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COPD

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Aging (Albany NY)

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. 2022 Oct 28;14(undefined).

doi: 10.18632/aging.204358. Online ahead of print.

Identification and validation of genetic signature associated with aging in chronic obstructive pulmonary disease

[Shanshan Chen](#)¹, [Yuan Zhan](#)¹, [Jinkun Chen](#)², [Jixing Wu](#)¹, [Yiya Gu](#)¹, [Qian Huang](#)¹, [Zhesong Deng](#)¹, [Xiaojie Wu](#)³, [Yongman Lv](#)⁴, [Jungang Xie](#)¹

Affiliations expand

- PMID: 36309899
- DOI: [10.18632/aging.204358](https://doi.org/10.18632/aging.204358)

Abstract

Aging plays an essential role in the development for chronic obstructive pulmonary disease (COPD). The aim of this study was to identify and validate the potential aging-related

genes of COPD through bioinformatics analysis and experimental validation. Firstly, we compared the gene expression profiles of aged and young COPD patients using two datasets (GSE76925 and GSE47460) from Gene Expression Omnibus (GEO), and identified 244 aging-related different expressed genes (DEGs), with 132 up-regulated and 112 down-regulated. Then, by analyzing the data for cigarette smoke-induced COPD mouse model (GSE125521), a total of 783 DEGs were identified between aged and young COPD mice, with 402 genes increased and 381 genes decreased. Additionally, functional enrichment analysis revealed that these DEGs were actively involved in COPD-related biological processes and function pathways. Meanwhile, six genes were identified as the core aging-related genes in COPD after combining the human DEGs and mouse DEGs. Eventually, five out of six core genes were validated to be up-regulated in the lung tissues collected from aged COPD patients than young COPD patients, namely NKG7, CKLF, LRP4, GDPD3 and CXCL9. Thereinto, the expressions of NKG7 and CKLF were negatively associated with lung function. These results may expand the understanding for aging in COPD.

Keywords: aging; bioinformatics analysis; chronic obstructive pulmonary disease; genetic signature.

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Handb Exp Pharmacol

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. 2022 Oct 29.

doi: 10.1007/164_2022_614. Online ahead of print.

[Metabolomics of Respiratory Diseases](#)

[Subhabrata Moitra](#)¹, [Arghya Bandyopadhyay](#)¹, [Paige Lacy](#)²

Affiliations expand

- PMID: 36306009
- DOI: [10.1007/164_2022_614](https://doi.org/10.1007/164_2022_614)

Abstract

Metabolomics is an expanding field of systems biology that is gaining significant attention in respiratory research. As a unique approach to understanding and diagnosing diseases, metabolomics provides a snapshot of all metabolites present in biological samples such as exhaled breath condensate, bronchoalveolar lavage, plasma, serum, urine, and other specimens that may be obtained from patients with respiratory diseases. In this article, we review the rapidly expanding field of metabolomics in its application to respiratory diseases, including asthma, chronic obstructive pulmonary disease (COPD), pneumonia, and acute lung injury, along with its more severe form, adult respiratory disease syndrome. We also discuss the potential applications of metabolomics for monitoring exposure to aerosolized occupational and environmental materials. With the latest advances in our understanding of the microbiome, we discuss microbiome-derived metabolites that arise from the gut and lung in asthma and COPD that have mechanistic implications for these diseases. Recent literature has suggested that metabolomics analysis using nuclear magnetic resonance (NMR) and mass spectrometry (MS) approaches may provide clinicians with the opportunity to identify new biomarkers that may predict progression to more severe diseases which may be fatal for many patients each year.

Keywords: Acute lung injury; Acute respiratory distress syndrome (ARDS); Asthma; Chronic obstructive pulmonary disease (COPD); Pneumonia.

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BMC Pulm Med

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. 2022 Oct 27;22(1):390.

doi: 10.1186/s12890-022-02187-5.

An observational study of the effects of smoking cessation earlier on the clinical characteristics and course of acute exacerbations of chronic obstructive pulmonary disease

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- PMID: 36303160
- PMCID: [PMC9615224](#)
- DOI: [10.1186/s12890-022-02187-5](#)

Free PMC article

Abstract

Background: Previous studies have focused on the negative effects of continued smoking on chronic obstructive pulmonary disease (COPD). However, few studies have investigated the positive effects of long-term smoking cessation on patients suffering from acute exacerbations of COPD.

Methods: The study recruited and followed current or former smokers who had been hospitalized and diagnosed with AECOPD. An in-depth analysis of clinical and laboratory indicators was conducted.

Results: 125 patients were covered, including 72 short-term quitters and 53 long-term quitters. The results showed that long-term smoking cessation may result in milder dyspnea and cough, a higher oxygenation index, a lower arterial partial pressure of carbon dioxide, and milder pulmonary hypertension, airflow restriction, and gas retention in patients with AECOPD. However, despite the lower treatment intensity for long-term quitters, improvement in dyspnea and an increase in oxygenation index were comparable to those achieved by short-term quitters. Furthermore, patients with mild phlegm, which accounted for 84% of all subjects, showed greater improvement in phlegm in AECOPD patients with long-term cessation of smoking.

Conclusion: It was found that in patients with AECOPD who quit smoking for a long period of time, there was a reduction in symptoms, improvement in lung function, reduction in treatment intensity, and better improvement in phlegm symptoms after therapy. It is beneficial and necessary to quit smoking early, even if you smoke a small amount of cigarettes.

Keywords: AECOPD; Smoking cessation; Therapeutics.

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Conflict of interest statement

The authors declare that they have no competing interests.

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Respiration

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. 2022 Oct 27;1-6.

doi: 10.1159/000527455. Online ahead of print.

Crossover Patient Outcomes for Targeted Lung Denervation in

Moderate to Severe Chronic Obstructive Pulmonary Disease: AIRFLOW-2

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Affiliations expand

- PMID: 36302345
- DOI: [10.1159/000527455](https://doi.org/10.1159/000527455)

Abstract

Background: Targeted Lung Denervation (TLD) is a potential new therapy for COPD. Radiofrequency energy is bronchoscopically delivered to the airways to disrupt pulmonary parasympathetic nerves, to reduce bronchoconstriction, mucus hypersecretion, and bronchial hyperreactivity.

Objectives: This work assesses the effect of TLD on COPD exacerbations (AECOPD) in crossover subjects in the AIRFLOW-2 trial.

Method: The AIRFLOW-2 trial is a multicentre, randomized, double-blind, sham-controlled crossover trial of TLD in COPD. Patients with symptomatic COPD on optimal medical therapy with an FEV1 of 30-60% predicted received either TLD or sham bronchoscopy in a 1:1 randomization. Those in the sham arm had the opportunity to cross into the treatment arm after 12 months. The primary end point was rate of respiratory adverse events. Secondary end points included adverse events, changes in lung function and health-related quality of life and symptom scores.

Results: Twenty patients were treated with TLD in the crossover phase and were subsequently followed up for 12 months (50% female, mean age 64.1 ± 6.9 years). After TLD, there was a trend towards a reduction in time to first AECOPD (hazard ratio 0.65, p = 0.28, not statistically significant) in comparison to sham follow-up period. There was also a reduction in time to first severe AECOPD in the crossover period (hazard ratio 0.38, p = 0.227, not statistically significant). Symptom scores and lung function showed stability.

Conclusions: AIRFLOW-2 crossover data support that of the randomization phase, showing trends towards reduction in COPD exacerbations with TLD.

Keywords: Bronchoscopy; Chronic obstructive pulmonary disease; Emphysema; Interventional pulmonology; Pulmonary medicine.

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Chronic Obstr Pulm Dis



. 2022 Oct 26;9(4):576-590.

doi: 10.15326/jcopdf.2022.0307.

[Interpreting Evaluating Respiratory Symptoms™ in COPD Diary Scores in Clinical Trials: Terminology, Methods, and Recommendations](#)

[Nancy K Leidy¹](#), [Donald M Bushnell¹](#), [Chau Thach²](#), [Carolina Hache²](#), [Florian S Gutzwiller²](#)

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- PMID: 36130315
- DOI: [10.15326/jcopdf.2022.0307](https://doi.org/10.15326/jcopdf.2022.0307)

Free article

Abstract

Accurately interpreting scores on patient-reported outcome (PRO) measures is essential to understanding and communicating treatment benefit. Over the years, terminology and methods for developing recommendations for PRO score interpretation in clinical trials have evolved, leading to some confusion in the field. The phrase "minimal clinically important difference (MCID)" has been simplified to "minimal important difference (MID)" and use of responder thresholds to interpret statistically significant treatment effects has increased. Anchor-based derivation methods continue to be the standard, with specific variations preferred by regulatory authorities for drug development programs. In the midst of these changes, the Evaluating Respiratory Symptoms™ in COPD (E-RS:COPD) was developed and qualified for use as an endpoint in chronic obstructive pulmonary disease (COPD) drug development programs. This paper summarizes the evolution of terminology and method preferences for the development of recommendations for interpreting scores from PRO measures used in clinical trials, and how these changes are reflected in the E-RS:COPD recommendations. The intent is to add clarity to discussions around PRO endpoints and facilitate use of the E-RS:COPD as a key efficacy endpoint in clinical trials of COPD.

Keywords: Evaluating Respiratory Symptoms (E-RS) in Chronic Obstructive Pulmonary Disease (COPD); PROs and clinical trials; interpretation recommendations for PRO measures; patient-reported outcome (PRO) measure; symptomatic relief.

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Chronic Obstr Pulm Dis

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. 2022 Oct 26;9(4):520-537.

doi: 10.15326/jcopdf.2022.0331.

Endurance Time During Constant Work Rate Cycle Ergometry in COPD: Development of an Integrated Database From Interventional Studies

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- PMID: 36066494
- DOI: [10.15326/jcopdf.2022.0331](https://doi.org/10.15326/jcopdf.2022.0331)

Free article

Abstract

Introduction: The COPD Biomarkers Qualification Consortium (CBQC) was formed under COPD Foundation management, with the goal of qualifying biomarkers and clinical outcome assessments through established regulatory processes for chronic obstructive pulmonary disease (COPD). Within CBQC, a working group evaluated opportunities for qualification of an exercise endurance measure. In a recent publication (*Chronic Obstr Pulm Dis.* 2022; 9[2]:252-265), we described a conceptual framework establishing exercise endurance's direct relationship to an individual with COPD's experience of physical functioning in daily life, and that increase in exercise endurance is a patient-centered, meaningful treatment benefit. We further proposed endurance time during constant work rate cycle ergometry (CWRCE) as a useful efficacy endpoint in clinical therapeutic intervention trials. In this current publication, we describe the process of assembling an integrated database of endurance time responses to interventions in COPD.

Methods: We sought participant-level data from published studies incorporating CWRCE as an outcome measure. A literature search screened 2993 publications and identified 553 studies for assessment. Two interventions had sufficient data across studies to warrant data

extraction: bronchodilators and rehabilitative exercise training. Investigators were contacted and requested to provide participant-by-participant data from their published studies.

Results: The final dataset included data from 8 bronchodilator studies (2166) participants and 15 exercise training studies (3488 participants). The database includes 71 variables per participant, comprising demographic, pulmonary function, and detailed physiologic response data. This paper provides a detailed description of the analysis population, while analysis supporting the validation/qualification process and addressing other scientific questions will be described in subsequent publications.

Keywords: bronchodilator; clinical outcome assessment; exercise endurance; exercise training; patient-centric.

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Chronic Obstr Pulm Dis

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. 2022 Oct 26;9(4):538-548.

doi: 10.15326/jcopdf.2022.0303.

[Beyond Access: Factors Associated With Spirometry Underutilization Among](#)

Patients With a Diagnosis of COPD in Urban Tertiary Care Centers

[Arianne K Baldomero](#)^{1,2,3}, [Ken M Kunisaki](#)^{1,2}, [Ann Bangerter](#)³, [David B Nelson](#)³, [Chris H Wendt](#)^{1,2}, [Spyridon Fortis](#)^{4,5}, [Hildi Hagedorn](#)³, [R Adams Dudley](#)^{1,2,3}

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- DOI: [10.15326/jcopdf.2022.0303](https://doi.org/10.15326/jcopdf.2022.0303)

Free article

Abstract

Rationale: Many patients with suspected chronic obstructive pulmonary disease (COPD) do not undergo spirometry to confirm the diagnosis. Underutilization is often attributed to barriers to accessing spirometry.

Objective: Our objective was to identify factors associated with spirometry underutilization for patients who are less likely to face access barriers related to travel, insurance, and availability of spirometry.

Methods: A retrospective analysis was conducted of patients enrolled in the Veterans Health Administration and living in urban areas with a new diagnosis of COPD between 2012 to 2015, reducing out-of-pocket cost and travel barriers, respectively. We included only patients whose primary care clinic was located in an academically affiliated tertiary level facility with spirometry available. We used logistic regression to estimate associations between patient characteristics and receipt of spirometry within 2 years before or after COPD diagnosis.

Results: Of 24,300 patients, 59.7% had spirometry. Compared to patients <55 years, patients 75-84 years had an adjusted odds ratio (aOR) of undergoing spirometry of 0.80 (95% confidence interval [CI]:0.72-0.90), while patients ≥85 years had an aOR of 0.47 (95%CI: 0.40-0.54). Compared to patients with a Charlson Comorbidity Index (CCI) ≥3, patients with a CCI of 0 had an aOR of 0.60 (95%CI:0.54-0.67). Patients who had not seen a pulmonary specialist had lower odds of receiving spirometry (aOR 0.38 [95%CI:0.35-0.41]).

Conclusion: Spirometry underutilization persists among patients who are less likely to have access barriers related to travel, insurance, and availability of spirometry. Spirometry

underutilization is associated with older age, not having received pulmonary care, and having fewer comorbidities. COPD care quality initiatives will need to address these factors.

Keywords: Veterans Affairs; chronic obstructive pulmonary disease; health care services; pulmonary disease; spirometry.

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. 2022 Oct 26;9(4):510-519.

doi: 10.15326/jcopdf.2022.0287.

[Impact of the Coronavirus Disease 2019 Pandemic on Physical and Mental Health of Patients With COPD: Results From a Longitudinal Cohort Study Conducted in the United States \(2020–2021\)](#)

[William Z Zhang](#)¹, [Stephanie L LaBedz](#)², [Janet T Holbrook](#)³, [Andrew Gangemi](#)⁴, [Ramasubramanian Baalachandran](#)⁵, [Michelle N Eakin](#)⁶, [Robert A Wise](#)⁶, [Kaharu Sumino](#)⁷, [American Lung Association Airways Clinical Research Centers](#)

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- PMID: 35998338
- DOI: [10.15326/jcopdf.2022.0287](https://doi.org/10.15326/jcopdf.2022.0287)

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Abstract

Background: Patients with chronic obstructive pulmonary disease (COPD) are at higher risk for severe coronavirus disease 2019 (COVID-19). From the pandemic's onset there has been concern regarding effects on health and well-being of high-risk patients.

Methods: This was an ancillary study to the Losartan Effects on Emphysema Progression (LEEP) Trial and was designed to collect descriptive information longitudinally about the health and wellbeing of COPD patients who were enrolled in a clinical trial. Participants were interviewed by telephone about their health status every 2 weeks and their mental health, knowledge, and behaviors every 8 weeks from June 2020 to April 2021. There were no pre-specified hypotheses.

Results: We enrolled 157 of the 220 participants from the parent LEEP trial. Their median age was 69 years, 55% were male, and 82% were White; median forced expiratory volume in 1 second (FEV₁)% predicted was 48%. Nine confirmed COVID-19 infections were reported, 2 resulting in hospitalization. Rates of elevated anxiety or depressive symptoms were 8% and 19% respectively in June 2020 and remained relatively stable during follow-up. By April 2021, 85% of participants said they were "very likely" to receive a vaccine; 91% were vaccinated (≥1 dose) by the end of December 2021.

Conclusion: Our select cohort of moderate to severe COPD patients who were well integrated into a health care network coped well with the COVID-19 pandemic. Few participants were diagnosed with COVID-19, levels of depression and anxiety were stable, most adopted accepted risk reduction behaviors, and did not become socially isolated; most were vaccinated by the end of 2021.

Keywords: COPD; COVID-19; anxiety; depression; vaccination; vaccine hesitancy.

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Chronic Obstr Pulm Dis

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. 2022 Oct 26;9(4):486-499.

doi: 10.15326/jcopdf.2022.0305.

[Varenicline for Gradual Versus Abrupt Smoking Cessation in Poorly Motivated Smokers With COPD: A Prematurely Terminated Randomized Controlled Trial](#)

[Abraham Bohadana](#)¹, [Ariel Rokach](#)¹, [Pascal Wild](#)², [Bela Peker](#)¹, [Yossi-Freier Dror](#)³, [Polina Babai](#)³, [Nissim Arish](#)¹, [Gabriel Izbicki](#)¹

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- PMID: 35877930
- DOI: [10.15326/jcopdf.2022.0305](https://doi.org/10.15326/jcopdf.2022.0305)

Free article

Abstract

Background: Although smoking is the leading cause of chronic obstructive pulmonary disease (COPD), many patients with COPD smoke, highlighting the need for effective smoking cessation interventions in this population. This study examined the efficacy and safety of varenicline in increasing smoking cessation rates through "gradual" versus "abrupt" cessation in COPD patients with low motivation to quit smoking.

Methods: A randomized, open label, 30-week, controlled trial (ClinicalTrials.gov identifier: [NCT02894957](https://clinicaltrials.gov/ct2/show/study/NCT02894957)) was conducted between January 2019 and October 2020 at a center in Israel. Smokers with COPD, poorly motivated to quit, were randomized to 6 weeks of varenicline for smoking reduction and a target quit day (TQD) at the end of week 6 (gradual cessation group) or *ad libitum* smoking for 5 weeks, 1 week of varenicline, and a TQD at the end of week 6 (abrupt cessation group). After the pre-quit phase, both groups received 12-week regular varenicline treatment and 12-week follow-up. Primary outcome was biochemically-validated continuous abstinence for weeks 6-30. Secondary outcomes were: (1) biochemically-confirmed 7-day point prevalence abstinence for weeks 4-30, (2) efficient smoking reduction ($\geq 50\%$ in number of cigarettes/day) in the pre-quit phase; and (3) number of cigarettes/day, motivation to quit, and changes in respiratory symptoms and spirometry from baseline through week 30.

Results: A drug recall issued by the study sponsor stopped the study after 70/242 (28.9%) patients had been enrolled. The gradual cessation group (n=29) had significantly higher continuous abstinence rates from TQD through week 30 versus the abrupt cessation group (n=41): 20.7% versus 4.9% (odds ratio [OR]=5.09; 95% confidence interval [CI] 0.89-29.17; $p=0.048$) and higher 7-day point prevalence abstinence levels at all time points but week 18 ($p=0.027$ at week 6, 0.056 at week 7, and 0.096 at week 9). Motivation to quit increased ($p=0.002$) and the number of cigarettes/day decreased ($p=0.002$) over time in both groups. Respiratory symptoms, but not spirometry, improved in both groups at week 30. Treatment was safe and well tolerated.

Conclusion: In poorly motivated smokers with COPD, using varenicline for a 6-week gradual smoking cessation before TQD, compared with abrupt cessation, significantly increased quit rates up to 6 months. Results were not affected by the smaller-than-expected sample size. Further studies are needed to confirm these data.

Keywords: chronic obstructive pulmonary disease; cigarette smoking; copd; smoking; smoking cessation; varenicline.

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Eur J Med Res

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. 2022 Oct 28;27(1):215.

doi: 10.1186/s40001-022-00861-2.

Transcriptome analysis of sputum cells reveals two distinct molecular phenotypes of "asthma and chronic obstructive pulmonary disease overlap" in the elderly

[Suh-Young Lee](#)^{1,2}, [Hyun-Seung Lee](#)³, [Heung-Woo Park](#)^{4,5,6}

Affiliations expand

- PMID: 36307832
- PMCID: [PMC9617312](#)
- DOI: [10.1186/s40001-022-00861-2](#)

Free PMC article

Abstract

Background: Little is known about the pathogenesis of asthma and chronic obstructive pulmonary disease (COPD) overlap (ACO). This study examined the molecular phenotypes of ACO in the elderly.

Methods: A genome-wide investigation of gene expression in sputum cells from the elderly with asthma, ACO, or COPD was performed using gene set variation analysis (GSVA) with predefined asthma- or COPD-specific gene signatures. We then performed a subsequent cluster analysis using enrichment scores (ESs) to identify molecular clusters in the elderly with ACO. Finally, a second GSVA was conducted with curated gene signatures to gain insight into the pathogenesis of ACO associated with the identified molecular clusters.

Results: Seventy elderly individuals were enrolled (17 with asthma, 41 with ACO, and 12 with COPD). Two distinct molecular clusters of ACO were identified. Clinically, ACO cluster 1 (N = 23) was characterized by male and smoker dominance, more obstructive lung function, and higher proportions of both neutrophil and eosinophil in induced sputum compared to ACO cluster 2 (N = 18). ACO cluster 1 had molecular features similar to both asthma and COPD, with mitochondria and peroxisome dysfunction as important mechanisms in the pathogenesis of these diseases. The molecular features of ACO cluster 2 differed from those of asthma and COPD, with enhanced innate immune reactions to microorganisms identified as being important in the pathogenesis of this form of ACO.

Conclusion: Recognition of the unique biological pathways associated with the two distinct molecular phenotypes of ACO will deepen our understanding of ACO in the elderly.

Keywords: Asthma; Asthma-chronic obstructive pulmonary disease overlap syndrome; Chronic obstructive pulmonary disease; Cluster analysis; Sputum; Transcriptome.

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Conflict of interest statement

The authors declare that they have no competing interests.

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doi: 10.1007/164_2022_614. Online ahead of print.

Metabolomics of Respiratory Diseases

[Subhabrata Moitra](#)¹, [Arghya Bandyopadhyay](#)¹, [Paige Lacy](#)²

Affiliations expand

- PMID: 36306009
- DOI: [10.1007/164_2022_614](https://doi.org/10.1007/164_2022_614)

Abstract

Metabolomics is an expanding field of systems biology that is gaining significant attention in respiratory research. As a unique approach to understanding and diagnosing diseases, metabolomics provides a snapshot of all metabolites present in biological samples such as exhaled breath condensate, bronchoalveolar lavage, plasma, serum, urine, and other specimens that may be obtained from patients with respiratory diseases. In this article, we review the rapidly expanding field of metabolomics in its application to respiratory diseases, including asthma, chronic obstructive pulmonary disease (COPD), pneumonia, and acute lung injury, along with its more severe form, adult respiratory disease syndrome. We also discuss the potential applications of metabolomics for monitoring exposure to aerosolized occupational and environmental materials. With the latest advances in our understanding of the microbiome, we discuss microbiome-derived metabolites that arise from the gut and lung in asthma and COPD that have mechanistic implications for these diseases. Recent literature has suggested that metabolomics analysis using nuclear magnetic resonance (NMR) and mass spectrometry (MS) approaches may provide clinicians with the opportunity to identify new biomarkers that may predict progression to more severe diseases which may be fatal for many patients each year.

Keywords: Acute lung injury; Acute respiratory distress syndrome (ARDS); Asthma; Chronic obstructive pulmonary disease (COPD); Pneumonia.

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Am J Respir Crit Care Med

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. 2022 Oct 27.

doi: 10.1164/rccm.202210-1953ED. Online ahead of print.

[Gastroesophageal Reflux, Atopic Dermatitis and Asthma—Finally Evidence for Causal Links?](#)

[Meghan D Althoff](#)¹, [Sunita Sharma](#)²

Affiliations expand

- PMID: 36301927
- DOI: [10.1164/rccm.202210-1953ED](https://doi.org/10.1164/rccm.202210-1953ED)

No abstract available

Keywords: GERD; asthma; atopic dermatitis; genetics.

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Allergy



. 2022 Oct 27.

doi: 10.1111/all.15566. Online ahead of print.

[Biomarkers of asthma relapse and lung function decline in adults with spontaneous asthma remission: a population-based cohort study](#)

[Daniel J Tan](#)¹, [Caroline J Lodge](#)¹, [E Haydn Walters](#)^{1,2}, [Adrian J Lowe](#)¹, [Dinh S Bui](#)¹, [Gayan Bowatte](#)^{1,3}, [Rangi Kandane-Rathnayake](#)⁴, [Fahad M Aldakheel](#)⁵, [Bircan Erbas](#)⁶, [Garun S Hamilton](#)^{4,7}, [Paul S Thomas](#)⁸, [Mark Hew](#)^{9,10}, [Mimi L K Tang](#)¹¹, [Michael J Abramson](#)⁹, [Jennifer L Perret](#)^{1,12}, [Shyamali C Dharmage](#)¹

Affiliations expand

- PMID: 36301194
- DOI: [10.1111/all.15566](https://doi.org/10.1111/all.15566)

Abstract

Background: The extent to which biomarkers of asthma activity persist in spontaneous asthma remission and whether such markers are associated with future respiratory

outcomes remained unclear. We investigated the association between sub-clinical inflammation in adults with spontaneous asthma remission and future asthma relapse and lung function decline.

Methods: The Tasmanian Longitudinal Health Study is a population-based cohort (n=8,583). Biomarkers of systemic inflammation were measured on participants at age 45 and latent profile analysis was used to identify cytokine profiles. Bronchial hyperresponsiveness (BHR) and nitric oxide products in exhaled breath condensate (EBC NOx) were measured at age 50. Participants with spontaneous asthma remission at ages 45 (n=466) and 50 (n=318) were re-evaluated at age 53, and associations between baseline inflammatory biomarkers and subsequent asthma relapse and lung function decline were assessed.

Results: We identified three cytokine profiles in adults with spontaneous asthma remission: average (34%), Th2-high (42%) and Th2-low (24%). Compared to the average profile, a Th2-high profile was associated with accelerated decline in post-BD FEV₁ /FVC (MD -0.18% predicted per-year; 95%CI -0.33, -0.02), while a Th2-low profile was associated with accelerated decline in both post-BD FEV₁ (-0.41%; -0.75, -0.06) and post-BD FVC (-0.31%; -0.62, 0.01). BHR and high TNF- α during spontaneous remission were associated with an increased risk of asthma relapse. In contrast, we found no evidence of association between EBC NOx and either asthma relapse or lung function decline.

Conclusion: BHR and serum inflammatory cytokines have prognostic value in adults with spontaneous asthma remission. At-risk individuals with BHR, Th2-high or Th2-low cytokine profiles may benefit from closer monitoring and on-going follow-up.

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J Asthma

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. 2022 Oct 27;1-14.

Use of FeNO to predict anti-IL-5 and IL-5R biologics efficacy in a real-world cohort of adults with severe eosinophilic asthma

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Affiliations expand

- PMID: 36301080
- DOI: [10.1080/02770903.2022.2136526](https://doi.org/10.1080/02770903.2022.2136526)

Abstract

Introduction: Severe eosinophilic asthma (SEA) is associated with multiple exacerbations. Fractional exhaled nitric oxide (FeNO), a biomarker of airway T2 inflammation, is known to be correlated with the risk of exacerbations. While the use of FeNO is well established to predict the therapeutic response to dupilumab (anti-IL-4/IL-13), it remains uncertain for biologics targeting the IL-5 pathway. **Methods:** We conducted an observational, retrospective, monocentric analysis of adults with SEA who started mepolizumab (anti-IL-5) or benralizumab (anti-IL-5-R) between January 1, 2016 and December 31, 2020. **Results:** Data were collected for 109 patients. All participants reported uncontrolled asthma with a median of 3 annual exacerbations and a median *Asthma Control Test* score of 12. They all had an initial blood eosinophilia >300/mm³, with a median at 610/mm³ (IQR 420-856). Patients with a baseline FeNO ≥50 ppb reported more exacerbations in the previous year than those with a FeNO <50 ppb ($p = 0.02$). After initiation of treatment, change in FeNO was not associated with therapeutic response. However, decrease in the annual number of exacerbations was significantly greater in patients with a baseline FeNO ≥50 ppb than in those with a baseline FeNO <50 ppb (-3.3 ± 2.7 vs -0.9 ± 2.4 , respectively; $p = 0.01$). There was no association between baseline FeNO values and subsequent lung function, asthma control or reduction of oral corticosteroids use. **Conclusion:** In this real-world cohort, adults with SEA who had a baseline FeNO ≥50 ppb experienced a greater decrease in exacerbations after 12 months of anti-IL-5 or IL-5-R biologics than those with a FeNO <50 ppb.

Keywords: benralizumab; exacerbation; exhaled nitric oxide; interleukin-5; mepolizumab; severe asthma.

FULL TEXT LINKS



RHINITIS

1

Fundam Clin Pharmacol



. 2022 Oct 31.

doi: 10.1111/fcp.12847. Online ahead of print.

[Survey the effect of drug treatment on modulation of cytokines gene expression in Allergic Rhinitis](#)

[Yan Ma](#)¹, [Xiao-Hong Yang](#)¹, [Yi Tu](#)¹, [Seyyed Shamsadin Athari](#)²

Affiliations expand

- PMID: 36314138
- DOI: [10.1111/fcp.12847](https://doi.org/10.1111/fcp.12847)

Abstract

Allergic rhinitis as common airway disease has high prevalence in all peoples worldwide. In allergic diseases, Th2 cells release type 2 cytokines which support the inflammation in airways. All the drugs used for allergic rhinitis, do not cure completely, and the choice of drugs according to cost and efficacy is very important in all groups of atopic patients. Therefore, in this study, the effect of commercial drugs on cytokine gene expression has been studied. Male Balb/c mice were divided into six groups. Allergic rhinitis was induced in five of the six groups with ovalbumin, and four of these five groups were treated with salbutamol, budesonide, theophylline and montelukast. The 5th group was used as positive

control group and the 6th group as negative control group. For the survey, RNA was extracted, cDNA was synthesized, and quantitative real time PCR was done for 21 genes. The four drugs had different effect on mRNA expression of cytokines (IL-1b, 2, 4, 5, 7, 8, 9, 11, 12, 13, 17, 18, 22, 25, 31, 33, 37, IFN- γ , TNF- α , TGF- β 1 and Eotaxin) in the allergic rhinitis groups. Salbutamol can be used during pregnancy and breastfeeding, but it has some side effects. Budesonide in the inhaled form is generally safe in pregnancy. Theophylline cannot control allergic attack in the long run. Montelukast is not useful in the treatment of acute. Immunomodulatory and anti-inflammatory effects of drugs in control of allergic rhinitis via Th2 cytokines can be new approaches in molecular medicine.

Keywords: allergy; asthma; beta2 Agonists; corticosteroid; drugs; leukotriene.

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J Clin Lab Anal

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. 2022 Oct 31;e24747.

doi: 10.1002/jcla.24747. Online ahead of print.

[Association between IL1RL1 gene polymorphisms and allergic rhinitis risk in the Chinese Han population](#)

[Zhengqing Li](#)¹, [Jiajia Ren](#)², [Jirong Zhang](#)³, [Xing Wang](#)⁴, [Yonglin Liu](#)², [Qiang Wang](#)⁵

Affiliations expand

- PMID: 36310516
- DOI: [10.1002/jcla.24747](https://doi.org/10.1002/jcla.24747)

Abstract

Background: Although it has been confirmed that IL1RL1 is involved in the occurrence of allergic rhinitis (AR), the role of IL1RL1 gene single nucleotide polymorphisms (SNPs) in AR is still unclear.

Methods: We performed a case-control study including 1000 AR patients and 1000 healthy controls. The four SNPs rs72823628 G > A, rs950881 G > T, rs72823641 T > A and rs3771175 T > A in IL1RL1 were chosen and genotyped using Agena MassARRAY platform. The relationship between IL1RL1 SNPs and AR risk was analyzed by logistic regression and assessed with odds ratios (ORs) and corresponding 95% confidence intervals (95% CIs).

Results: Overall analysis revealed that IL1RL1 gene rs72823628, rs950881 and rs3771175 were associated with a reduced AR risk. Stratified analysis showed that the three SNPs (rs72823628, rs950881 and rs3771175) were obviously linked to a reduced risk of AR in males. Moreover, no correlation was observed between haplotypes and reduced AR risk after the false discovery rate (FDR) correction. The false positive report probability (FPRP) analysis was used to further validate significant findings.

Conclusion: Our study is the first to indicate that IL1RL1 gene polymorphisms (rs72823628, rs950881 and rs3771175) may be correlated with decreased risk of AR in the Chinese Han population.

Keywords: IL1RL1; Chinese Han population; allergic rhinitis; polymorphisms; risk.

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NPJ Prim Care Respir Med

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. 2022 Oct 29;32(1):47.

doi: 10.1038/s41533-022-00313-8.

Validation of the Spanish language version of the control of allergic rhinitis and asthma test

[Quijano Diana](#)¹, [Ali Abraham](#)², [Arevalo Yaicith](#)³, [Orejuela Peter](#)⁴, [Trujillo Juan](#)⁵

Affiliations expand

- PMID: 36309520
- PMCID: [PMC9617860](#)
- DOI: [10.1038/s41533-022-00313-8](#)

Abstract

Allergic rhinitis and asthma are common diseases that frequently coexist, referred to as unified airway disease. There is currently no validated scale in Spanish, which allows simultaneous evaluation of both conditions. A translation from Portuguese to Spanish was therefore performed. It was administered to 120 patients aged between 18 and 70 years whose native language was Spanish and presented a diagnosis of allergic rhinitis and asthma. The reliability, validity and sensitivity to instrument change validations were carried out, as well as the values of minimally relevant clinical differences. Reliability was evaluated using Cronbach's alpha test on CARAT-global: 0.83 [IC 95% 0.79-0.88]; test and retest evaluation was done with Pearson's correlation coefficient: 0.6 [IC 95% 0.32-0.77] and the standard error of measurement 3.5 ($p < 0.005$). A confirmatory factor analysis was performed corroborating two factors. Correlation coefficients were not high in the longitudinal validation. Concurrent validity showed an acceptable correlation between CARAT10 asthma ACQ5 and low between allergic rhinitis-VAS. There was a milestone of the controlled disease in the discriminant validity of CARAT10 rhinitis ≥ 8 mean an adequate control, CARAT10-asthma > 16 In this case, CARAT10-asthma value < 16 are interpreted as an inadequate or partial control and values ≥ 16 mean an adequate control and CARAT10-global ≥ 18 , patients evaluated with CARAT10 with a result ≥ 18 , which would be a patient with both conditions controlled. The minimally relevant clinically important average difference found in the CARAT10 scale was 3.25 (SD 3.77). The CARAT10

scale in Spanish is a standardised, reliable and valid evaluation method on patients with unified airway disease.

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Conflict of interest statement

The authors declare no competing interests.

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

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Acta Biomed

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. 2022 Oct 26;93(5):e2022211.

doi: 10.23750/abm.v93i5.12633.

[Rhinosinusitis: clinical-based phenotyping](#)

[Giorgio Ciprandi](#)¹, [Desiderio Passali](#)², [Luisa Maria Bellussi](#)³, [Francesco Maria Passali](#)⁴

Affiliations expand

- PMID: 36300245
- DOI: [10.23750/abm.v93i5.12633](https://doi.org/10.23750/abm.v93i5.12633)

Abstract

Rhinosinusitis (RS) is a common disease and is currently classified into two main types: acute RS (ARS) and chronic RS (CRS), which in turn includes CRS with or without nasal polyps. Different guidelines consider this classification. However, in clinical practice, other phenotypes exist. The current article would propose new clinical-based phenotyping of RS, including the following clinical phenotypes: simple catarrhal RS, Acute RS, acute bacterial RS, severe (complicated) acute RS, chronic RS, and recurrent chronic RS. Treatment strategy should be tailored considering the clinical phenotype and could include phytomedicines, intranasal non-pharmacological remedies, and local bacteriotherapy. In conclusion, RS requires thorough diagnostic work-up, and the therapeutic approach should be mainly based on appropriate management.

SUPPLEMENTARY INFO

MeSH termsexpand

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Eur J Pediatr

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. 2022 Oct 27.

doi: 10.1007/s00431-022-04679-2. Online ahead of print.

[Probability of successful inhaled corticosteroids cessation in preschool wheezers: a predictive score](#)

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Affiliations expand

- PMID: 36289097

- DOI: [10.1007/s00431-022-04679-2](https://doi.org/10.1007/s00431-022-04679-2)

Abstract

Nearly all asthma predictive tools estimate the future risk of asthma development. However, there is no tool to predict the probability of successful ICS cessation at an early age. Therefore, we aimed to determine the predictors of successful ICS cessation in preschool wheezers, and developed a simple predictive tool for clinical practice. This was a retrospective cohort study involving preschool wheezers who had undergone an ICS therapeutic trial during 2015-2020 at the University Hospital, Southern, Thailand. A predictive scoring system was developed using a nomogram to estimate the probability of successful ICS cessation. We calculated area under ROC curve and used a calibration plot for assessing the tool's performance. A total of 131 medical records were eligible for analysis. Most of the participants were male (68.9%). More than half of the preschool wheezers had successful ICS cessation after an initial therapeutic trial regimen. The predictors of less successful ICS cessation were perinatal oxygen use [OR 0.10 (0.01, 0.70), $P = 0.02$], allergic rhinitis [OR 0.20 (0.08, 0.56), $P = 0.002$], blood eosinophil count > 500 cell/mm³ [OR 0.20 (0.06, 0.67), $P = 0.008$], and previous ICS use > 6 months [OR 0.30 (0.09, 0.72), $P = 0.009$].

Conclusions: Predictors of less successful ICS cessation were the following: perinatal oxygen use, allergic rhinitis, blood eosinophil count > 500 cell/mm³, and previous ICS use > 6 months. A simple predictive score developed in this study may help general practitioners to be more confident in making a decision regarding the discontinuation of ICS after initial therapeutic trials.

What is known: • Early allergic sensitization is associated with reduced chances of inhaled corticosteroid cessation at school age. • Prolonged ICS is associated with the emergence of adverse effect and discontinuing too early can result in recurrence symptoms.

What is new: • Requirement of oxygen support within 7 days after birth in term neonate is a postnatal factor associated with less successful ICS cessation. • We propose a simple predictive tool with easily available clinical parameters (perinatal oxygen use, allergic rhinitis, blood eosinophil count, parental asthma history, and duration of previous ICS use) to determine the timing of inhalational corticosteroid cessation in preschool wheezers.

Keywords: Childhood asthma; Inhaled corticosteroid therapeutic trials; Nomogram; Predictive tool; Preschool wheezing.

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Meta-Analysis

J Ethnopharmacol

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. 2022 Oct 28;297:115169.

doi: 10.1016/j.jep.2022.115169. Epub 2022 Mar 4.

[Efficacy and safety of the Chinese herbal medicine Xiao-qing-long-tang for allergic rhinitis: A systematic review and meta-analysis of randomized controlled trials](#)

[Yajie Yan](#)¹, [Jiajun Zhang](#)², [Haolan Liu](#)³, [Ze Lin](#)⁴, [Qiulan Luo](#)⁵, [Yunying Li](#)⁶, [Yan Ruan](#)⁷, [Shiqing Zhou](#)⁸

Affiliations expand

- PMID: 35257842
- DOI: [10.1016/j.jep.2022.115169](https://doi.org/10.1016/j.jep.2022.115169)

Abstract

Ethnopharmacological relevance: The classic Chinese herbal medicine formula Xiao-qing-long-tang (XQLT) is commonly recommended to manage allergic rhinitis (AR), but the treatment efficacy and safety of XQLT are uncertain.

Aim of the study: This study aimed to evaluate the effectiveness and safety of XQLT in treating AR.

Materials and methods: Nine databases were searched from their inception to April 2021. Randomized controlled trials (RCTs) evaluating XQLT for AR were included. The methodological quality of the studies was assessed using the Cochrane risk-of-bias tool. A meta-analysis and a subgroup meta-analysis were conducted to evaluate the effectiveness of XQLT.

Results: Twenty-four RCTs were included in this meta-analysis. XQLT was compared to both placebo and Western medicine (WM), and XQLT combined with WM was compared with WM alone. Meta-analyses were conducted for total nasal symptom scores (TNSS), four individual nasal symptom scores, quality of life (QoL), effective rate, and recurrence rate. The TNSS decreased after XQLT treatment and combination treatment (mean difference (MD): -0.79; 95% confidence interval (CI) [-1.20, -0.38], standardized mean difference (SMD): -1.42; 95% CI [-1.59, -1.24], and SMD: -1.84; 95% CI [-2.08, -1.60]). The two individual nasal symptom scores decreased after XQLT treatment and combination treatment; these nasal symptoms comprised rhinorrhea (SMD: -0.30; 95% CI [-0.58, -0.02] and SMD: -0.48; 95% CI [-0.70, -0.26]), and nasal obstruction (SMD: -0.54; 95% CI [-0.78, -0.30] and SMD: -0.54; 95% CI [-0.76, -0.32]). XQLT and XQLT combined with WM achieved a better effective rate than WM (risk ratio (RR): 1.18; 95% CI [1.11, 1.25] and RR: 1.16; 95% CI [1.10, 1.23]) and a lower recurrence rate than WM (RR: 0.24; 95% CI [0.13, 0.43] and RR: 0.47; 95% CI [0.31, 0.72]). XQLT was well tolerated in patients being treated for AR.

Conclusion: Our results indicated that oral XQLT may alleviate the TNSS, rhinorrhea scores, and nasal obstruction scores of AR and is safe to use in clinical practice. However, more RCTs that follow rigorous methodologies and evaluate well-accepted outcome measures are required to evaluate the effectiveness of XQLT.

Keywords: Allergic rhinitis; Chinese herbal medicine; Meta-analysis; RCT; Systematic review; Xiao-qing-long-tang.

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SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS



CHRONIC COUGH

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Neurosci Lett

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. 2022 Oct 26;136934.

doi: 10.1016/j.neulet.2022.136934. Online ahead of print.

Mini-Review: Hypertussivity and Allotussivity in Chronic Cough Endotypes

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

Affiliations expand

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

Abstract

In recent years our understanding of the neurophysiological basis of cough has increased substantially. In conjunction, concepts around the drivers of chronic coughing in patients have also significantly evolved. Increasingly it is recognised that dysregulation of the neuronal pathways mediating cough play an important role in certain phenotypes of chronic cough and therefore pathological processes affecting the nervous system are likely to represent key endotypes in patients. Taking inspiration from the study of neuropathic pain, the term hypertussia has been employed to describe the phenomenon of abnormal excessive coughing in response to airway irritation and allotussia to describe coughing in response to stimuli not normally provoking cough. This review aims to summarise current clinical evidence supporting a role for the hyperexcitability of neuronal pathways contributing to chronic coughing and suggest how these might align with the clinical features observed in patients.

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Conflict of interest statement

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

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BMC Pulm Med



. 2022 Oct 27;22(1):390.

doi: 10.1186/s12890-022-02187-5.

[An observational study of the effects of smoking cessation earlier on the clinical characteristics and course of acute exacerbations of chronic obstructive pulmonary disease](#)

[Xiaolong Li](#)^{#1}, [Zhen Wu](#)^{#1}, [Mingyue Xue](#)¹, [Wei Du](#)^{2,3,4}

Affiliations expand

- PMID: 36303160

- PMCID: [PMC9615224](#)

- DOI: [10.1186/s12890-022-02187-5](https://doi.org/10.1186/s12890-022-02187-5)

Free PMC article

Abstract

Background: Previous studies have focused on the negative effects of continued smoking on chronic obstructive pulmonary disease (COPD). However, few studies have investigated the positive effects of long-term smoking cessation on patients suffering from acute exacerbations of COPD.

Methods: The study recruited and followed current or former smokers who had been hospitalized and diagnosed with AECOPD. An in-depth analysis of clinical and laboratory indicators was conducted.

Results: 125 patients were covered, including 72 short-term quitters and 53 long-term quitters. The results showed that long-term smoking cessation may result in milder dyspnea and cough, a higher oxygenation index, a lower arterial partial pressure of carbon dioxide, and milder pulmonary hypertension, airflow restriction, and gas retention in patients with AECOPD. However, despite the lower treatment intensity for long-term quitters, improvement in dyspnea and an increase in oxygenation index were comparable to those achieved by short-term quitters. Furthermore, patients with mild phlegm, which accounted for 84% of all subjects, showed greater improvement in phlegm in AECOPD patients with long-term cessation of smoking.

Conclusion: It was found that in patients with AECOPD who quit smoking for a long period of time, there was a reduction in symptoms, improvement in lung function, reduction in treatment intensity, and better improvement in phlegm symptoms after therapy. It is beneficial and necessary to quit smoking early, even if you smoke a small amount of cigarettes.

Keywords: AECOPD; Smoking cessation; Therapeutics.

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Conflict of interest statement

The authors declare that they have no competing interests.

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Review

Rev Environ Health

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. 2022 Oct 28.

doi: 10.1515/reveh-2022-0154. Online ahead of print.

[Exploring the links between indoor air pollutants and health outcomes in South Asian countries: a systematic review](#)

[Laiba Rafiq](#)¹, [Syeda Hamayal Zahra Naqvi](#)¹, [Laila Shahzad](#)¹, [Syed Mustafa Ali](#)²

Affiliations expand

- PMID: 36302378
- DOI: [10.1515/reveh-2022-0154](https://doi.org/10.1515/reveh-2022-0154)

Abstract

Indoor air pollution (IAP) has adverse effects on the health of people, globally. The objective of this systematic review was to present the range of health problems studied in association with indoor air pollutants in South Asian countries. We searched five databases, including PubMed, Web of Science, Scopus, Google Scholar, and CAB Direct for articles published between the years 2000 and 2020. We retrieved 5,810 articles, out of which we included 90 articles in our review. Among South Asian countries, only five countries have published results related to relationship between indoor air pollutants and adverse health conditions. All studies have shown adversity of indoor air pollutants on human's health. We found indoor solid fuel burning as a key source of indoor air pollution in the included studies, while women and children were most affected by their exposure to solid fuel burning. More than half of the studies accounted particulate matter responsible for indoor air pollution bearing negative health effects. In the included studies, eyes and lungs were the most commonly affected body organs, exhibiting common symptoms like cough, breathing difficulty and wheezing. This might have developed into common conditions like respiratory tract infection, chronic obstructive pulmonary diseases and eye cataract. In addition to promote research in South Asian countries, future research should focus on novel digital ways of capturing effects of indoor air pollutants among vulnerable segments of the population. As a result of this new knowledge, public health agencies should develop and test interventions to reduce people's exposure levels and prevent them to develop adverse health outcomes.

Keywords: South Asia; child health; indoor air pollution; negative health effects; systematic review; woman health.

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Curr Opin Support Palliat Care



. 2022 Oct 28.

doi: 10.1097/SPC.0000000000000623. Online ahead of print.

The burden and impact of chronic cough in severe disease

[Össur Ingi Emilsson](#)^{1,2}

Affiliations expand

- PMID: 36302225
- DOI: [10.1097/SPC.0000000000000623](https://doi.org/10.1097/SPC.0000000000000623)

Abstract

Purpose of review: Chronic cough is common in severe diseases, such as COPD, interstitial lung disease, lung cancer and heart failure, and has a negative effect on quality of life. In spite of this, patients with cough sometimes feel their cough is neglected by healthcare workers. This review aims to briefly describe cough mechanisms, highlight the burden chronic cough can be for the individual, and the clinical impact of chronic cough.

Recent findings: Chronic cough is likely caused by different mechanisms in different diseases, which may have therapeutic implications. Chronic cough, in general, has a significant negative effect on quality of life, both with and without a severe comorbid disease. It can lead to social isolation, recurrent depressive episodes, lower work ability, and even conditions such as urinary incontinence. Cough may also be predictive of more frequent exacerbations among patients with COPD, and more rapid lung function decline in idiopathic pulmonary fibrosis. Cough is sometimes reported by patients to be underappreciated by healthcare.

Summary: Chronic cough has a significant negative impact on quality of life, irrespective of diagnosis. Some differences are seen between patients with and without severe disease. Healthcare workers need to pay specific attention to cough, especially patients with severe disease.

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