnea Patients: The O2VERLAP Study

[Sergio Martinez](#)<sup>1</sup>, [Jamie Sullivan](#)<sup>1</sup>, [Cara Pasquale](#)<sup>1</sup>, [Bill Clark](#)<sup>1</sup>, [Elisha Malanga](#)<sup>1</sup>, [Sean Deering](#)<sup>2</sup>, [Lin Liu](#)<sup>2</sup>, [Carl J Stepnowsky](#)<sup>2</sup>

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- PMID: 35797447
- DOI: [10.15326/jcopdf.2022.0293](https://doi.org/10.15326/jcopdf.2022.0293)

**Free article**

## Abstract

**Background:** Obstructive sleep apnea (OSA), a sleep disorder prevalent in >10% of individuals diagnosed with chronic obstructive pulmonary disease (COPD). Continuous positive airway pressure (CPAP) is the first-line therapy for OSA, but many don't use it enough during sleep to effectively manage OSA. The study compared Proactive Care (PC; structured web-based peer-coaching education and support intervention) vs Reactive Care (RC; education and support based on limited scheduled interactions and patient-initiated contacts).

**Methods:** Participants were primarily recruited from patient communities (COPD, OSA, and PCORnet) through electronic methods. Inclusion criteria: ≥40 years old, diagnosis of both COPD and OSA, and currently using CPAP. Participants were then randomly assigned to either the PC or RC group, with outcomes assessed at baseline, 6 and 12 weeks. The primary study outcome was CPAP adherence (hours of use/night) and secondary outcomes

were daytime functioning, sleep quality, and daytime sleepiness. Changes in outcomes over time were examined using random effects models.

**Results:** The study enrolled 332 participants of which 294 were randomized. While groups differed significantly in CPAP adherence at baseline (PC:  $6.1 \pm 3.1$ , RC:  $7.3 \pm 2.4$  hours/night;  $P < 0.001$ ), there were no significant differences in change of primary and secondary outcomes at either 6 or 12 weeks.

**Conclusion:** In this group of patients with both COPD and OSA on CPAP therapy, no difference was found between the provision of PC and RC. The study did find unexpectedly high baseline CPAP adherence levels, which suggests that any improvement from the intervention would have been very small and difficult to detect.

**Keywords:** COPD.

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Infect Dis (Lond)

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. 2022 Jul 6;1-10.

doi: 10.1080/23744235.2022.2092648. Online ahead of print.

## [Impact of bacterial strain acquisition in the lung of patients with COPD: the AERIS study](#)

[Lucio Malvisi](#)<sup>1</sup>, [Aparna Yarraguntla](#)<sup>2</sup>, [Marie-Cécile Mortier](#)<sup>3</sup>, [Karen Osman](#)<sup>4</sup>, [David W Cleary](#)<sup>4,5</sup>, [Béatrice Sente](#)<sup>3</sup>, [Thierry G Pascal](#)<sup>2</sup>, [Vincent Weynants](#)<sup>2</sup>, [Stuart C Clarke](#)<sup>4,6</sup>, [Laura Taddei](#)<sup>1</sup>, [Tom M A Wilkinson](#)<sup>4,5,6</sup>, [Jeanne-Marie Devaster](#)<sup>3</sup>, [Nathalie Devos](#)<sup>3</sup>, [AERIS Study Group](#)

Collaborators, Affiliations expand

- PMID: 35794793
- DOI: [10.1080/23744235.2022.2092648](https://doi.org/10.1080/23744235.2022.2092648)

## Abstract

**Background:** Bacterial infections are associated with acute exacerbations of chronic obstructive pulmonary disease (AECOPD), but the mechanism is incompletely understood.

**Method:** In a COPD observational study ([NCT01360398](#)), sputum samples were collected monthly at the stable state and exacerbation. *Post-hoc* analyses of 1307 non-typeable *Haemophilus influenzae* (NTHi) isolates from 20 patients and 756 *Moraxella catarrhalis* isolates from 38 patients in one year of follow-up were conducted by multilocus sequence typing (MLST). All isolates came from cultured sputum samples that were analyzed for bacterial species presence, apparition (infection not detected at the preceding visit), or acquisition (first-time infection), with the first study visit as a baseline. Strain apparition or new strain acquisition was analyzed by MLST. The odds ratio (OR) of experiencing an exacerbation vs. stable state was estimated by conditional logistic regression modelling, stratified by patient.

**Results:** The culture results confirmed a significant association with exacerbation only for NTHi species presence (OR 2.28; 95% confidence interval [CI]: 1.12-4.64) and strain apparition (OR 2.38; 95% CI: 1.08-5.27). For *M. catarrhalis*, although confidence intervals overlapped, the association with exacerbation for first-time species acquisition (OR 5.99; 2.75-13.02) appeared stronger than species presence (OR 3.67; 2.10-6.40), new strain acquisition (OR 2.94; 1.43-6.04), species apparition (OR 4.18; 2.29-7.63), and strain apparition (OR 2.78; 1.42-5.42). This may suggest that previous *M. catarrhalis* colonization may modify the risk of exacerbation associated with *M. catarrhalis* infection.

**Conclusions:** The results confirm that NTHi and *M. catarrhalis* infections are associated with AECOPD but suggest different dynamic mechanisms in triggering exacerbations.

**Keywords:** Exacerbation; *Moraxella catarrhalis*; acquisition; apparition; bacteria; non-typeable *Haemophilus influenzae*.

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. 2022 Jul 6.

doi: 10.1007/s41030-022-00194-9. Online ahead of print.

# [Respiratory Symptoms among US Adults: a Cross-Sectional Health Survey Study](#)

[Roy A Pleasants](#)<sup>1</sup>, [Khosrow Heidari](#)<sup>2</sup>, [Jill Ohar](#)<sup>3</sup>, [James F Donohue](#)<sup>4</sup>, [Njira L Lugogo](#)<sup>5</sup>, [Sarojini M Kanotra](#)<sup>6</sup>, [Monica Kraft](#)<sup>7</sup>, [David M Mannino](#)<sup>8</sup>, [Charlie B Strange](#)<sup>9</sup>

Affiliations expand

- PMID: 35794458
- DOI: [10.1007/s41030-022-00194-9](https://doi.org/10.1007/s41030-022-00194-9)

## Abstract

**Introduction:** Data collected through ongoing, state-based, cross-sectional health surveys could be used to better understand the contribution of respiratory symptoms to impaired health among the US adult population.

**Methods:** We used the 2015 Behavioral Risk Factor Surveillance System telephone health survey in four states (Kentucky, Florida, South Carolina, Texas) to describe the relationship between symptoms, associated factors such as tobacco smoking, and health impairments. Self-reported productive cough, shortness of breath (SOB), and dyspnea on exertion (DOE)

were categorized as minimal, moderate, or severe. Data were analyzed using multiple logistic regression models with age as a covariate to assess relationships of symptoms with other factors.

**Results:** Among adults  $\geq 18$  years, respiratory impairment [current asthma, chronic obstructive pulmonary disease (COPD), or a current moderate or severe symptom] occurred in 39.1% of the population. More than half of adults reporting moderate or severe symptoms had not been diagnosed with asthma or COPD, particularly with DOE and productive cough. Subjects were at greater risk of moderate and severe SOB or productive cough with increasing age, prolonged smoking duration ( $\geq 20$  years), being an ever-smoker, or if reporting COPD, current asthma, or any other comorbidity except cancer. Morbid obesity [body mass index (BMI)  $> 35$  kg/m<sup>2</sup>] was associated with severe DOE at a rate similar to current asthma or COPD (25.6%, 95% CI 20.9-30.3%; 20.8%, 95% CI 16.4-25.1%; 21.3%, 95% CI 17.5-25.1%, respectively); it was the most common cause of DOE. SOB was associated with worse general health impairment and limited ambulation compared with other symptoms. Tobacco smoking prevalence and race varied among states, affecting symptom prevalence.

**Conclusion:** In the largest US survey in decades, we provide a current perspective of respiratory symptoms among adults of all ages. While known risk factors were apparent, low-risk persons also frequently reported symptoms and impairments.

**Keywords:** Asthma; Behavioral Risk Factor Surveillance System; COPD; Cross-sectional health survey; Dyspnea on exertion; Obesity; Productive cough; Quality of life; Shortness of breath; Smoking duration.

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NPJ Prim Care Respir Med

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. 2022 Jul 6;32(1):24.

doi: 10.1038/s41533-022-00287-7.

# The Timed Up and Go test predicts frailty in patients with COPD

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Affiliations expand

- PMID: 35794130
- DOI: [10.1038/s41533-022-00287-7](https://doi.org/10.1038/s41533-022-00287-7)

**Free article**

## Abstract

The Timed Up and Go (TUG) is a global measure of mobility and has the ability to detect frail individuals. Frail patients with chronic obstructive pulmonary disease (COPD) are usually undiagnosed. We hypothesised that the TUG would identify frail patients with COPD. Frailty was assessed in 520 patients diagnosed with COPD and 150 controls using a Comprehensive Geriatric Assessment questionnaire and frailty index (FI) was derived. The TUG was used to assess physical mobility. All participants were assessed for lung function and body composition. A ROC curve was used to identify how well TUG discriminates between frail and non-frail patients with COPD. The patients with COPD and controls were similar in age, sex and BMI but the patients with COPD were more frail, mean  $\pm$  SD FI  $0.16 \pm 0.08$  than controls  $0.05 \pm 0.03$ ,  $P < 0.001$ . Frail patients with COPD had a greater TUG time ( $11.55 \pm 4.03$  s) compared to non-frail patients ( $9.2 \pm 1.6$  sec), after controlling for age and lung function ( $F = 15.94$ ,  $P < 0.001$ ), and both were greater than the controls ( $8.3 \pm 1.2$  sec),  $P < 0.001$ . The TUG discriminated between frail and non-frail patients with COPD with an area under the curve of 72 (95% CI: 67-76), and a diagnostic odds ratio of 2.67 (95% CI: 1.5-4.6),  $P < 0.001$ . The TUG showed the ability to discriminate between frail and non-frail patients with COPD, independent of age and severity of the airflow obstruction. The TUG is a simple, easy and quick measure that could be easily applied in restricted settings to screen for frailty in COPD.

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- [36 references](#)

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JAMA



. 2022 Jul 5;328(1):69-70.

doi: 10.1001/jama.2022.8492.

# [Diagnosis and Treatment of Combined Pulmonary Fibrosis and Emphysema in 2022](#)

[Masahiro Nemoto](#)<sup>1,2</sup>, [Chi Wan Koo](#)<sup>3</sup>, [Jay H Ryu](#)<sup>4</sup>

Affiliations expand

- PMID: 35788808
- DOI: [10.1001/jama.2022.8492](https://doi.org/10.1001/jama.2022.8492)

*No abstract available*

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MeSH termsexpand

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BMC Pulm Med



. 2022 Jul 4;22(1):262.

doi: 10.1186/s12890-022-02053-4.

# [Causes of death following small cell lung cancer diagnosis: a population-based analysis](#)

[Xue-Qin Wu](#)<sup>1,2,3</sup>, [Jing-Yi Li](#)<sup>1,2,3</sup>, [Wen-Jing Du](#)<sup>4,5,6</sup>

Affiliations expand

- PMID: 35787685
- PMCID: [PMC9254402](#)
- DOI: [10.1186/s12890-022-02053-4](#)

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## Abstract

**Purpose:** To examine the distribution of causes of death (CODs) in patients with small cell lung cancer (SCLC).

**Methods:** Patients diagnosed with SCLC were identified from the Surveillance, Epidemiology, and End Results Program database during 2004-2015. Standardized

mortality rates (SMRs) were performed for each COD to present changes in risk for a particular COD following SCLC diagnosis.

**Results:** A total of 44,506 patients diagnosed with SCLC were identified in this study, and 42,476 patients died during the follow-up. Of total deaths, 69.5% occurred within the first years after diagnosis, 26% occurred from 1 to 3 years, and 4.5% individuals survived longer than 3 years. In addition, 88.7% of deaths were caused by SCLC, followed by non-cancer causes (7.1%) and other cancers (4.2%). Moreover, non-cancer CODs increased from 6.3 to 30% over time after 3 years of diagnosis. As for non-cancer CODs, cardiovascular diseases, COPD, and septicemia were the most common in SCLC.

**Conclusion:** Non-cancer CODs, such as cardiovascular events, COPD and septicemia, contribute to a considerable proportion of deaths among long-term SCLC survivors, supporting the involvement of multidisciplinary care for the follow-up strategy in SCLC.

**Keywords:** Cause of death; Lung cancer; SCLC; SEER.

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## Conflict of interest statement

The authors declare that they have no competing interests.

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

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IEEE Trans Biomed Eng

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. 2022 Jul 4;PP.

doi: 10.1109/TBME.2022.3188173. Online ahead of print.

# Direct Visualization and Quantitative Imaging of Small Airway Anatomy In Vivo Using Deep Learning Assisted Diffractive OCT

[Wu Yuan](#), [Jeffrey Thiboutot](#), [Hyeon-Cheol Park](#), [Ang Li](#), [Jeffrey Loubé](#), [Wayne Mitzner](#), [Lonny Yarmus](#), [Robert H Brown](#), [Xingde Li](#)

- PMID: 35786546
- DOI: [10.1109/TBME.2022.3188173](https://doi.org/10.1109/TBME.2022.3188173)

## Abstract

**Objective/background:** In vivo imaging and quantification of the microstructures of small airways in three dimensions (3D) allows a better understanding and management of airway diseases, such as asthma and chronic obstructive pulmonary disease (COPD). At present, the resolution and contrast of the currently available conventional optical coherence tomography (OCT) imaging technologies operating at 1300 nm remain challenging to directly visualize the fine microstructures of small airways in vivo.

**Methods:** We developed an ultrahigh-resolution diffractive endoscopic OCT at 800 nm to afford a resolving power of 1.7  $\mu\text{m}$  (in tissue) with an improved contrast and a custom deep residual learning based image segmentation framework to perform accurate and automated 3D quantification of airway anatomy.

**Results:** The 800-nm diffractive OCT enabled the direct delineation of the structural components in the small airway wall in vivo. We further first demonstrated the 3D anatomic quantification of critical tissue compartments of small airways in sheep using the automated segmentation method.

**Conclusion:** The deep learning assisted diffractive OCT provides a unique ability to access the small airways, directly visualize and quantify the important tissue compartments, such as airway smooth muscle, in the airway wall in vivo in 3D.

**Significance:** These pilot results suggest a potential technology for calculating volumetric measurements of small airways in patients in vivo.

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. 2022 Jul 4;1-10.

doi: 10.1159/000524996. Online ahead of print.

# [Endoscopic Lung Volume Reduction with One-Way Valves in Patients with Severe Chronic Obstructive Pulmonary Disease with Hypercapnia](#)

[Pavlina Lenga](#)<sup>1</sup>, [Christian Grah](#)<sup>2</sup>, [Christoph Ruwwe-Glösenkamp](#)<sup>3</sup>, [Jacopo Saccomanno](#)<sup>3</sup>, [Jens Rückert](#)<sup>4</sup>, [Stephan Eggeling](#)<sup>5</sup>, [Sven Gläser](#)<sup>6</sup>, [Sylke Kurz](#)<sup>7</sup>, [Stephan Eisenmann](#)<sup>8</sup>, [Marcus Krüger](#)<sup>9</sup>, [Bernd Schmidt](#)<sup>10</sup>, [Paul Schneider](#)<sup>10</sup>, [Stefan Andreas](#)<sup>11</sup>, [Marc Hinterthaler](#)<sup>12</sup>, [Joachim Pfannschmidt](#)<sup>13</sup>, [Andreas Gebhardt](#)<sup>14</sup>, [Franz Stanzel](#)<sup>15</sup>, [Angélique Holland](#)<sup>16</sup>, [Andreas Kirschbaum](#)<sup>17</sup>, [Birgit Becke](#)<sup>18</sup>, [Ralf-Harto Hübner](#)<sup>3</sup>, [Lung Emphysema Registry Study Group](#)

Affiliations expand

- PMID: 35785772
- DOI: [10.1159/000524996](https://doi.org/10.1159/000524996)

# Abstract

**Background:** Robust clinical evidence on the efficacy and safety of endoscopic lung volume reduction (ELVR) with one-way valves in patients with severe lung emphysema with chronic hypercapnic respiratory failure is lacking.

**Objective:** The aim of this study was to compare patient characteristics, clinical outcome measures, and incidences of adverse events between patients with severe COPD undergoing ELVR with one-way valves and with either a partial pressure of carbon dioxide (pCO<sub>2</sub>) of ≤45 mm Hg or with pCO<sub>2</sub> >45 mm Hg.

**Methods:** This was a multicentre prospective study of patients with severe lung disease who were evaluated based on lung function, exercise capacity (6-min walk test [6-MWT]), and quality-of-life tests.

**Results:** Patients with pCO<sub>2</sub> ≤45 mm Hg (n = 157) and pCO<sub>2</sub> >45 mm Hg (n = 40) showed similar baseline characteristics. Patients with pCO<sub>2</sub> ≤45 mm Hg demonstrated a significant increase in forced expiratory volume in 1 s (p < 0.001), a significant decrease in residual volume (RV) (p < 0.001), and significant improvements in the quality of life and 6-MWT at the 3-month follow-up. Patients with pCO<sub>2</sub> >45 mm Hg had significant improvements in RV only (p < 0.05). There was a significant decrease in pCO<sub>2</sub> between baseline and follow-up in hypercapnic patients, relative to the decrease in patients with pCO<sub>2</sub> ≤45 mm Hg (p = 0.008). Patients who were more hypercapnic at baseline showed a greater reduction in pCO<sub>2</sub> after valve placement (r = -0.38, p < 0.001). Pneumothorax was the most common adverse event in both groups.

**Conclusions:** ELVR with one-way valves seems clinically beneficial with a remarkably good safety profile for patients with chronic hypercapnic respiratory failure.

**Keywords:** Chronic obstructive pulmonary disease; Endoscopic lung volume reduction; Hypercapnia; Valves.

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Med Clin (Barc)

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. 2022 Jul 8;159(1):33-39.

doi: 10.1016/j.medcli.2022.01.021. Epub 2022 Mar 9.

# Beyond the COPD–tobacco binomium: New opportunities for the prevention and early treatment of the disease

[Article in English, Spanish]

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Affiliations expand

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- DOI: [10.1016/j.medcli.2022.01.021](https://doi.org/10.1016/j.medcli.2022.01.021)

## Abstract

Chronic obstructive pulmonary disease (COPD) has been traditionally understood as a self-inflicted disease cause by tobacco smoking occurring in individuals older than 50-60 years. This traditional paradigm has changed over the last decade because new scientific evidence showed that there are many genetic (G) and environmental (E) factors associated with reduced lung function, that vary, accumulate, and interact over time (T), even before birth (G×E×T). This new perspective opens novel windows of opportunity for the prevention, early diagnosis, and personalized treatment of COPD. This review presents the evidence that supports this proposal, as well as its practical implications, with particular emphasis on the need that clinical histories in patients with suspected COPD should investigate early life events and that spirometry should be used much more widely as a global health marker.

**Keywords:** Aging; Bronchitis; Bronquitis; Chronic obstructive pulmonary disease; Desarrollo pulmonar; Early ages; Edades tempranas; Enfermedad pulmonar obstructiva crónica; Envejecimiento; Lung development; Prevención; Prevention.

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SUPPLEMENTARY INFO

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## ASTHMA

Ann Am Thorac Soc



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doi: [10.1513/AnnalsATS.202109-1053OC](https://doi.org/10.1513/AnnalsATS.202109-1053OC). Online ahead of print.

# [Comparing the Effect of Acute Moderate and Vigorous Exercise on Inflammation in Adults with Asthma: A Randomized Controlled Trial](#)

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Affiliations expand

- PMID: 35802811
- DOI: [10.1513/AnnalsATS.202109-1053OC](https://doi.org/10.1513/AnnalsATS.202109-1053OC)

## Abstract

**Rationale:** Exercise is associated with improvements in asthma, however the mechanisms responsible are not clear. Exercise induces changes in systemic inflammation, and it is possible that these inflammatory effects extend to the airways of people with asthma. Studies in healthy adults suggest inflammatory responses are dependent on exercise intensity: while acute moderate exercise is anti-inflammatory, acute vigorous exercise appears to be neutral or pro-inflammatory. The effect of exercise intensity on inflammation has not been investigated in people with asthma.



**Objectives:** To compare acute changes in airway and systemic inflammation following a bout of moderate or vigorous exercise in physically inactive adults with asthma, and to establish whether these effects differ according to asthma phenotype.

**Methods:** Participants were randomised to either 1) control (no intervention), 2) 45 minutes of moderate exercise, or 3) 30 minutes of vigorous exercise. Induced sputum and blood samples were collected at baseline and four hours post-intervention.

**Results:** Fifty-six participants [75% female, mean age 33.4 (9.9) years] completed the trial. Moderate exercise induced a significant reduction in sputum eosinophil count [-173 (-337 to -10),  $p=0.032$ ] and sputum %eosinophils [-2.2 (-4.9 to 0.5),  $p=0.049$ ], relative to control. Vigorous exercise had no effect on airway inflammation. The anti-inflammatory effects of moderate exercise were greatest in participants with eosinophilic asthma, with larger reductions in sputum eosinophils and larger increases in plasma IL-1ra compared to participants with non-eosinophilic asthma. Vigorous exercise induced a systemic pro-inflammatory response in participants with eosinophilic asthma, indicated by an increase in serum IL-5 and IL-1 $\beta$ ; however, this had no effect on airway inflammation.

**Conclusions:** Exercise intensity modifies the acute inflammatory response to exercise in adults with asthma. While a bout of moderate exercise is associated with a reduction in eosinophilic airway inflammation, vigorous exercise has no effect on airway inflammation. Interestingly, the effects of moderate exercise vary by asthma phenotype, with greater anti-inflammatory effects in participants with eosinophilic asthma. Future studies should examine the impact of exercise training at different intensities on inflammation and clinical asthma outcomes.

**Clinical trial registration:** Australian New Zealand Clinical Trials Registry: ACTRN12615000294550.

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J Asthma

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. 2022 Jul 7;1-12.

doi: 10.1080/02770903.2022.2097919. Online ahead of print.

[Potential for repurposing oral hypertension/diabetes drugs to decrease asthma risk in obesity](#)

[Akshay Sood](#)<sup>1</sup>, [Clifford Qualls](#)<sup>2</sup>, [Allison Murata](#)<sup>2</sup>, [Phillip J Kroth](#)<sup>3</sup>, [Jenny Mao](#)<sup>4</sup>, [David S Schade](#)<sup>5</sup>, [Glen Murata](#)<sup>2</sup>

Affiliations expand

- PMID: 35796615
- DOI: [10.1080/02770903.2022.2097919](https://doi.org/10.1080/02770903.2022.2097919)

## Abstract

**Objective:** Risk for asthma in the overweight/obese may be mediated by adiponectin and peroxisome proliferator activated receptor pathways, and may be reduced by the use of oral drugs impacting these pathways, such as angiotensin converting enzyme inhibitors (ACE-I), thiazolidinediones (TZD) and angiotensin receptor blockers (ARB). Our study objective was to determine whether ACE-I, TZD and/or ARB use in overweight/obese adults with diabetes mellitus and/or hypertension is associated with a lower risk for incident asthma.

**Methods:** Using an existing cohort of American veterans, we performed a longitudinal data analysis over 15 years. Exposure was defined by the prescription pickup of ACE-I, TZD and/or ARB for at least 4 weeks. The outcome, time until new-onset of clinician-diagnosed asthma, was studied using survival analysis. Propensity scoring method controlled for treatment selection bias.

**Results:** 2.83 million eligible veterans, including 77,278 with incident asthma, were studied. As compared to those unexposed, the use of ACE-I alone, TZD alone, or their combination were each associated with decreased risk for incident asthma (hazard ratios of 0.88, 0.74, and 0.20, respectively;  $p < 0.001$  for all analyses in the fully adjusted statistical models). TZD lowered the risk among racial/ethnic minority subjects more than among White participants ( $p < 0.001$ ). On the other hand, ARB use alone or in combination with TZD was associated with a higher risk for incident asthma.

**Conclusions:** Use of ACE-I and/or TZD was associated with a lower risk for incident asthma in overweight/obese patients with diabetes mellitus and/or hypertension.

**Keywords:** adiponectin; angiotensin converting enzyme inhibitor; angiotensin receptor blocker; incident asthma; peroxisome proliferator-activated receptor; thiazolidinediones.

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. 2022 Jul 7.

doi: 10.1111/jdv.18415. Online ahead of print.

# Adults with concomitant atopic dermatitis and asthma have more frequent urgent health care utilization and less frequent scheduled follow-up visits than adults with atopic dermatitis or asthma only: A nationwide cohort study

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- PMID: 35796157
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## Abstract

**Background:** Atopic dermatitis (AD) and asthma often co-occur in the same patient, and health care utilization is related to disease severity of these diseases.

**Objective:** To investigate differences in healthcare utilization in adults with concomitant AD and asthma compared to patients with asthma or AD only.

**Methods:** All Danish adults with a hospital-diagnosis of AD, asthma or concomitant AD and asthma recorded in national registries were included. Health care utilization data were obtained in 3-month intervals from two year prior to index date (the date of the first hospital diagnosis), and to five years after.

**Results:** A total of 12,409 patients with AD were included (11,590 with AD only and 819 with concomitant AD and asthma), and 65,539 with asthma only. Adults with concomitant AD and asthma had higher risk of hospitalization for AD (OR 1.38, 95% CI (1.15-1.67), p=0.001) and

asthma (OR 1.16, 95% CI (1.00-1.35),  $p=0.047$ ) compared to patients with only AD and asthma, respectively. These patients also had fewer visits in outpatient clinics for AD (OR 0.10, 95% CI (0.08-0.12),  $p<0.001$ ) and asthma (OR 0.34, 95% CI (0.29-0.39),  $P<0.001$ ) compared to patients with only AD or asthma. Outpatient clinic visits for rhinitis were more frequent among patients with concomitant AD and asthma compared to patients with only AD or asthma.

**Conclusion:** Adults with concomitant AD and asthma had different patterns of healthcare utilization compared to adults with AD or asthma alone, suggesting that improvements in management and monitoring may reduce unscheduled health care visits, and lower healthcare costs.

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Environ Health



. 2022 Jul 6;21(1):63.

doi: 10.1186/s12940-022-00871-x.

## [Birch pollen, air pollution and their interactive effects on airway symptoms and peak expiratory flow in allergic asthma during pollen season - a panel study in Northern and Southern Sweden](#)

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- PMID: 35794604

- DOI: [10.1186/s12940-022-00871-x](https://doi.org/10.1186/s12940-022-00871-x)

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## Abstract

**Background:** Evidence of the role of interactions between air pollution and pollen exposure in subjects with allergic asthma is limited and need further exploration to promote adequate preventive measures. The objective of this study was to assess effects of exposure to ambient air pollution and birch pollen on exacerbation of respiratory symptoms in subjects with asthma and allergy to birch.

**Methods:** Thirty-seven subjects from two Swedish cities (Gothenburg and Umeå) with large variation in exposure to both birch-pollen and air pollutants, participated in the study. All subjects had confirmed allergy to birch and self-reported physician-diagnosed asthma. The subjects recorded respiratory symptoms such as rhinitis or eye irritation, dry cough, dyspnoea, the use of any asthma or allergy medication and peak respiratory flow (PEF), daily for five consecutive weeks during two separate pollen seasons and a control season without pollen. Nitrogen oxides (NO<sub>x</sub>), ozone (O<sub>3</sub>), particulate matter (PM<sub>2.5</sub>), birch pollen counts, and meteorological data were obtained from an urban background monitoring stations in the study city centres. The data were analysed using linear mixed effects models.

**Results:** During pollen seasons all symptoms and medication use were higher, and PEF was reduced in the subjects. In regression analysis, exposure to pollen at lags 0 to 2 days, and lags 0 to 6 days was associated with increased ORs of symptoms and decreased RRs for PEF. Pollen and air pollution interacted in some cases; during low pollen exposure, there were no associations between air pollution and symptoms, but during high pollen exposure, O<sub>3</sub> concentrations were associated with increased OR of rhinitis or eye irritation, and PM<sub>2.5</sub> concentrations were associated with increased ORs of rhinitis or eye irritation, dyspnea and increased use of allergy medication.

**Conclusions:** Pollen and air pollutants interacted to increase the effect of air pollution on respiratory symptoms in allergic asthma. Implementing the results from this study, advisories for individuals with allergic asthma could be improved, minimizing the morbidities associated with the condition.

**Keywords:** Allergic asthma; Betula; Birch; O<sub>3</sub>; PM<sub>2.5</sub>; Panel study; Pollen season.

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- [42 references](#)

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Pulm Ther



. 2022 Jul 6.

doi: 10.1007/s41030-022-00194-9. Online ahead of print.

# [Respiratory Symptoms among US Adults: a Cross-Sectional Health Survey Study](#)

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- PMID: 35794458
- DOI: [10.1007/s41030-022-00194-9](https://doi.org/10.1007/s41030-022-00194-9)

## Abstract

**Introduction:** Data collected through ongoing, state-based, cross-sectional health surveys could be used to better understand the contribution of respiratory symptoms to impaired health among the US adult population.

**Methods:** We used the 2015 Behavioral Risk Factor Surveillance System telephone health survey in four states (Kentucky, Florida, South Carolina, Texas) to describe the relationship between symptoms, associated factors such as tobacco smoking, and health impairments. Self-reported productive cough, shortness of breath (SOB), and dyspnea on exertion (DOE) were categorized as minimal, moderate, or severe. Data were analyzed using multiple logistic regression models with age as a covariate to assess relationships of symptoms with other factors.

**Results:** Among adults  $\geq 18$  years, respiratory impairment [current asthma, chronic obstructive pulmonary disease (COPD), or a current moderate or severe symptom] occurred in 39.1% of the population. More than half of adults reporting moderate or severe symptoms had not been diagnosed with asthma or COPD, particularly with DOE and productive cough. Subjects were at greater risk of moderate and severe SOB or productive cough with increasing age, prolonged smoking duration ( $\geq 20$  years), being an ever-smoker, or if reporting COPD, current asthma, or any other comorbidity except cancer. Morbid obesity [body mass index (BMI)  $> 35$  kg/m<sup>2</sup>] was associated with severe DOE at a rate similar to current asthma or COPD (25.6%, 95% CI 20.9-30.3%; 20.8%, 95% CI 16.4-25.1%; 21.3%, 95% CI 17.5-25.1%, respectively); it was the most common cause of DOE. SOB was associated with worse general health impairment and limited ambulation compared with other symptoms. Tobacco smoking prevalence and race varied among states, affecting symptom prevalence.

**Conclusion:** In the largest US survey in decades, we provide a current perspective of respiratory symptoms among adults of all ages. While known risk factors were apparent, low-risk persons also frequently reported symptoms and impairments.

**Keywords:** Asthma; Behavioral Risk Factor Surveillance System; COPD; Cross-sectional health survey; Dyspnea on exertion; Obesity; Productive cough; Quality of life; Shortness of breath; Smoking duration.

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- [55 references](#)

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Respiration

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. 2022 Jul 6;1-8.

doi: 10.1159/000525549. Online ahead of print.

## [Distribution of the Clinical Manifestations of Alpha 1 Antitrypsin Deficiency in Respiratory Outpatients from an Area of Northern Italy](#)

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Affiliations expand

- PMID: 35793662
- DOI: [10.1159/000525549](https://doi.org/10.1159/000525549)

## Abstract

**Background:** Alpha 1 antitrypsin deficiency (AATD) is an autosomal codominant genetic condition that affects Caucasians of the European population due to the presence of a deficient allele of the SERPINA1 gene. A frequency of about 1/5,000 individuals has been estimated in Italy.

**Objectives:** The aim of the study was to evaluate the distribution of the clinical manifestations of severe and intermediate genetic AATD in the geographic area around Parma in Northern Italy.

**Method:** 238 subjects were submitted to molecular analysis of the SERPINA1 gene, and data on anthropometric variables, smoking habits, number of packs per year, AAT serum concentration, and clinical manifestations were recorded and presented as mean  $\pm$  SD or median values (1st quartile; 3rd quartile).

**Results:** The results show a distribution of genetic AATD of 4.1% of the screened population in the area encompassing the city of Parma. PI\*MS and PI\*MZ were the most common genotypes at 40.9% and 28.2% of the population with genetic AATD, and asthma and emphysema were the most represented clinical manifestations.

**Conclusion:** Our study allowed to increase the knowledge of the distribution of genetic AATD in Northern Italy providing information regarding frequencies of genotypes and clinical manifestations of the disorder.

**Keywords:** Alpha 1 antitrypsin; Alpha 1 antitrypsin deficiency; Clinical manifestations; Genotype.

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# From the Global Initiative for Asthma report and asthma guidelines to real-life asthma control: is there room for improvement?

[Elio Novembre<sup>1</sup>](#), [Mattia Giovannini<sup>2</sup>](#), [Simona Barni<sup>1</sup>](#), [Francesca Mori<sup>1</sup>](#)

Affiliations [expand](#)

- PMID: 35790997
- PMCID: [PMC9258205](#)
- DOI: [10.1186/s13052-022-01304-8](#)

**Free PMC article**

## Abstract

Available guidelines for asthma management represent an important and suitable tool to make the entire medical process evidence-based, effective, and safe for patients. Their purpose is to help doctors and patients formulate the best decisions in regard to asthma management by choosing the most appropriate strategies in each specific clinical situation. The Global Initiative for Asthma (GINA) document, together with other national and international recommendations, is one of the main documents used for asthma prevention and management in Italy, but several studies reported that these recommendations are often not applied in real-life clinical practice, which consequently results in inadequate asthma control. In this context, a substantial simplification of the GINA document and asthma guidelines may represent a feasible strategy to be pursued to ameliorate the knowledge among GPs, primary care pediatricians, and specialists taking care of children and adults with asthma. On the other hand, another critical factor that may explain unsatisfactory control of asthma is the limited importance that all recommendations place on asthma heterogeneity. In the era of personalized medicine and target therapies, phenotype-driven asthma management may become a

desirable approach for optimizing the management of asthmatic patients. In addition, digital health strategies have been investigated in the literature to improve asthma monitoring and may represent a promising tool in the future from this point of view. Relevant stakeholders should continue to investigate how to optimize real-life asthma control to propose novel solutions to translate into clinical practice.

**Keywords:** Asthma; Global Initiative for Asthma; Improvement; Pediatrics; Real-life.

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## Conflict of interest statement

The authors declare that they have no competing interests to disclose in relation to this paper.

- [15 references](#)

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. 2022 Jul 5;thoraxjnl-2021-217389.

doi: 10.1136/thoraxjnl-2021-217389. Online ahead of print.

# [In vivo bronchial epithelial interferon responses are augmented in asthma on day 4 following experimental rhinovirus infection](#)

[Hugo Farne](#)<sup>#1</sup>, [Lijing Lin](#)<sup>#2</sup>, [David J Jackson](#)<sup>#1,3,4</sup>, [Magnus Rattray](#)<sup>2</sup>, [Angela Simpson](#)<sup>5</sup>, [Adnan Custovic](#)<sup>6</sup>, [Shilpy Joshi](#)<sup>7</sup>, [Paul A Wilson](#)<sup>7</sup>, [Rick Williamson](#)<sup>7</sup>, [Michael R Edwards](#)<sup>1</sup>, [Aran Singanayagam](#)<sup>8</sup>, [Sebastian L Johnston](#)<sup>9</sup>

Affiliations expand

- PMID: 35790388
- DOI: [10.1136/thoraxjnl-2021-217389](https://doi.org/10.1136/thoraxjnl-2021-217389)

## Abstract

Despite good evidence of impaired innate antiviral responses in asthma, trials of inhaled interferon- $\beta$  given during exacerbations showed only modest benefits in moderate/severe asthma. Using human experimental rhinovirus infection, we observe robust in vivo induction of bronchial epithelial interferon response genes 4 days after virus inoculation in 25 subjects with asthma but not 11 control subjects. This signature correlated with virus loads and lower respiratory symptoms. Our data indicate that the in vivo innate antiviral response is dysregulated in asthma and open up the potential that prophylactic rather than therapeutic interferon therapy may have greater clinical benefit.

**Keywords:** Asthma; Asthma Mechanisms; Innate Immunity; Viral infection.

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## Conflict of interest statement

Competing interests: HF and LL report no competing interests. DJJ reports personal fees from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, and Novartis outside the submitted work. MR and AnS report personal fees from AstraZeneca outside the submitted work. AC reports personal fees from Novartis, Thermo Fisher Scientific, Philips, Sanofi, Stallergenes Greer, and AstraZeneca outside the submitted work. SJ, PAW and RW are GlaxoSmithKline employees. MRE is a Virtus Respiratory Research employee. SLJ personal fees from Virtus Respiratory Research, Myelo Therapeutics, Bayer, Synairgen, Novartis, Boehringer Ingelheim, Chiesi, Gerson Lehrman Group, resTORbio, Bioforce, Matera Medical Holdings, PrepBio Pharma, Pulmotect, Virion Health, Lallemand Pharma, and AstraZeneca outside the submitted work; in addition SLJ is an author on patents relating to use of interferons in treatment of exacerbations of airway disease.

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# Cigarette smoke aggravates asthma by inducing memory-like type 3 innate lymphoid cells

[Jongho Ham](#)<sup>#1,2</sup>, [Jihyun Kim](#)<sup>#1,3</sup>, [Kyoung-Hee Sohn](#)<sup>4</sup>, [In-Won Park](#)<sup>5</sup>, [Byoung-Whui Choi](#)<sup>5,6</sup>, [Doo Hyun Chung](#)<sup>2,7,8</sup>, [Sang-Heon Cho](#)<sup>3,9</sup>, [Hye Ryun Kang](#)<sup>3,9</sup>, [Jae-Woo Jung](#)<sup>10</sup>, [Hye Young Kim](#)<sup>11,12,13</sup>

Affiliations expand

- PMID: 35789151
- PMCID: [PMC9253141](#)
- DOI: [10.1038/s41467-022-31491-1](#)

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## Abstract

Although cigarette smoking is known to exacerbate asthma, only a few clinical asthma studies have been conducted involving smokers. Here we show, by comparing paired sputum and blood samples from smoking and non-smoking patients with asthma, that smoking associates with significantly higher frequencies of pro-inflammatory, natural-cytotoxicity-receptor-non-expressing type 3 innate lymphoid cells (ILC3) in the sputum and memory-like, CD45RO-expressing ILC3s in the blood. These ILC3 frequencies positively correlate with circulating neutrophil counts and M1 alveolar macrophage frequencies, which are known to increase in uncontrolled severe asthma, yet do not correlate with circulating eosinophil frequencies that characterize allergic asthma. In vitro exposure of ILCs to cigarette smoke extract induces expression of the memory marker CD45RO in ILC3s. Cigarette smoke extract also impairs the barrier function of airway epithelial cells and increases their production of IL-1 $\beta$ , which is a known activating factor for ILC3s. Thus, our study suggests that cigarette smoking increases local and circulating frequencies of activated ILC3 cells, plays a role in their activation, thereby aggravating non-allergic inflammation and the severity of asthma.

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## Conflict of interest statement

The authors declare no competing interests.

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

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Am J Physiol Lung Cell Mol Physiol

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. 2022 Jul 5.

doi: 10.1152/ajplung.00132.2022. Online ahead of print.

# [Obesity Elicits a Unique Metabolomic Signature in Human Airway Smooth Muscle Cells](#)

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- PMID: 35787188

- DOI: [10.1152/ajplung.00132.2022](https://doi.org/10.1152/ajplung.00132.2022)

## Abstract

Obesity can aggravate asthma by enhancing airway hyperresponsiveness (AHR) and attenuating response to treatment. However, the precise mechanisms linking the obesity and asthma remain unknown. Human airway smooth muscle (HASM) cells exhibit amplified excitation-contraction (EC) coupling and force generation in obesity. Therefore, we posit that airway smooth muscle (ASM) cells obtained from obese donors manifest a metabolomic phenotype distinct from that of non-obese donor cells and that a differential metabolic phenotype, at least in part, drives enhanced ASM cell E-C coupling. HASM cells derived from age, sex and race-matched non-obese (BMI  $\leq$  24.9 kg.m<sup>-2</sup>) and obese (BMI  $\geq$  29.9 kg.m<sup>-2</sup>) lung donors were subject to unbiased metabolomic screening. The unbiased metabolomic screening identified differentially altered metabolites linked to glycolysis and citric acid cycle in obese donor-derived cells compared to non-obese donor cells. The Seahorse® assay measured the bioenergetic profile based on glycolysis, mitochondrial respiration, palmitate oxidation, and glutamine oxidation rates in HASM cells. Glycolytic rate and capacity were elevated in obese donor-derived HASM cells, while mitochondrial respiration, palmitate oxidation, and glutamine oxidation rates were comparable between obese and non-obese groups. PFKFB3 mRNA and protein expression levels were also elevated in obese donor-derived HASM cells. Furthermore, pharmacological inhibition of PFKFB3 attenuated agonist-induced myosin light chain (MLC) phosphorylation in HASM cells derived from obese and non-obese donors. Our findings identify elevated glycolysis as a signature metabolic phenotype of obesity and inhibition of glycolysis attenuates MLC phosphorylation in HASM cells. These findings identify novel therapeutic targets to mitigate AHR in obesity-associated asthma.

**Keywords:** airway smooth muscle; metabolomics; obesity.

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. 2022 Jul 7;1-18.

# Investigational approaches for unmet need in severe asthma

[David Watchorn](#)<sup>1</sup>, [Andrew Menzies-Gow](#)<sup>1</sup>

Affiliations expand

- PMID: 35786146
- DOI: [10.1080/17476348.2022.2096593](https://doi.org/10.1080/17476348.2022.2096593)

## Abstract

**Introduction:** Molecular antibodies (mAb) targeting inflammatory mediators are effective in T2-high asthma. The recent approval of Tezepelumab presents a novel mAb therapeutic option for those with T2-low asthma.

**Areas covered:** We discuss a number of clinical problems pertinent to severe asthma that are less responsive to current therapies, such as persistent airflow obstruction and airway hyperresponsiveness. We discuss selected investigational approaches, including a number of candidate therapies under investigation in two adaptive platform trials currently in progress, with particular reference to this unmet need, as well as their potential in phenotypes such as neutrophilic asthma and obese asthma, which may or may not overlap with a T2-high phenotype.

**Expert opinion:** The application of discrete targeting approaches to T2-low molecular phenotypes, including those phenotypes in which inflammation may not arise within the airway, has yielded variable results to date. Endotypes associated with T2-low asthma are likely to be diverse but await validation. Investigational therapeutic approaches must, likewise, be diverse if the goal of remission is to become attainable for all those living with asthma.

**Keywords:** Airway hyper-responsiveness; Charcot-Leyden crystals; OM-85 BV; astegolimab; dexpropimpraxole; galectin-10; glucagon-like peptide 1; mucus plugging; neutrophilic asthma; obese asthma.

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Allergy

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. 2022 Jul 4.

doi: 10.1111/all.15426. Online ahead of print.

# The impact of type 2 immunity and allergic diseases in atherosclerosis

[Nieves Fernández-Gallego](#)<sup>#1,2</sup>, [Raquel Castillo-González](#)<sup>#1,2,3</sup>, [Nerea Méndez-Barbero](#)<sup>4,5</sup>, [Celia López-Sanz](#)<sup>2</sup>, [David Obeso](#)<sup>6,7</sup>, [Alma Villaseñor](#)<sup>6,7</sup>, [María M Escribese](#)<sup>6</sup>, [Beatriz López-Melgar](#)<sup>8</sup>, [Jorge Salamanca](#)<sup>8</sup>, [Amparo Benedicto-Buendía](#)<sup>8</sup>, [Luis Jesús Jiménez-Borreguero](#)<sup>5,8</sup>, [Borja Ibañez](#)<sup>5,9,10</sup>, [Joaquín Sastre](#)<sup>11,12</sup>, [María Teresa Belver](#)<sup>13</sup>, [Francisco Vega](#)<sup>13</sup>, [Carlos Blanco](#)<sup>13</sup>, [Domingo Barber](#)<sup>6</sup>, [Francisco Sánchez-Madrid](#)<sup>1,2,5</sup>, [Hortensia de la Fuente](#)<sup>2,5</sup>, [Pilar Martín](#)<sup>1,5</sup>, [Vanessa Esteban](#)<sup>11,14</sup>, [Rodrigo Jiménez-Saiz](#)<sup>2,15,16,17</sup>

Affiliations expand

- PMID: 35781885
- DOI: [10.1111/all.15426](https://doi.org/10.1111/all.15426)

## Abstract

Allergic diseases are allergen-induced immunological disorders characterized by the development of type 2 immunity and IgE responses. The prevalence of allergic diseases has been on the rise alike cardiovascular disease (CVD), which affects arteries of different organs such as the heart, the kidney and the brain. The underlying cause of CVD is often atherosclerosis, a disease distinguished by endothelial dysfunction, fibrofatty material accumulation in the intima of the artery wall, smooth muscle cell proliferation, and Th1 inflammation. The opposed T-cell identity of allergy and atherosclerosis implies an atheroprotective role for Th2 cells by counteracting Th1 responses. Yet, the clinical association between allergic disease and CVD argues against it. Within, we review different phases of allergic pathology, basic immunological mechanisms of atherosclerosis and the clinical association between allergic diseases (particularly asthma, atopic dermatitis, allergic rhinitis and food allergy) and CVD. Then, we discuss putative atherogenic mechanisms of type 2 immunity and allergic inflammation including acute allergic reactions (IgE, IgG1, mast cells, macrophages and allergic mediators such as vasoactive components, growth factors and those derived from the complement, contact and coagulation systems) and late phase inflammation (Th2 cells, eosinophils, type 2 innate-like lymphoid cells, alarmins, IL-4, IL-5, IL-9, IL-13 and IL-17).



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Curr Opin Allergy Clin Immunol



. 2022 Jul 4.

doi: [10.1097/ACI.0000000000000829](https://doi.org/10.1097/ACI.0000000000000829). Online ahead of print.

# [Severe asthma and personalized approach in the choice of biologic](#)

[Danilo Di Bona](#)<sup>1</sup>, [Federico Spataro](#)<sup>1</sup>, [Palma Carlucci](#)<sup>1</sup>, [Giovanni Paoletti](#)<sup>2,3</sup>, [Giorgio W Canonica](#)<sup>2,3</sup>

Affiliations [expand](#)

- PMID: 35779061
- DOI: [10.1097/ACI.0000000000000829](https://doi.org/10.1097/ACI.0000000000000829)

## Abstract

**Purpose of review:** Severe asthma requires intensive pharmacological treatment to achieve disease control. Oral corticosteroids are effective, but their use is burdened with important side effects. Biologics targeting the specific inflammatory pathways underpinning the disease have been shown to be effective but not all patients respond equally well. As we treat more patients than those who can respond, our inability to predict responders has important healthcare costs considering that

biologics are expensive drugs. Thus, a more precise choice of the 'right patients' to be prescribed with the 'right biologics' would be desirable.

**Recent findings:** Machine learning techniques showed that it is possible to increase our ability to predict outcomes in patients treated with biologics. Recently, we identified by cluster analysis four different clusters within the T2 high phenotype with differential benralizumab response. Two of these clusters, characterized by higher levels of inflammatory markers, showed the highest response rate (80-90%).

**Summary:** Machine learning holds promise for asthma research enabling us to predict which patients will respond to which drug. These techniques can facilitate the diagnostic workflow and increase the chance of selecting the more appropriate treatment option for the individual patient, enhancing patient care and satisfaction.

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J Asthma

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. 2022 Jul 7;1-10.

doi: 10.1080/02770903.2022.2094804. Online ahead of print.

## [Trends in seasonal pollen and asthma-related morbidity among adults and children in a U.S. high-density urban center, 2001-2020](#)

[Kyle Mani](#)<sup>1</sup>, [Raphael Miller](#)<sup>2</sup>, [Juan Lin](#)<sup>3</sup>, [Jai Shahani](#)<sup>4</sup>, [Sunit Jariwala](#)<sup>5</sup>

Affiliations expand

- PMID: 35758000
- DOI: [10.1080/02770903.2022.2094804](https://doi.org/10.1080/02770903.2022.2094804)

## Abstract

**Objective:** To analyze the long-term trends in pollen counts and asthma-related emergency department visits (AREDV) in adult and pediatric populations in the Bronx.

**Methods:** Daily values of adult and pediatric AREDV were retrospectively obtained from three major Bronx hospitals using ICD-10 codes and pollen counts were obtained from the Armonk station from 2001-2020. Wilcoxon Ranked Sum was applied to compare median values, while Spearman correlation was employed to examine the association between these variables, for both decades and each season.

**Results:** The median value of pediatric AREDV increased by 200% from the 1st to 2nd decade ( $p < 0.001$ ) and AREDV peak shifted from predominantly the spring season in the 1st decade to the fall and winter seasons in the 2nd decade. Seasonal patterns were consistent over 20 years with summer AREDV lower than all other seasons (9 vs. 17 per day) ( $p < 0.001$ ). Spring tree pollen peaks were correlated with AREDV peaks ( $\rho = 0.34$ ) ( $p < 0.001$ ). Tree pollen exceeding 100 grains/m<sup>3</sup> corresponded to a median of 19.0 AREDVs while all other tree pollen (0 - 99 grains/m<sup>3</sup>) corresponded to a median of 15.0 AREDVs ( $p < 0.001$ ). AREDVs sharply declined in 2020, coinciding with the emergence of COVID-19.

**Conclusions:** Pollen and AREDVs peak earlier in the spring and are more strongly interconnected, while asthma rates among children are rapidly rising, particularly in the fall and winter. These findings can advise targeted awareness campaigns for better management of asthma related morbidity.

**Keywords:** Asthma; emergency department visits; epidemiology; pollen; surveillance; urban.

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J Breath Res

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. 2022 Jul 5;16(4).

doi: 10.1088/1752-7163/ac7a57.

# Short- and medium-term effect of inhaled corticosteroids on exhaled breath biomarkers in severe asthma

Fahad H Alahmadi<sup>1</sup>, Max Wilkinson<sup>2</sup>, Brian Keevil<sup>2</sup>, Rob Niven<sup>2</sup>, Stephen J Fowler<sup>2</sup>

Affiliations expand

- PMID: 35724643
- DOI: [10.1088/1752-7163/ac7a57](https://doi.org/10.1088/1752-7163/ac7a57)

## Abstract

Inhaled corticosteroids (ICS) are the mainstay of therapy in asthma, but benefits vary due to disease heterogeneity. Steroid insensitivity is a particular problem in severe asthma, where patients may require systemic corticosteroids and/or biologics. Biomarkers sensitive to ICS over a short period of time could inform earlier and more personalised treatment choices. To investigate how exhaled breath biomarkers change over two-hours and one-week following monitored ICS dosing in severe asthma patients with evidence of uncontrolled airway inflammation. Patients with severe asthma and elevated fractional exhaled nitric oxide (FeNO) ( $\geq 45$  ppb, indicative of active airway inflammation) were recruited. Exhaled breath biomarkers were evaluated using (FeNO), exhaled breath temperature (EBT), particles in exhaled air (PExA) and volatile organic compounds (VOCs). Samples were collected over 2 h following observed inhalation of 1000 mcg fluticasone propionate, and at a second visit 1 week after taking the same dose daily via an inhaler monitoring device that recorded correct actuation and inhalation. Changes in parameters over 2 h were analysed by the Friedman test and 1 week by Wilcoxon's test ( $p$ -value for significance set at 0.05; for VOCs false discovery rate  $q$  of 0.1 by Benjamini-Hochberg method applied). 17 participants (9 male) were recruited, but three could not complete PExA and two FeNO testing, as they were unable to comply with the necessary technique; complete datasets were available from 12 (9 male) with median (interquartile range) age 45 (36-59) yrs. EBT ( $p < 0.05$ ) and levels of six VOCs ( $q < 0.1$ ) fell over the 2 h after high dose ICS; there were no changes in FeNO or PExA. After one week of using high dose ICS, there were falls in FeNO, EBT and two VOCs ( $p < 0.05$ ), but no changes in PExA. Reduction in EBT over the short and medium term after high dose ICS may reflect airway vascular changes, and this, together with the observed changes in exhaled VOCs, merits further investigation as potential markers of ICS use and effectiveness.

**Keywords:** asthma; exhaled breath biomarkers; exhaled breath temperature; fractional exhaled breath nitric oxide; inhaled corticosteroids; particles in exhaled breath; volatile organic compounds.

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SUPPLEMENTARY INFO

MeSH terms, Substances expand

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Eur Respir J



. 2022 Jul 7;60(1):2004361.

doi: 10.1183/13993003.04361-2020. Print 2022 Jul.

# [Lysyl oxidase like 2 is increased in asthma and contributes to asthmatic airway remodelling](#)

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- PMID: 34996828
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Free article

## Abstract

**Background:** Airway smooth muscle (ASM) cells are fundamental to asthma pathogenesis, influencing bronchoconstriction, airway hyperresponsiveness and airway remodelling. The extracellular matrix (ECM) can influence tissue remodelling pathways; however, to date no study has investigated the effect of ASM ECM stiffness and cross-linking on the development of asthmatic airway remodelling. We hypothesised that transforming growth factor- $\beta$  (TGF- $\beta$ ) activation by ASM cells is influenced by ECM in asthma and sought to investigate the mechanisms involved.

**Methods:** This study combines *in vitro* and *in vivo* approaches: human ASM cells were used *in vitro* to investigate basal TGF- $\beta$  activation and expression of ECM cross-linking enzymes. Human bronchial biopsies from asthmatic and nonasthmatic donors were used to confirm lysyl oxidase like 2 (LOXL2) expression in ASM. A chronic ovalbumin (OVA) model of asthma was used to study the effect of LOXL2 inhibition on airway remodelling.

**Results:** We found that asthmatic ASM cells activated more TGF- $\beta$  basally than nonasthmatic controls and that diseased cell-derived ECM influences levels of TGF- $\beta$  activated. Our data demonstrate that the ECM cross-linking enzyme LOXL2 is increased in asthmatic ASM cells and in bronchial biopsies. Crucially, we show that LOXL2 inhibition reduces ECM stiffness and TGF- $\beta$  activation *in vitro*, and can reduce subepithelial collagen deposition and ASM thickness, two features of airway remodelling, in an OVA mouse model of asthma.

**Conclusion:** These data are the first to highlight a role for LOXL2 in the development of asthmatic airway remodelling and suggest that LOXL2 inhibition warrants further investigation as a potential therapy to reduce remodelling of the airways in severe asthma.

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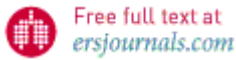
## Conflict of interest statement

Conflict of interest: J. Ramis has a patent “Industrial Synthesis of Modified Crosslinkable Biopolymer” pending. Conflict of interest: R. Middlewick has nothing to disclose. Conflict of interest: F. Pappalardo has nothing to disclose. Conflict of interest: J.T. Cairns has nothing to disclose. Conflict of interest: I.D. Stewart has nothing to disclose. Conflict of interest: A.E. John has nothing to disclose. Conflict of interest: S-U-N. Naveed has nothing to disclose. Conflict of interest: R. Krishnan has nothing to disclose. Conflict of interest: S. Miller has nothing to disclose. Conflict of interest: D.E. Shaw has nothing to disclose. Conflict of interest: C.E. Brightling has nothing to disclose. Conflict of interest: L. Buttery has nothing to disclose. Conflict of interest: F. Rose has nothing to disclose. Conflict of interest: G. Jenkins reports personal fees and other (sponsored research agreement paid to institution) from Biogen, GlaxoSmithKline and MedImmune, personal fees from Galapagos, Heptares, Boehringer Ingelheim, Pliant, Roche/InterMune, PharmAkea, Bristol Myers Squibb, Chiesi and Roche/Promedior, other (sponsored research agreement paid to institution) from Galecto, other (collaborative awards) from RedX and Nordic Biosciences, other (advisory board membership) from NuMedii, outside the submitted work; is supported by a National Institute of Health Research Professorship (RP-2017-08-ST2-014); and is a trustee for Action for Pulmonary Fibrosis. Conflict of interest: S.R. Johnson reports grants from the Medical Research Council (MRC), during the conduct of the study; grants from the National Institute of Health Research, MRC and Pfizer, personal fees from AstraZeneca, outside the submitted work. Conflict of interest: A.L. Tatler reports personal fees for consultancy from Pliant Therapeutics, outside the submitted work.

SUPPLEMENTARY INFO

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Practice Guideline

Med Clin (Barc)



. 2022 Jul 8;159(1):53.e1-53.e14.

doi: 10.1016/j.medcli.2021.04.028. Epub 2021 Jul 3.

# [Expert consensus recommendations for the management of asthma in older adults](#)

[Article in English, Spanish]

[Miguel Perpiñá<sup>1</sup>](#), [Ana Gómez-Bastero<sup>2</sup>](#), [Andrea Trisán<sup>3</sup>](#), [Eva Martínez-Moragón<sup>4</sup>](#), [Francisco Javier Álvarez-Gutiérrez<sup>5</sup>](#), [Isabel Urrutia<sup>6</sup>](#), [Marina Blanco-Aparicio<sup>7</sup>](#)

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- DOI: [10.1016/j.medcli.2021.04.028](https://doi.org/10.1016/j.medcli.2021.04.028)

## Abstract

Asthma is a public health problem in patients of any age, although there is still a tendency to erroneously assume that it is almost always confined to children and young people. Epidemiological

studies indicate that, from the sixth decade of life, the prevalence of this disease in countries such as Spain reaches 6-10%, with a higher prevalence among women aged 64 to 75 years. In addition, two-thirds of asthma deaths occur at this stage of life, resulting in a substantial number of hospital admissions, longer hospital stays and, from a finance point of view, significant direct economic costs. Asthma in older adults (65 years or older) is now a matter of great concern, the reality of which is underestimated and undertreated. It is therefore essential to establish appropriate recommendations for the diagnosis and treatment of asthma in the aging population. This consensus, which brings together the latest evidence available, was conceived with this objective. The proposed recommendations/conclusions are the result of a nominal consensus developed throughout 2019 and validated by panellists in successive rounds of voting.

**Keywords:** Asma; Asthma; Comorbidities; Comorbilidades; Diagnóstico diferencial; Differential diagnosis; Immunosenescence; Inmunosenescencia; Older adults; Personas mayores; Tratamiento; Treatment.

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SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS



## RHINITIS

1

Allergy

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. 2022 Jul 8.

doi: 10.1111/all.15430. Online ahead of print.

# [Role of Dietary Fiber in Promoting Immune Health – An EAACI Position Paper](#)

[Carina Venter](#), [Rosan W Meyer](#)<sup>1</sup>, [Matthew Greenhawt](#)<sup>2,3</sup>, [Isabella Pali-Schöll](#)<sup>4</sup>, [Bright Nwaru](#)<sup>5</sup>, [Caroline Roduit](#)<sup>6,7</sup>, [Eva Untersmayer](#)<sup>8</sup>, [Karine Adel-Patient](#)<sup>9</sup>, [Ioana Agache](#)<sup>10</sup>, [Carlo](#)



[Agostoni](#)<sup>11 12</sup>, [Cezmi A Akdis](#)<sup>7 13</sup>, [Mary Feeney](#)<sup>14 15</sup>, [Karin Hoffmann-Sommergruber](#)<sup>8</sup>, [Nonhlanhla Lunjani](#)<sup>16 17</sup>, [Kate Grimshaw](#)<sup>18</sup>, [Imke Reese](#)<sup>19</sup>, [Peter K Smith](#)<sup>20</sup>, [Milena Sokolowska](#)<sup>13</sup>, [Emilia Vassilopoulou](#)<sup>21</sup>, [Berber Vlieg-Boerstra](#)<sup>22 23</sup>, [Shriya Amara](#)<sup>24</sup>, [Jens Walter](#)<sup>16 25 26</sup>, [Liam O'Mahony](#)<sup>16 25 26</sup>

Affiliations expand

- PMID: 35801383
- DOI: [10.1111/all.15430](https://doi.org/10.1111/all.15430)

## Abstract

Microbial metabolism of specific dietary components, such as fiber, contribute to the sophisticated inter-kingdom dialogue in the gut that maintains a stable environment with important beneficial physiological, metabolic, and immunological effects on the host. Historical changes in fiber intake may be contributing to the increase of allergic and hypersensitivity disorders as fiber-derived metabolites are evolutionarily hardwired into the molecular circuitry governing immune cell decision making processes. In this review, we highlight the importance of fiber as a dietary ingredient, its effects on the microbiome, its effects on immune regulation, the importance of appropriate timing of intervention to target any potential window of opportunity, and potential mechanisms for dietary fibers in the prevention and management of allergic diseases. In addition, we review the human studies examining fiber or prebiotic interventions on asthma and respiratory outcomes, allergic rhinitis, atopic dermatitis, and overall risk of atopic disorders. While exposures, interventions and outcomes were too heterogeneous for meta-analysis, there is significant potential for using fiber in targeted manipulations of the gut microbiome and its metabolic functions in promoting immune health.

**Keywords:** allergy; diet; fiber; nutrition; prebiotics.

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Int Forum Allergy Rhinol

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. 2022 Jul 7.

doi: 10.1002/alr.23058. Online ahead of print.

# [Correlation between middle turbinate insertion in relation to sphenopalatine foramen and failure rates of cryotherapy and radiofrequency treatment for chronic rhinitis](#)

[Timothy Fan](#)<sup>1</sup>, [Megha Chandna](#)<sup>1</sup>, [Daniel Gorelik](#)<sup>2</sup>, [Masayoshi Takashima](#)<sup>2</sup>, [Michael T Yim](#)<sup>3</sup>, [Nicholas R Rowan](#)<sup>4</sup>, [Prachi Dubey](#)<sup>5</sup>, [Jordan J Garner](#)<sup>2</sup>, [Jason F Ohlstein](#)<sup>6</sup>, [Arthur W Wu](#)<sup>7</sup>, [Omar G Ahmed](#)<sup>2</sup>

Affiliations expand

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- DOI: [10.1002/alr.23058](https://doi.org/10.1002/alr.23058)

*No abstract available*

**Keywords:** Chronic rhinitis; Cryotherapy; Middle turbinate Nonallergic rhinitis; Radiofrequency therapy; Vasomotor rhinitis.

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. 2022 Jul 6;21(1):63.

doi: 10.1186/s12940-022-00871-x.

# [Birch pollen, air pollution and their interactive effects on airway symptoms and peak expiratory flow in allergic asthma during pollen season – a panel study in Northern and Southern Sweden](#)

[Hanne Krage Carlsen](#)<sup>1</sup>, [Susanna Lohman Haga](#)<sup>2</sup>, [David Olsson](#)<sup>1,3</sup>, [Annelie F Behndig](#)<sup>4</sup>, [Lars Modig](#)<sup>3</sup>, [Kadri Meister](#)<sup>5</sup>, [Bertil Forsberg](#)<sup>3</sup>, [Anna-Carin Olin](#)<sup>2</sup>

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- DOI: [10.1186/s12940-022-00871-x](https://doi.org/10.1186/s12940-022-00871-x)

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## Abstract

**Background:** Evidence of the role of interactions between air pollution and pollen exposure in subjects with allergic asthma is limited and need further exploration to promote adequate preventive measures. The objective of this study was to assess effects of exposure to ambient air pollution and birch pollen on exacerbation of respiratory symptoms in subjects with asthma and allergy to birch.

**Methods:** Thirty-seven subjects from two Swedish cities (Gothenburg and Umeå) with large variation in exposure to both birch-pollen and air pollutants, participated in the study. All subjects had confirmed allergy to birch and self-reported physician-diagnosed asthma. The subjects recorded respiratory symptoms such as rhinitis or eye irritation, dry cough, dyspnoea, the use of any asthma or allergy medication and peak respiratory flow (PEF), daily for five consecutive weeks during two separate pollen seasons and a control season without pollen. Nitrogen oxides (NO<sub>x</sub>), ozone (O<sub>3</sub>), particulate matter (PM<sub>2.5</sub>), birch pollen counts, and meteorological data were obtained from an urban background monitoring stations in the study city centres. The data were analysed using linear mixed effects models.

**Results:** During pollen seasons all symptoms and medication use were higher, and PEF was reduced in the subjects. In regression analysis, exposure to pollen at lags 0 to 2 days, and lags 0 to 6 days was associated with increased ORs of symptoms and decreased RRs for PEF. Pollen and air pollution interacted in some cases; during low pollen exposure, there were no associations between air pollution and symptoms, but during high pollen exposure, O<sub>3</sub> concentrations were associated with increased OR of rhinitis or eye irritation, and PM<sub>2.5</sub> concentrations were associated with increased ORs of rhinitis or eye irritation, dyspnea and increased use of allergy medication.

**Conclusions:** Pollen and air pollutants interacted to increase the effect of air pollution on respiratory symptoms in allergic asthma. Implementing the results from this study, advisories for individuals with allergic asthma could be improved, minimizing the morbidities associated with the condition.

**Keywords:** Allergic asthma; Betula; Birch; O<sub>3</sub>; PM<sub>2.5</sub>; Panel study; Pollen season.

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- [42 references](#)

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[Review](#)

Allergy

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. 2022 Jul 4.

doi: 10.1111/all.15426. Online ahead of print.

# The impact of type 2 immunity and allergic diseases in atherosclerosis

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- DOI: [10.1111/all.15426](https://doi.org/10.1111/all.15426)

## Abstract

Allergic diseases are allergen-induced immunological disorders characterized by the development of type 2 immunity and IgE responses. The prevalence of allergic diseases has been on the rise alike cardiovascular disease (CVD), which affects arteries of different organs such as the heart, the kidney and the brain. The underlying cause of CVD is often atherosclerosis, a disease distinguished by endothelial dysfunction, fibrofatty material accumulation in the intima of the artery wall, smooth muscle cell proliferation, and Th1 inflammation. The opposed T-cell identity of allergy and atherosclerosis implies an atheroprotective role for Th2 cells by counteracting Th1 responses. Yet, the clinical association between allergic disease and CVD argues against it. Within, we review different phases of allergic pathology, basic immunological mechanisms of atherosclerosis and the clinical association between allergic diseases (particularly asthma, atopic dermatitis, allergic rhinitis and food allergy) and CVD. Then, we discuss putative atherogenic mechanisms of type 2 immunity and allergic inflammation including acute allergic reactions (IgE, IgG1, mast cells, macrophages and allergic mediators such as vasoactive components, growth factors and those derived from the complement, contact and coagulation systems) and late phase inflammation (Th2 cells, eosinophils, type 2 innate-like lymphoid cells, alarmins, IL-4, IL-5, IL-9, IL-13 and IL-17).

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Curr Opin Allergy Clin Immunol



. 2022 Jul 4.

doi: 10.1097/ACI.0000000000000830. Online ahead of print.

# [LNIT-Local nasal immunotherapy in allergic rhinitis: revisited evidence and perspectives](#)

[Dichapong Kanjanawasee](#)<sup>1,2</sup>, [Pongsakorn Tantilipikorn](#)<sup>1,3</sup>

Affiliations expand

- PMID: 35779069
- DOI: [10.1097/ACI.0000000000000830](https://doi.org/10.1097/ACI.0000000000000830)

## Abstract

**Purpose of review:** Allergen immunotherapy (AIT) is a personalized treatment approach for the allergic airway disease. The most common routes of administration are subcutaneous and sublingual. Local nasal immunotherapy (LNIT) presents another alternative route for allergen desensitization. Nasal mucosa is the first entry site of pathogens and numerous lymphoid organs are located in this area, making LNIT a favorable method for triggering immune tolerance. LNIT has shown promising results in reducing symptoms and medication use in allergic rhinitis patients. Over time, difficulties in

dosing adjustments have made this method less popular. Recent advances in intranasal drug delivery systems warrant re-examination of LNIT as a viable option for the treatment of the allergic airway disease.

**Recent findings:** The scope of the review includes evidences of LNIT in human trials including comparison with placebo and conventional method of immunotherapy. Recent articles regarding the mechanism of LNIT and the challenges of intranasal drug delivery are reviewed. Advances in the LNIT delivery system which have overcome previous limitations demonstrate promising effects.

**Summary:** LNIT presents a judicious alternative for noninjection AIT. The evidences from previous clinical trials and the novel improvement of drug delivery system will lead into the future allergen vaccine production.

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- [59 references](#)

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## CHRONIC COUGH

Pulm Ther

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doi: 10.1007/s41030-022-00194-9. Online ahead of print.

# Respiratory Symptoms among US Adults: a Cross-Sectional Health Survey Study

[Roy A Pleasants<sup>1</sup>](#), [Khosrow Heidari<sup>2</sup>](#), [Jill Ohar<sup>3</sup>](#), [James F Donohue<sup>4</sup>](#), [Njira L Lugogo<sup>5</sup>](#), [Sarojini M Kanotra<sup>6</sup>](#), [Monica Kraft<sup>7</sup>](#), [David M Mannino<sup>8</sup>](#), [Charlie B Strange<sup>9</sup>](#)

Affiliations expand

- PMID: 35794458

- DOI: [10.1007/s41030-022-00194-9](https://doi.org/10.1007/s41030-022-00194-9)

## Abstract

**Introduction:** Data collected through ongoing, state-based, cross-sectional health surveys could be used to better understand the contribution of respiratory symptoms to impaired health among the US adult population.

**Methods:** We used the 2015 Behavioral Risk Factor Surveillance System telephone health survey in four states (Kentucky, Florida, South Carolina, Texas) to describe the relationship between symptoms, associated factors such as tobacco smoking, and health impairments. Self-reported productive cough, shortness of breath (SOB), and dyspnea on exertion (DOE) were categorized as minimal, moderate, or severe. Data were analyzed using multiple logistic regression models with age as a covariate to assess relationships of symptoms with other factors.

**Results:** Among adults  $\geq 18$  years, respiratory impairment [current asthma, chronic obstructive pulmonary disease (COPD), or a current moderate or severe symptom] occurred in 39.1% of the population. More than half of adults reporting moderate or severe symptoms had not been diagnosed with asthma or COPD, particularly with DOE and productive cough. Subjects were at greater risk of moderate and severe SOB or productive cough with increasing age, prolonged smoking duration ( $\geq 20$  years), being an ever-smoker, or if reporting COPD, current asthma, or any other comorbidity except cancer. Morbid obesity [body mass index (BMI)  $> 35$  kg/m<sup>2</sup>] was associated with severe DOE at a rate similar to current asthma or COPD (25.6%, 95% CI 20.9-30.3%; 20.8%, 95% CI 16.4-25.1%; 21.3%, 95% CI 17.5-25.1%, respectively); it was the most common cause of DOE. SOB was associated with worse general health impairment and limited ambulation compared with other symptoms. Tobacco smoking prevalence and race varied among states, affecting symptom prevalence.

**Conclusion:** In the largest US survey in decades, we provide a current perspective of respiratory symptoms among adults of all ages. While known risk factors were apparent, low-risk persons also frequently reported symptoms and impairments.

**Keywords:** Asthma; Behavioral Risk Factor Surveillance System; COPD; Cross-sectional health survey; Dyspnea on exertion; Obesity; Productive cough; Quality of life; Shortness of breath; Smoking duration.

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