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

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BMC Public Health

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. 2023 Apr 14;23(1):698.

doi: 10.1186/s12889-023-15535-9.

Burden of smoking on disease-specific mortality, DALYs, costs: the case of a high-income European country

Renato Farcher^{#1}, Maria Eleni Syleouni^{#1}, Linda Vinci², Renato Mattli¹

Affiliations expand

• PMID: 37060054

• DOI: [10.1186/s12889-023-15535-9](https://doi.org/10.1186/s12889-023-15535-9)

Abstract

Background: Smoking is a major risk factor for chronic diseases causing early death and disability. Smoking prevalence over the past 25years has remained high in Switzerland. Evidence about the burden of disease and cost of illness attributable to smoking can support tobacco control. The aim of the present paper is to quantify from a societal perspective the mortality, disability-adjusted life years (DALYs), medical costs and productivity losses attributable to smoking in Switzerland in 2017.

Methods: Smoking attributable fractions (SAFs) were calculated based on the prevalence of current and former active smoking in the latest Swiss Health Survey from 2017 and relative risks from the literature. The SAFs were then multiplied with the number of deaths, DALYs, medical costs and productivity losses in the total population.

Results: In the Swiss population in 2017 smoking accounted for 14.4% of all deaths, for 29.2% of the deaths due to smoking-related diseases, 36.0% of the DALYs, 27.8% of the medical costs and 27.9% of productivity losses. Total costs amounted to CHF 5.0 billion which equals CHF 604 per capita per year. The highest disease burden in terms of mortality and DALYs attributable to smoking was observed for lung cancer and chronic obstructive pulmonary disease (COPD), whereas the highest cost of illness in terms of medical costs was observed for coronary heart diseases and lung cancer and in terms of productivity losses for COPD and coronary heart diseases. Sex and age group differences were found.

Conclusions: We provide an estimate of the burden of smoking on disease-specific mortality, DALYs, medical costs and productivity losses in Switzerland that could be prevented through evidence-based tobacco prevention and control policies as well as regular monitoring of tobacco consumption.

Keywords: Burden of disease; Chronic disease; Cost of illness; Smoking.

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[Medicine \(Baltimore\)](#)

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. 2023 Apr 14;102(15):e33537.

doi: 10.1097/MD.00000000000033537.

Efficacy of acupuncture therapy for stable chronic obstructive pulmonary disease: A systematic review and meta-analysis

Su Fan¹, Zhenyu Zhang¹, Qinglin Wang²

Affiliations expand

- PMID: 37058051
- PMCID: [PMC10101258](#)
- DOI: [10.1097/MD.00000000000033537](#)

Abstract

Background: Acupuncture therapy (AT) is a widely used, alternative medicine in China. AT is an effective treatment for many diseases, but its efficacy in stable chronic obstructive pulmonary disease (COPD) remains controversial. Therefore, we performed the present meta-analysis to evaluate the efficacy of AT in stable COPD patients.

Methods: Randomized controlled trials (RCTs) for AT efficacy in stable COPD patients were searched in literature databases from the inception to December 31, 2021. Pooled effect sizes of outcome measurements with respect to lung function (forced vital capacity [FVC], forced expiratory volume in 1 second [FEV1], FEV1 in predicted value [FEV1%], FEV1/FVC), quality of life (St. George respiratory questionnaire [SGRQ]), exercise capacity (6-minute walking distance [6MWD]) and effective rate were estimated by calculating weighted mean difference (WMD) or odds ratio (OR) with corresponding 95% confidence interval (95% CI), respectively, by a random-effect model.

Results: A total of 28 RCTs with 2130 COPD patients were included. AT group had significant improvement in FVC (WMD = 0.29 L, 95% CI: 0.22-0.36, $P < .001$), FEV1 (WMD = 0.33 L, 95% CI: 0.23-0.43, $P < .001$), FEV1% (WMD = 3.30%, 95% CI: 3.30-4.64, $P < .001$), FEV1/FVC (WMD = 5.45%, 95% CI: 4.41-6.49, $P < .001$), 6MWD (WMD = 45.48 m, 95% CI: 28.21-62.16, $P < .001$), SGRQ (WMD = -7.79, 95% CI: -12.34 to -3.24, $P < .001$), and a higher effective rate (OR = 3.71, 95% CI: 2.50-5.52, $P < .001$) compared to the control group. Subgroup analysis stratified by comparison model (AT combined with other treatments vs other treatments, AT alone vs sham AT) and treatment duration (≥ 8 weeks, < 8 weeks) also showed more improvement in AT arm than control arm without significant between-subgroup difference. Adverse events were reported in a few studies and only mild reactions were observed.

Conclusion: AT is effective in improving lung function, quality of life and exercise capacity, and can be used as an adjunctive treatment in patients with stable COPD.

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Conflict of interest statement

The authors have no conflicts of interest to disclose.

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ERJ Open Res

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. 2023 Apr 11;9(2):00412-2022.

doi: 10.1183/23120541.00412-2022. eCollection 2023 Mar.

Effect of acetazolamide on pulmonary vascular haemodynamics in patients with COPD going to altitude: a randomised, placebo-controlled, double-blind trial

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Affiliations expand

- PMID: 37057079
- PMID: [PMC10086691](#)
- DOI: [10.1183/23120541.00412-2022](#)

Abstract

Background: COPD may predispose to symptomatic pulmonary hypertension at high altitude. We investigated haemodynamic changes in lowlanders with COPD ascending to 3100 m and evaluated whether preventive acetazolamide treatment would attenuate the altitude-induced increase in pulmonary artery pressure (PAP).

Methods: In this randomised, placebo-controlled, double-blind, parallel-group trial, patients with COPD Global Initiative for Chronic Obstructive Lung Disease grades 2-3 who were living <800 m and had peripheral oxygen saturation (S_{pO_2}) >92% and arterial carbon dioxide tension <6 kPa were randomised to receive either acetazolamide (125-250 mg·day⁻¹) or placebo capsules, starting 24 h before ascent from 760 m and during a 2-day stay at

3100 m. Echocardiography, pulse oximetry and clinical assessments were performed at 760 m and after the first night at 3100 m. Primary outcome was PAP assessed by tricuspid regurgitation pressure gradient (TRPG).

Results: 112 patients (68% men, mean±sd age 59±8 years, forced expiratory volume in 1 s (FEV₁) 61±12% pred, S_{pO₂} 95±2%) were included. Mean±sd TRPG increased from 22±7 to 30±10 mmHg in 54 patients allocated to placebo and from 20±5 to 24±7 mmHg in 58 patients allocated to acetazolamide (both p<0.05) resulting in a mean (95% CI) treatment effect of -5 (-9 to -1) mmHg (p=0.015). In patients assigned to placebo at 760/3100 m, mean±sd S_{pO₂} was 95±2%/88±3%; in the acetazolamide group, the respective values were 94±2%/90±3% (both p<0.05), resulting in a treatment effect of +2 (1 to 3)% (p=0.001).

Conclusions: In lowlanders with COPD travelling to 3100 m, preventive acetazolamide treatment attenuated the altitude-induced rise in PAP and improved oxygenation.

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Conflict of interest statement

Conflict of interest: M. Lichtblau received funding from the Swiss Lung League for this study. S. Ulrich reports grants from the Swiss National Science Foundation and Lung Zuerich. K.E. Bloch was supported by Swiss National Science Foundation (grant ID: 172980). S. Saxer, L. Mayer, U. Sheraliev, M. Mademilov, M. Furian, A. Buergin, P.M. Schweiwiller, S.R. Schneider, F.C. Tanner and T. Sooronbaev have nothing to declare.

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[Review](#)

Clin Respir J

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. 2023 Apr 13.

doi: 10.1111/crj.13610. Online ahead of print.

From the infant to the geriatric patient- Strategies for inhalation therapy in asthma and chronic obstructive pulmonary disease

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Affiliations expand

- PMID: 37054701
- DOI: [10.1111/crj.13610](https://doi.org/10.1111/crj.13610)

Abstract

Inhalation therapy represents the standard of care in children, adolescents as well as in young, middle-aged and geriatric adults with asthma or chronic obstructive pulmonary disease. However, there are only few recommendations for the choice of inhalation devices, which consider both, age-specific limitations in young and geriatric patients. Transition concepts are lacking. In this narrative review, the available device technologies and the evidence for age-specific problems are discussed. Pressurized metered-dose inhalers may be favoured in patients who fulfill all cognitive, coordinative and manual power requirements. Breath-actuated metered-dose inhalers, soft-mist inhalers or the use of add-on devices such as spacers, face masks and valved holding chambers may be suitable for patients with mild to moderate impairments of these variables. In these cases, available resources of personal assistance by educated family members or caregivers should be used to allow metered-dose inhaler therapy. Dry powder inhalers may be reserved for patients with a sufficient peak inspiratory flow and good cognitive and manual abilities. Nebulizers may be indicated in persons who are either unwilling or unable to use handheld inhaler devices. After initiation of a specific inhalation therapy, close monitoring is essential to reduce handling mistakes. An algorithm is developed that considers age and relevant comorbidities to support the decision-making process for the choice of an inhaler device.

Keywords: age; comorbidity; inhalation device; obstructive airway disease.

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J Racial Ethn Health Disparities

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. 2023 Apr 13;1-8.

doi: 10.1007/s40615-023-01588-4. Online ahead of print.

Telehealth for Chronic Disease Management Among Vulnerable Populations

Cynthia Williams¹, Di Shang²

Affiliations expand

- PMID: 37052797
- PMID: [PMC10100602](#)
- DOI: [10.1007/s40615-023-01588-4](#)

Abstract

Chronic diseases disproportionately affect patients in low-income minority groups who traditionally use in-person healthcare services. COVID-19 disrupted their routines and limited options for people to receive care; this could exacerbate health inequities. The study examined telehealth chronic disease management among low-income minority groups. We used Florida Medicaid claims data from March to December 2020 and the American Consumer Survey to examine the study objectives. Data were analyzed using Linear and Logistic Regression. We retrieved claim records of 52,904 unique patients; 31,999 were female and 49% of the sample had at least one telehealth visit. Medicaid patients were 8% less likely to use telehealth and 21% more likely to have audio visits when compared to Medicare patients. The analyses suggest that Non-Hispanic Black patients and individuals with a lack of education experience significant health inequities. People with chronic obstructive pulmonary disease (5%) and heart failure (14%) were less likely to use telehealth than patients with diabetes. Telehealth will continue to be a health delivery option; thus we recommend that strategies are enacted to educate, and resources are provided to promote equity among Non-Hispanic Black patients. Without priority

attention to people among low-income minority populations, health inequities will continue to plague this community.

Keywords: COVID19; Chronic disease management; Health inequity; Medicaid; Poverty; Telehealth.

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Conflict of interest statement

The authors declare no conflict of interest.

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

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J Osteopath Med

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. 2023 Apr 12;98(s12):s7-s10.

doi: 10.1515/jom-1998-0124. eCollection 1998 Dec 1.

Smoking in women

Loretta Mueller¹, Carman A Ciervo

Affiliations expand

- PMID: 37043745
- DOI: [10.1515/jom-1998-0124](https://doi.org/10.1515/jom-1998-0124)

Free article

Abstract

Smoking has numerous increased health risks for women, including the risks for cancer, cardiovascular disease, chronic obstructive pulmonary disease, gastric and duodenal ulcers, reduced fertility, ovulatory dysfunction, ectopic pregnancy, spontaneous abortion, sudden infant death, and earlier menopause. Such health risks, smoking cessation therapy, and unique obstacles to smoking cessation in women are the focus of this article.

Keywords: health risks; nicotine replacement; smoking; women.

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supplementary info

MeSH terms, Substances expand
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Respir Care

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. 2023 Apr 11;respcare.10614.

doi: 10.4187/respcare.10614. Online ahead of print.

Delivery of Aerosolized Bronchodilators by High-Flow Nasal Cannula During COPD Exacerbation

Nicolás Colaianni-Alfonso¹, Ronan MacLoughlin^{2,3,4}, Ariel Espada⁵, Yasmine Saa⁵, Mariano Techera⁵, Ada Toledo⁵, Guillermo Montiel⁵, Mauro Castro-Sayat⁵

Affiliations expand

- PMID: 37041023
- DOI: [10.4187/respcare.10614](https://doi.org/10.4187/respcare.10614)

Abstract

Background: Bronchodilator delivery via a high-flow nasal cannula (HFNC) has generated great interest in recent years. The efficacy of in-line vibrating mesh nebulizers with an HFNC during COPD exacerbation is limited. The aim of this study was to evaluate the clinical response of subjects with COPD exacerbation who require bronchodilator therapy (anticholinergic and β -agonist) by using a vibrating mesh nebulizer in line with an HFNC.

Methods: This was a prospective single-center study performed in a respiratory intermediate care unit that enrolled patients with a diagnosis of COPD exacerbation who required noninvasive ventilation on admission. All the subjects underwent noninvasive

ventilation breaks with an HFNC. After clinical stability, pulmonary function tests were performed to assess changes in FEV₁ and clinical parameters before and after bronchodilation by using a vibrating mesh nebulizer in line with an HFNC.

Results: Forty-six patients with COPD exacerbation were admitted. Five patients who did not use noninvasive ventilation and 10 patients who did not receive bronchodilator treatment with a vibrating mesh nebulizer were excluded. Thirty-one were selected, but 1 subject was secondarily excluded due to loss of data. Finally, 30 subjects were included. The primary outcome was spirometric changes in FEV₁. The mean \pm SD FEV₁ before receiving bronchodilator treatment by using a vibrating mesh nebulizer in line with an HFNC was 0.74 ± 0.10 L, and, after receiving treatment, the mean \pm SD FEV₁ changed to 0.88 ± 0.12 L ($P < .001$). Similarly, the mean \pm SD FVC increased from 1.75 ± 0.54 L to 2.13 ± 0.63 L ($P < .001$). Considerable differences were observed in breathing frequency and heart rate after receiving bronchodilator treatment. No relevant changes were observed in the Borg scale or S_p O₂ after treatment. The mean clinical stability recorded was 4 d.

Conclusions: In the subjects with COPD exacerbation, bronchodilator treatment by using a vibrating mesh nebulizer in line with an HFNC showed a mild but significant improvement in FEV₁ and FVC. In addition, a decrease in breathing frequency was observed, which suggests a reduction in loads imposed by dynamic hyperinflation.

Keywords: COPD; aerosol; high-flow nasal cannula oxygen; nebulization; respiratory function tests.

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Am J Respir Crit Care Med



. 2023 Apr 11.

doi: 10.1164/rccm.202209-1774OC. Online ahead of print.

Exacerbation Risk and Mortality in COPD GOLD Group A and B Patients with and without Exacerbation History

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Affiliations expand

- PMID: 37040482
- DOI: [10.1164/rccm.202209-1774OC](https://doi.org/10.1164/rccm.202209-1774OC)

Abstract

Rationale: Risk stratification of patients according to COPD severity is clinically important and forms the basis of therapeutic recommendations. No studies have examined the association for GOLD group A and B patients with (A1, B1) and without (A0, B0) an exacerbation in the last year with future exacerbations, hospitalizations, and mortality in perspective of the new GOLD ABE classification.

Methods: In this nationwide cohort study, we identified patients with a diagnosis of COPD, aged ≥ 30 years, registered in the Swedish National Airway Register between January 2017 and August 2020. Patients were stratified in GOLD groups A0, A1, B0, B1 and E, and followed until January 2021 for exacerbations, hospitalization, and mortality in national registries.

Results: The 45350 eligible patients included 25% A0, 4% A1, 44% B0, 10% B1, and 17% E. Moderate exacerbations, all-cause and respiratory hospitalizations, and all-cause and respiratory mortality increased by GOLD group A0-A1-B0-B1-E, except for moderate exacerbations which was higher in A1 than B0. Group B1 had substantially higher hazard ratio of future exacerbation (2.56, 95%CI 2.40-2.74), all-cause hospitalization (1.28, 1.21-1.35), respiratory hospitalization (1.44, 1.27-1.62), but not all-cause (1.04, 0.91-1.18) or respiratory mortality (1.13, 0.79-1.64) than group B0. The exacerbation rate for group B1 was 0.6 events/patient-year versus 0.2 for B0 (rate ratio 2.73, 95%CI 2.57-2.79). Results were similar for group A1 versus A0.

Conclusion: Stratification of GOLD A and B patients with one or no exacerbation in the last year provides valuable information on future risk, which should influence treatment recommendations for preventive strategies.

Keywords: COPD; Exacerbation; GOLD classification; Mortality; Registry.

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[Editorial](#)

Respirology

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. 2023 Apr 11.

doi: 10.1111/resp.14507. Online ahead of print.

Dynamics of hyperinflation

Jorrit B A Welling^{1,2}, Dirk-Jan Slebos^{1,2}

Affiliations expand

- PMID: 37039738

- DOI: [10.1111/resp.14507](https://doi.org/10.1111/resp.14507)

No abstract available

Keywords: COPD; bronchoscopic lung volume reduction; dynamic hyperinflation; emphysema; endobronchial valve treatment.

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[Review](#)

Tuberc Respir Dis (Seoul)

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. 2023 Apr 11.

doi: 10.4046/trd.2023.0015. Online ahead of print.

COPD AND THE AIRWAY MICROBIOME: WHAT RESPIROLOGISTS NEED TO KNOW

Don D Sin¹

Affiliations expand

- PMID: 37038880
- DOI: [10.4046/trd.2023.0015](https://doi.org/10.4046/trd.2023.0015)

Free article

Abstract

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide. The lower airways contain a rich and diverse microbiome, which may play a significant regulatory role in both health and disease. In COPD, the microbiome becomes perturbed, causing dysbiosis. Increased representation of members in the Proteobacteria phylum and certain members in the Firmicutes phylum has been associated with increased risk of exacerbations and mortality. Therapies such as inhaled corticosteroids and azithromycin may modulate the airway microbiome or its metabolites in patients with COPD. This paper provides an up-to-date overview of the airway microbiome and its importance in the pathophysiology of COPD and as potential therapeutic target in the future.

Keywords: COPD; airway microbiome; dysbiosis; sequencing.

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[Editorial](#)

J Korean Med Sci

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. 2023 Apr 10;38(14):e123.
doi: 10.3346/jkms.2023.38.e123.

Chronic Obstructive Pulmonary Disease in Super-Aged Society: A Letter From the Near Future

Hun-Gyu Hwang¹

Affiliations expand

- PMID: 37038647
- PMCID: [PMC10086378](#)
- DOI: [10.3346/jkms.2023.38.e123](#)

Free PMC article

No abstract available

Conflict of interest statement

The author has no potential conflicts of interest to disclose.

Comment on

- [Recent Prevalence of and Factors Associated with Chronic Obstructive Pulmonary Disease in a Rapidly Aging Society: Korea National Health and Nutrition Examination Survey 2015-2019](#)
- [5 references](#)

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Disabil Rehabil

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. 2023 Apr 10;1-9.

doi: 10.1080/09638288.2023.2196095. Online ahead of print.

Effect of internet-based pulmonary rehabilitation on physical capacity and health-related life quality in patients with chronic obstructive pulmonary disease-a systematic review and meta-analysis

Xin Zhang^{1,2}, Gongwei Jia¹, Liping Zhang^{1,2}, Yilin Liu^{1,2}, Sanrong Wang¹, Li Cheng³

Affiliations expand

- PMID: 37036029
- DOI: [10.1080/09638288.2023.2196095](https://doi.org/10.1080/09638288.2023.2196095)

Abstract

Purpose: Pulmonary rehabilitation (PR) is now recognized as the most effective treatments for individuals with chronic obstructive pulmonary disease (COPD), internet-based PR arises a promising method. The aim of this study was to conduct a systematic review and meta-analysis for assessing the effect of internet-based PR programs on physical capacity and health-related quality of life in patients with COPD.

Materials and methods: Randomized controlled trials were identified through systematically searches in PubMed, EMBASE, web of science, CENTRAL, Cochrane Library, and Google Scholar databases.

Results: Twelve studies (1433 patients) were included. For physical capacity, there was no significant difference between groups was found according to the 6-min walk test (6MWT) (MD 10.42, 95% CI -2.92 to 23.77, $p = 0.13$, $I^2 = 0\%$). For the health-related quality of life, no significant difference between groups was found regarding the St George's Respiratory Questionnaire (SGRQ) (MD -0.64, 95% CI -3.52 to 2.23, $p = 0.66$), COPD assessment test (CAT) (MD -0.34, 95% CI -1.62 to 0.94, $p = 0.60$), modified Medical Research Council scale (mMRC) (MD 0.17, 95% CI -0.06 to 0.39, $p = 0.15$) and Chronic Respiratory Questionnaire (CRQ) (MD 1.32 95% CI -5.88 to 8.53, $p = 0.72$).

Conclusions: This study has established the potential for delivery of PR via the internet in demonstrating non-inferiority of physical capacity and health-related quality of life (HRQoL) compared with conventional PR. IMPLICATIONS FOR REHABILITATION Long-term rehabilitation training for patients with chronic obstructive pulmonary disease needs a more convenient and feasible way. In this study, internet-based rehabilitation showed similar effects as conventional rehabilitation on physical activity and health-related quality of life. Internet-based rehabilitation strategies would be helpful for this population. All internet-based rehabilitation strategies should be simple and sustainable.

Keywords: Internet; chronic obstructive respiratory disease; physical capacity health-related quality of life; pulmonary rehabilitation; telemedicine.

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Am J Respir Crit Care Med

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. 2023 Apr 15;207(8):1095-1097.

doi: 10.1164/rccm.202210-1949LE.

Clinicians' and Researchers' Perspectives on a New Chronic Obstructive Pulmonary Disease Exacerbation Definition: Rome Wasn't Built in a Day

Malik A Althobiani^{1,2}, Amar J Shah³, Bilal Khan¹, John R Hurst¹

Affiliations expand

- PMID: 36656550
- DOI: [10.1164/rccm.202210-1949LE](https://doi.org/10.1164/rccm.202210-1949LE)

No abstract available

supplementary info

Publication types, Grant support expand

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Randomized Controlled Trial

Sci Total Environ

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. 2023 Apr 10;868:161573.

Principal stratification analysis to determine health benefit of indoor air pollution reduction in a randomized environmental intervention in COPD: Results from the CLEAN AIR study

Han Woo¹, Kirsten Koehler², Nirupama Putcha³, Wendy Lorizio³, Meredith McCormack⁴, Roger Peng⁵, Nadia N Hansel⁴

Affiliations expand

- PMID: 36669663
- PMID: PMC9975085 (available on 2024-04-10)
- DOI: [10.1016/j.scitotenv.2023.161573](https://doi.org/10.1016/j.scitotenv.2023.161573)

Abstract

Background: Indoor air quality represents a modifiable exposure to Chronic Obstructive Pulmonary Disease (COPD) health. In a randomized controlled trial (CLEAN AIR study), air cleaner assignment had causal effect in improving COPD outcomes. It is unclear, however, what is the treatment effect among those for whom intervention reduced air pollution and whether it was reduction in fine particulate matter (PM_{2.5}) or nitrogen dioxide (NO₂) that contributed to such improvement. Because pollution is a posttreatment variable, treatment effect cannot be assessed while controlling for pollution using intention-to-treat (ITT) analysis.

Objective: Using principal stratification method, we assess indoor pollutants as the intermediate variable, and determine the causal effect of reducing indoor air pollution on COPD health.

Method: In randomized controlled trial, former smokers with COPD received either active or placebo HEPA air cleaners and were followed for 6 months. Saint George's Respiratory Questionnaire (SGRQ) was the primary outcome and secondary measures included SGRQ subscales, COPD assessment test (CAT), dyspnea (mMRC), and breathlessness, cough, and sputum scale (BCSS). Indoor PM_{2.5} and NO₂ were measured. Principal stratification analysis was performed to assess the treatment effect while controlling for pollution reduction.

Results: Among those showing at least 40 % PM_{2.5} reduction through air cleaners, the intervention showed improvement in respiratory symptoms for the active (vs. placebo), and the size of treatment effect shown for this subgroup was larger than that for the overall sample. In this subgroup, those with active air cleaners (vs. placebo) showed 7.7 points

better SGRQ (95%CI: -14.3, -1.1), better CAT ($\beta = -5.5$; 95%CI: -9.8, -1.2), mMRC ($\beta = -0.6$; 95%CI: -1.1, -0.1), and BCSS ($\beta = -1.8$; 95%CI: -3.0, -0.5). Among those showing at least 40 % NO₂ reduction through air cleaners, there was no intervention difference in outcomes.

Conclusion: Air cleaners caused clinically significant improvement in respiratory health for individuals with COPD through reduction in indoor PM_{2.5}.

Trial registration: ClinicalTrials.gov: [NCT02236858](https://clinicaltrials.gov/ct2/show/study/NCT02236858).

Keywords: Air cleaners; COPD; Environment; Particulate matter; Principal stratification; Randomized controlled trial.

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

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. 2023 Apr 11;163406.

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Ambient air pollution and incidence, progression to multimorbidity and death of hypertension, diabetes, and chronic kidney disease: A national prospective cohort

Gan Wu¹, Miao Cai¹, Chongjian Wang², Hongtao Zou¹, Xiaojie Wang¹, Junjie Hua³, Hualiang Lin⁴

Affiliations expand

• PMID: 37054795

• DOI: [10.1016/j.scitotenv.2023.163406](https://doi.org/10.1016/j.scitotenv.2023.163406)

Abstract

Background: The link between ambient air pollution and the incidence of hypertension, diabetes, and chronic kidney disease (CKD) has been widely studied. However, the associations of air pollution with the dynamic progression to multimorbidity and mortality of these diseases are unknown.

Methods: This study included 162,334 participants from the UK Biobank. Multimorbidity was defined as the coexistence of at least two of hypertension, diabetes, and CKD. Land use regression was used to estimate annual concentrations of particulate matter (PM_{2.5}), PM₁₀, nitrogen dioxide (NO₂), and nitrogen oxides (NO_x). Multi-state models were used to assess the association between ambient air pollutants and the dynamic progression of hypertension, diabetes, and CKD.

Results: During a median follow-up of 11.7 years, 18,496 participants experienced at least one of hypertension, diabetes, and CKD, 2216 experienced multimorbidity, and 302 died afterwards. We observed differential associations of four air pollutants on different transitions from healthy status to incident disease (hypertension, diabetes, or CKD), to multimorbidity, and to death. The hazard ratios (HRs) of each IQR increment in PM_{2.5}, PM₁₀, NO₂, and NO_x for the transition to incident disease were 1.07 [95 % confidence intervals (CI): 1.04, 1.09], 1.02 (1.00, 1.03), 1.07 (1.04, 1.09), and 1.05 (1.03, 1.07), but the associations with the transition to death were significant for NO_x only [HR: 1.04 (95 % CI: 1.01, 1.08)].

Conclusions: Air pollution exposure might be one important determinant for the incidence and dynamic progression of hypertension, diabetes, and CKD, suggesting that more attention should be paid to ambient air pollution control in the prevention of hypertension, diabetes, and CKD, as well as their progression.

Keywords: Air pollution; CKD; Diabetes; Hypertension; Multi-state model; Multimorbidity.

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Scand J Prim Health Care

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. 2023 Apr 13;1-10.

doi: 10.1080/02813432.2023.2197951. Online ahead of print.

Disparities in prevalence of heart failure between the genders in relation to age, multimorbidity and socioeconomic status in southern Sweden: a cross-sectional study

Mia Scholten¹, Patrik Midlöv¹, Anders Halling¹

Affiliations expand

- PMID: 37052877
- DOI: [10.1080/02813432.2023.2197951](https://doi.org/10.1080/02813432.2023.2197951)

Abstract

Objective: Prior studies have reported that heart failure typically affects elderly, multimorbid and socioeconomically deprived men. Women with heart failure are generally older, have a higher EF (ejection fraction) and have more heart failure-related symptoms than men. This study explored the disparities in the prevalence of heart failure between men and women in relation to age, multimorbidity level and socioeconomic status of the population in southern Sweden.

Design: A register-based, cross-sectional cohort study. **Setting and subjects:** The inhabitants from 20 years of age onwards ($N = 981,383$) living in southern Sweden in 2015. **Main outcome measure:** Prevalence and mean probability of having heart failure in both genders. CNI (Care Need Index) percentiles depend on the socioeconomic status of their listed primary healthcare centres.

Results: Men had a higher OR for HF - 1.70 (95% CI 1.65-1.75) - than women. The probability of men having heart failure increased significantly compared to women with advancing age and multimorbidity levels. At all CNI levels, the multimorbid patients had a higher prevalence of heart failure in men than in women. The disparity in the mean probability of heart failure between the most affluent and deprived CNI percentile was more apparent in women compared to men, especially from 80 years.

Conclusions: The prevalence of heart failure differs significantly between the genders. Men had an increasing mean probability of heart failure with advancing age and multimorbidity level compared to women. Socioeconomic deprivation was more strongly associated with heart failure in women than in men. The probability of having heart failure differs between the genders in several aspects. **Key Points** Independently of socioeconomic status, men had a higher prevalence of heart failure than women among the multimorbid patients. The mean probability of men having heart failure increased significantly compared to women

with advancing age and multimorbidity level. Socioeconomic status was more strongly associated with heart failure in women than in men.

Keywords: Heart failure (HF); multimorbidity (MM); prevalence; primary health care; probability.

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Review

BMC Prim Care



. 2023 Apr 12;24(1):98.

doi: 10.1186/s12875-023-02050-4.

Primary healthcare competencies needed in the management of person-centred integrated care for chronic illness and multimorbidity: Results of a scoping review

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Affiliations expand

- PMID: 37046190
- PMID: [PMC10091550](#)
- DOI: [10.1186/s12875-023-02050-4](#)

Free PMC article

Abstract

Background: Chronic disease management is important in primary care. Disease management programmes focus primarily on the respective diseases. The occurrence of multimorbidity and social problems is addressed to a limited extent. Person-centred integrated care (PC-IC) is an alternative approach, putting the patient at the centre of care. This asks for additional competencies for healthcare professionals involved in the execution of PC-IC. In this scoping review we researched which competencies are necessary for healthcare professionals working in collaborative teams where the focus lies within the concept of PC-IC. We also explored how these competencies can be acquired.

Methods: Six literature databases and grey literature were searched for guidelines and peer-reviewed articles on chronic illness and multimorbidity in primary care. A data synthesis was carried out resulting in an overview of the competencies that healthcare professionals need to deliver PC-IC.

Results: Four guidelines and 21 studies were included and four core competencies could be derived through the synthesis: 1. interprofessional communication, 2. interprofessional collaborative teamwork, 3. leadership and 4. patient-centred communication. Included papers mostly lack a clear description of the competencies in terms of knowledge, skills and attitudes which are necessary for a PC-IC approach and on how these competencies can be acquired.

Conclusion: This review provides insight on competencies necessary to provide PC-IC within primary care. Research is needed in more depth on core concepts of these competencies which will then benefit educational programmes to ensure that healthcare professionals in primary care are better equipped to deliver PC-IC for patients with chronic illness and multimorbidity.

Keywords: Chronic illness; Competencies; Multimorbidity; Person-centred integrated care and interprofessional collaboration; Primary care.

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Conflict of interest statement

The authors declare that they have no competing interests.

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

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

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. 2023 Apr 14.

doi: 10.1111/all.15743. Online ahead of print.

Assessment of dupilumab in children with moderate-to-severe type 2 asthma with or without evidence of allergic asthma

Nikolaos G Papadopoulos¹, Stanley J Szeffler², Leonard B Bacharier³, Jorge F Maspero⁴, Christian Domingo⁵, Alessandro Fiocchi⁶, Jason K Lee⁷, Nadia Daizadeh⁸, David J Lederer⁹, Megan Hardin⁸, Rebecca Gall⁹, Michel Djandji⁸, Shahid Siddiqui⁹, Juby A Jacob-Nara¹⁰, Yamo Deniz⁹, Paul J Rowe¹⁰

Affiliations expand

- PMID: 37059696

- DOI: [10.1111/all.15743](https://doi.org/10.1111/all.15743)

Abstract

Background: Cytokines, such as interleukins (IL)-4/5/13, play a key role in multiple type 2 inflammatory diseases, including allergic asthma. Dupilumab, a human monoclonal antibody, blocks the shared receptor component for IL-4/IL-13, inhibiting signaling. In this post hoc analysis of VOYAGE ([NCT02948959](https://clinicaltrials.gov/ct2/show/study/NCT02948959)), dupilumab efficacy was evaluated in patients aged 6-11 years with type 2 asthma with or without evidence of allergic asthma (baseline serum total IgE ≥ 30 IU/mL and ≥ 1 perennial aeroallergen-specific IgE ≥ 0.35 kU/L).

Methods: Annualized rate of severe exacerbations (AER) and changes in pre-bronchodilator (Pre-BD) forced expiratory volume in one second (FEV₁), percent-predicted pre-BD FEV₁ (ppFEV₁), and Asthma Control Score (ACQ)-7 were assessed during the treatment period.

Results: 350 children (261 with and 89 without evidence of allergic asthma) were included. Dupilumab vs placebo significantly reduced AER in patients with (0.24 vs 0.62, relative risk reduction [RRR]: 62% [95% CI, 39-76], $p < .0001$) and without (0.39 vs 0.80, RRR: 51% [95% CI, 0-76], $p < .05$) evidence of allergic asthma. Significant improvements in ppFEV₁, pre-bronchodilator FEV₁, and ACQ-7 scores were observed in dupilumab vs placebo throughout the treatment period in patients with evidence of allergic asthma. In patients without evidence of allergic asthma, numerical improvements in pre-bronchodilator FEV₁ and asthma control were observed by Week 52.

Conclusion: Dupilumab vs placebo reduced asthma exacerbations in children with type 2 asthma irrespective of evidence of allergic asthma; similar trends were observed in changes in lung function. Significant improvement in asthma control was observed in patients with evidence of allergic asthma, but not in those without.

Keywords: Asthma; allergic; exacerbation; percentage predicted FEV1, dupilumab.

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. 2023 Apr 12;S0761-8425(23)00107-9.

doi: 10.1016/j.rmr.2023.03.002. Online ahead of print.

[Lung manifestations of sickle-cell disease]

[Article in French]

[A Hamzaoui](#)¹, [S Louhaichi](#)², [B Hamdi](#)²

Affiliations expand

- PMID: 37059617
- DOI: [10.1016/j.rmr.2023.03.002](https://doi.org/10.1016/j.rmr.2023.03.002)

Abstract

Sickle-cell disease is an autosomal recessive genetic disorder of hemoglobin that causes systemic damage. Hypoxia is the main actor of sickle-cell disease. It initiates acutely the pathogenic cascade leading to tissue damages that in turn induce chronic hypoxia. Lung lesions represent the major risk of morbidity and mortality. Management of sickle-cell disease requires a tight collaboration between hematologists, intensivists and chest physicians. Recurrent episodes of thrombosis and hemolysis characterize the disease. New therapeutic protocols, associating hydroxyurea, transfusion program and stem cell

transplantation in severe cases allow a prolonged survival until the fifth decade. However, recurrent pain, crisis, frequent hospital admissions due to infection, anemia or acute chest syndrome and chronic complications leading to organ deficiencies degrade the patients' quality of life. In low-income countries where the majority of sickle-cell patients are living, the disease is still associated with a high mortality in childhood. This paper focuses on acute chest syndrome and chronic lung manifestations.

Keywords: Acute chest syndrome; Apnées du sommeil; Asthma; Asthme; Drépanocytose; Hypertension pulmonaire; Pulmonary hypertension; Sickle-cell disease; Sleep apneas; Syndrome thoracique aigu.

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. 2023 Apr 11;9(2):00499-2022.

doi: 10.1183/23120541.00499-2022. eCollection 2023 Mar.

Association of genetic risk and lifestyle with incident adult-onset asthma in the UK Biobank cohort

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Affiliations expand

- PMID: 37057096
- PMID: [PMC10086697](#)
- DOI: [10.1183/23120541.00499-2022](#)

Abstract

Background: Both genetic and lifestyle factors contribute to the development of asthma, but whether unfavourable lifestyle is associated with similar increases in risk of developing asthma among individuals with varying genetic risk levels remains unknown.

Methods: A healthy lifestyle score was constructed using body mass index, smoking status, physical activities and dietary pattern to further categorise into ideal, intermediate and poor groups. Genetic risk of asthma was also categorised as three groups based on the tertiles of polygenic risk score established using 212 reported and verified single-nucleotide polymorphisms of European ancestry in the UK Biobank study. We examined the risk of incident asthma related with each lifestyle level in each genetic risk group by Cox regression models.

Results: Finally, 327 124 participants without baseline asthma were included, and 157 320 (48.1%) were male. During follow-up, 6238 participants (1.9%) developed asthma. Compared to ideal lifestyle in a low genetic risk group, poor lifestyle was associated with a hazard ratio of up to 3.87 (95% CI, 2.98-5.02) for developing asthma in a high genetic risk group. There was interaction between genetic risk and lifestyle, and the population-attributable fraction of lifestyle and genetic risk were 30.2% and 30.0% respectively.

Conclusion: In this large contemporary population, lifestyle and genetic factors jointly play critical roles in the development of asthma, and the effect values of lifestyle on incident adult-onset asthma were greater than that of genetic risk. Our findings highlighted the necessity of a comprehensive intervention for the prevention of asthma despite the genetic risk.

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Conflict of interest statement

Conflict of interest: The authors declare no conflict of interests.

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. 2023 Apr 11;9(2):00559-2022.

doi: 10.1183/23120541.00559-2022. eCollection 2023 Mar.

Clinical response to benralizumab can be predicted by combining clinical outcomes at 3 months with baseline characteristics

Johannes A Kroes^{1,2}, Kim de Jong³, Simone Hashimoto⁴, Sander W Zielhuis¹, Eric N van Roon^{1,2}, Jacob K Sont⁵, Anneke Ten Brinke⁶

Affiliations expand

- PMID: 37057095
- PMCID: [PMC10086738](#)
- DOI: [10.1183/23120541.00559-2022](#)

Abstract

Background: Benralizumab is highly effective in many, but not all, patients with severe asthma. Baseline characteristics alone are insufficient to predict an individual's probability of long-term benralizumab response. The objectives of the present study were to: 1) study whether parameters at 3 months, in addition to baseline characteristics, contribute to the prediction of benralizumab response at 1 year; and 2) develop an easy-to-use prediction tool to assess an individual's probability of long-term response.

Methods: We assessed the effect of benralizumab treatment in 192 patients from the Dutch severe asthma registry (RAPSODI). To investigate predictors of long-term benralizumab response ($\geq 50\%$ reduction in maintenance oral corticosteroid (OCS) dose or annual exacerbation frequency) we used logistic regression, including baseline characteristics and 3-month Asthma Control Questionnaire (ACQ-6) score and maintenance OCS dose.

Results: Benralizumab treatment significantly improved several clinical outcomes, and 144 (75%) patients were classified as long-term responders. Response prediction improved significantly when 3-month outcomes were added to a predictive model with baseline characteristics only (area under the receiver-operating characteristic (AUROC) 0.85 *versus* 0.72, $p=0.001$). Based on this model, a prediction tool using sex, prior biologic use, baseline blood eosinophils, forced expiratory volume in 1 s, and at 3 months OCS dose and ACQ-6 was developed which classified patients into three categories with increasing probability of long-term response (95% CI): 25% (3-65%), 67% (57-77%) and 97% (91-99%), respectively.

Conclusion: In addition to baseline characteristics, treatment outcomes at 3 months contribute to the prediction of benralizumab response at 1 year in patients with severe eosinophilic asthma. Prediction tools as proposed in this study may help physicians optimise the use of costly biologics.

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Conflict of interest statement

Conflict of interest: J.A. Kroes reports a grant from AstraZeneca. Conflict of interest: K. De Jong has nothing to disclose. Conflict of interest: S. Hashimoto has nothing to disclose. Conflict of interest: S.W. Zielhuis reports a grant from AstraZeneca, and personal fees from Novartis, GlaxoSmithKline, Sanofi-Genzyme Regeneron, Eli-Lilly and Merck Sharp & Dohme. Conflict of interest: E.N. Van Roon has nothing to disclose. Conflict of interest: J.K. Sont reports a grant from AstraZeneca. Conflict of interest: A. Ten Brinke reports grants from AstraZeneca, GlaxoSmithKline, TEVA and Sanofi-Genzyme Regeneron, and personal fees from GlaxoSmithKline, TEVA, AstraZeneca and Sanofi-Genzyme Regeneron, unrelated to this work.

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. 2023 Apr 11;9(2):00548-2022.

doi: 10.1183/23120541.00548-2022. eCollection 2023 Mar.

Associations between maternal complications during pregnancy and childhood asthma: a retrospective cohort study

Ying Ma^{1,2}, Yu Wu^{3,2}, Yi Zhang^{4,2}, Ting Jiao⁴, Shuangshuang Guo⁴, Dongying Zhang⁵, Jiewen Yang⁶, Nali Deng⁷, Zhijiang Liang⁸, Harry H X Wang⁹, Wei Bao¹⁰, Ruoling Chen¹¹, Jie Tang⁴, Xiaoqin Liu¹²

Affiliations expand

- PMID: 37057092
- PMCID: [PMC10086685](#)
- DOI: [10.1183/23120541.00548-2022](#)

Abstract

Background: Studies on the associations between maternal complications during pregnancy and childhood asthma are exclusively conducted in Western countries. The findings are mixed and may not be translated to other populations. We aimed to investigate the associations among the Chinese population and to determine whether the associations were mediated through pre-term birth, caesarean delivery, low birthweight and not breastfeeding in the first 6 months.

Methods: We conducted a retrospective cohort study of 166 772 children in Guangzhou, China. Information on maternal gestational hypertension, gestational diabetes and gestational anaemia during pregnancy was extracted from medical records. Ever-diagnosis of asthma in children aged 6-12 years was obtained by questionnaire. Logistic regression models and mediation analyses were used to estimate the adjusted odds ratios (aORs) and 95% confidence intervals for childhood asthma.

Results: Gestational hypertension, gestational diabetes and gestational anaemia during pregnancy were associated with an increased risk of ever-diagnosed childhood asthma: aOR 1.48 (95% CI 1.37-1.60), 1.71 (95% CI 1.65-1.78) and 1.34 (95% CI 1.26-1.45), respectively. A stronger association was observed for two or three gestational complications (aOR 2.02 (95% CI 1.93-2.16)) than one gestational complication (aOR 1.64 (95% CI 1.52-1.77)). The aOR for the three gestational complications was 1.35 (95% CI 1.26-1.45), 1.63 (95% CI 1.58-1.70) and 1.32 (95% CI 1.24-1.43), respectively, after controlling for the mediators, including pre-term birth, caesarean delivery, low birthweight and not breastfeeding in the first 6 months.

Conclusions: Gestational hypertension, gestational diabetes and gestational anaemia were associated with childhood asthma, and the associations were partially explained by the mediation effects.

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Conflict of interest statement

Conflict of interest: None declared.

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. 2023 Apr 11;9(2):00485-2022.

doi: 10.1183/23120541.00485-2022. eCollection 2023 Mar.

Precision Medicine Intervention in Severe Asthma (PRISM) study: molecular phenotyping of patients with severe asthma and response to biologics

Ji-Hyang Lee¹, Piers Dixey², Pank Bhavsar², Katie Raby², Nazanin Kermani², Marc Chadeau-Hyam³, Ian M Adcock², Woo-Jung Song¹, Hyouk-Soo Kwon¹, Sei-Won Lee⁴, You Sook Cho¹, Kian Fan Chung², Tae-Bum Kim¹

Affiliations [expand](#)

- PMID: 37057090
- PMCID: [PMC10086686](#)
- DOI: [10.1183/23120541.00485-2022](#)

Abstract

Severe asthma represents an important clinical unmet need despite the introduction of biologic agents. Although advanced omics technologies have aided researchers in identifying clinically relevant molecular pathways, there is a lack of an integrated omics approach in severe asthma particularly in terms of its evolution over time. The collaborative Korea-UK research project Precision Medicine Intervention in Severe Asthma (PRISM) was launched in 2020 with the aim of identifying molecular phenotypes of severe asthma by analysing multi-omics data encompassing genomics, epigenomics, transcriptomics, proteomics, metagenomics and metabolomics. PRISM is a prospective, observational,

multicentre study involving patients with severe asthma attending severe asthma clinics in Korea and the UK. Data including patient demographics, inflammatory phenotype, medication, lung function and control status of asthma will be collected along with biological samples (blood, sputum, urine, nasal epithelial cells and exhaled breath condensate) for omics analyses. Follow-up evaluations will be performed at baseline, 1 month, 4-6 months and 10-12 months to assess the stability of phenotype and treatment responses for those patients who have newly begun biologic therapy. Standalone and integrated omics data will be generated from the patient samples at each visit, paired with clinical information. By analysing these data, we will identify the molecular pathways that drive lung function, asthma control status, acute exacerbations and the requirement for daily oral corticosteroids, and that are involved in the therapeutic response to biological therapy. PRISM will establish a large multi-omics dataset of severe asthma to identify potential key pathophysiological pathways of severe asthma.

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Conflict of interest statement

Conflict of interest: W-J. Song is deputy chief editor of this journal. All other authors declare no conflicts of interest.

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. 2023 Apr 11;9(2):00248-2022.

doi: 10.1183/23120541.00248-2022. eCollection 2023 Mar.

Roles of real-world evidence in severe asthma treatment: challenges and opportunities

Youngsoo Lee¹, Ji-Hyang Lee², So Young Park³, Ji-Ho Lee⁴, Joo-Hee Kim⁵, Hyun Jung Kim⁶, Sang-Heon Kim⁷, Kian Fan Chung⁸, Woo-Jung Song²

Affiliations expand

- PMID: 37057082
- PMCID: [PMC10086725](#)
- DOI: [10.1183/23120541.00248-2022](#)

Abstract

Recent advances in asthma research have led to the development of novel biologicals that hinder the pathological actions of key molecules in severe asthma. Traditional randomised controlled studies (RCTs), the gold standard for evaluating the efficacy and safety of medical interventions with excellent internal validity, have proven the clinical benefits and favourable safety profiles of type 2 biologicals in severe asthma. However, RCTs are not always ideal because of shortcomings such as limited external validity and practical issues in the management of severe asthma that cannot be solved through strictly designed clinical trials. Thus, the applicability of their findings may be questioned because treatment adherence is frequently poor in the real world. Real-world evidence includes a wide range of real-world data (RWD) collected from multiple sources in clinical practice, such as electronic medical records, healthcare insurance claims and retrospective or prospective patient registries. RWD may help clinicians decide how to manage patients with severe asthma. Real-world evidence is also gaining attention in addressing clinical questions not answered by traditional RCTs. Because there are various types of RWD with different possibilities and limitations, it is important to decide which type of RWD could be "fit for purpose" to address a specific question. This narrative review discusses the challenges and opportunities of RWD for evaluating the effectiveness and clinical outcomes of biological treatments for severe asthma.

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Conflict of interest statement

Conflict of interest: W-J. Song is Deputy Chief Editor of this journal. Other authors have nothing to declare.

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Clin Exp Allergy

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. 2023 Apr 13.

doi: 10.1111/cea.14316. Online ahead of print.

Mepolizumab therapy decreases epithelial-derived cytokine concentrations in exhaled breath condensates from patients with severe eosinophilic asthma

Aleksandra Likońska¹, Alicja Nowak-Jurek¹, Adrian Gajewski¹, Monika Antczak-Marczak¹, Karolina Frachowicz-Guerreiro¹, Aleksandra Wardzyńska¹, Maciej Chałubiński¹

Affiliations expand

- PMID: 37055938

- DOI: [10.1111/cea.14316](https://doi.org/10.1111/cea.14316)

No abstract available

Keywords: IL-25; IL-33; anti-IL-5 treatment; asthma; exhale breath condensates; mepolizumab; periostin.

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J Allergy Clin Immunol Pract

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. 2023 Apr 11;S2213-2198(23)00398-7.

doi: 10.1016/j.jaip.2023.03.046. Online ahead of print.

Safety and effectiveness of as-needed formoterol in asthma patients taking ICS-formoterol or ICS-salmeterol maintenance therapy

Helen K Reddel¹, Guy Brusselle², Rosa Lamarca³, Per Gustafson⁴, Gary P Anderson⁵, Carin Jorup⁶

Affiliations expand

- PMID: 37054881
- DOI: [10.1016/j.jaip.2023.03.046](https://doi.org/10.1016/j.jaip.2023.03.046)

Abstract

Background: As-needed low-dose inhaled corticosteroid (ICS)-formoterol reliever is recommended in asthma patients prescribed maintenance ICS-formoterol. Clinicians often ask whether ICS-formoterol reliever can be used with other maintenance ICS-long-acting β_2 -agonists (LABAs).

Objective: To evaluate safety and effectiveness of as-needed formoterol in patients taking maintenance ICS-formoterol or ICS-salmeterol from the RELIEF study.

Methods: RELIEF (SD-037-0699) was a 6-month, open-label study that randomized 18,124 patients with asthma to as-needed formoterol 4.5 μ g or salbutamol 200 μ g on top of maintenance therapy. This post hoc analysis included patients on maintenance ICS-formoterol or ICS-salmeterol (n=5,436). The primary safety outcome was a composite of serious adverse events (SAEs) and/or adverse events leading to discontinuation (DAEs); the primary effectiveness outcome was time-to-first exacerbation.

Results: For both maintenance groups and both relievers, similar numbers of patients had ≥ 1 SAE and/or DAE. In patients taking maintenance ICS-salmeterol, but not ICS-formoterol, significantly more non-asthma-related and non-serious DAEs occurred with as-needed formoterol versus as-needed salbutamol (p=0.0066 and p=0.0034, respectively). In patients taking maintenance ICS-formoterol, there was a significantly lower risk in time-to-first exacerbation with as-needed formoterol versus as-needed salbutamol (HR 0.82; 95% CI 0.70, 0.95; p=0.007). In patients taking ICS-salmeterol maintenance, time-to-first exacerbation was not significantly different between treatment arms (HR 0.95; 95% CI 0.84, 1.06; p=0.35).

Conclusions: As-needed formoterol significantly reduced exacerbation risk compared with as-needed salbutamol when added to maintenance ICS-formoterol, but not to maintenance ICS-salmeterol. More DAEs were seen with ICS-salmeterol maintenance

therapy plus as-needed formoterol. Further research is needed to assess whether this is relevant to as-needed combination ICS-formoterol.

Keywords: Asthma; ICS; budesonide-formoterol; effectiveness; exacerbations; formoterol; reliever; safety; salbutamol; salmeterol.

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. 2023 Apr 13.

doi: 10.1111/crj.13610. Online ahead of print.

From the infant to the geriatric patient- Strategies for inhalation therapy in asthma and chronic obstructive pulmonary disease

Lars Hagmeyer^{1,2,3}, Silke van Koningsbruggen-Rietschel^{4,3}, Sandhya Matthes², Ernst Rietschel^{4,3}, Winfried Randerath^{1,2,3}

Affiliations expand

- PMID: 37054701

- DOI: [10.1111/crj.13610](https://doi.org/10.1111/crj.13610)

Abstract

Inhalation therapy represents the standard of care in children, adolescents as well as in young, middle-aged and geriatric adults with asthma or chronic obstructive pulmonary disease. However, there are only few recommendations for the choice of inhalation devices, which consider both, age-specific limitations in young and geriatric patients.

Transition concepts are lacking. In this narrative review, the available device technologies and the evidence for age-specific problems are discussed. Pressurized metered-dose inhalers may be favoured in patients who fulfill all cognitive, coordinative and manual power requirements. Breath-actuated metered-dose inhalers, soft-mist inhalers or the use of add-on devices such as spacers, face masks and valved holding chambers may be suitable for patients with mild to moderate impairments of these variables. In these cases, available resources of personal assistance by educated family members or caregivers should be used to allow metered-dose inhaler therapy. Dry powder inhalers may be reserved for patients with a sufficient peak inspiratory flow and good cognitive and manual abilities. Nebulizers may be indicated in persons who are either unwilling or unable to use handheld inhaler devices. After initiation of a specific inhalation therapy, close monitoring is essential to reduce handling mistakes. An algorithm is developed that considers age and relevant comorbidities to support the decision-making process for the choice of an inhaler device.

Keywords: age; comorbidity; inhalation device; obstructive airway disease.

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J Asthma

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. 2023 Apr 12;1-12.

doi: 10.1080/02770903.2023.2200844. Online ahead of print.

A narrative review on asthma and pest sensitization (cockroach, mouse and rat allergens): a social issue besides the medical problem

Gennaro Liccardi¹, Matteo Martini^{2,3}, Maria Beatrice Bilò^{3,4}, Manlio Milanese⁵, Luigino Calzetta⁶, Rossella Laitano⁷, Paola Rogliani^{1,7}

Affiliations expand

- PMID: 37042228
- DOI: [10.1080/02770903.2023.2200844](https://doi.org/10.1080/02770903.2023.2200844)

Abstract

Objective: Among animals defined as "pests", cockroaches and rodents (mouse and rat) represent the most common cause of airway allergic sensitization and bronchial asthma worldwide. Their frequency of sensitization has been widely assessed in US and other countries but poorly in Western Europe. This narrative review aims to provide a synthesis of data resulting in MEDLINE concerning allergic sensitization/asthma to pests as well as their related environmental/social risk factors, specifically in the European area. **Data**

Sources: We performed a literature research in MEDLINE for clinical trials, randomized controlled trials, systematic reviews and meta-analyses. **Study Selections:** We selected studies to the following key words: allergic sensitization, allergic rhinitis, bronchial asthma, cockroach, hypersensitivity, integrated pest management, material hardship, medication compliance, mouse, pest, poverty, rat, rodents.

Results: Current evidence indicates that residence in poor and urban areas, exposure to outdoor/indoor pollutants and tobacco smoke, poverty, material hardship, poor-quality housing, differences in health care quality, medication compliance, health care access contribute to increased pest-related allergic sensitization and asthma morbidity.

Conclusion: Further research should be done on many aspects of pest allergy such as a better characterization of allergens and epidemiological aspects. Relevant social actions should be carried out against poverty, healthcare disparities, psycho-social stress, poor compliance to therapy, with economic contributions to improve private and public living environments. Allergic sensitization to pests and pest-allergic respiratory diseases like asthma are "paradoxical" conditions, as they typically affect the poorest communities but can only be corrected by high-cost (diagnostic and preventive) interventions. We hope that progress can be made in this direction in the future.

Keywords: Allergic sensitization; allergic rhinitis; bronchial asthma; cockroach; hypersensitivity; integrated pest management; material hardship; medication compliance; mouse; pest; poverty; rat; rodents.

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Allergy

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. 2023 Apr 11.

doi: 10.1111/all.15740. Online ahead of print.

Patient-centred digital biomarkers for allergic respiratory diseases and asthma: the ARIA-EAACI approach

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Affiliations expand

- PMID: 37042071

- DOI: [10.1111/all.15740](https://doi.org/10.1111/all.15740)

Abstract

Biomarkers for the diagnosis, treatment and follow-up of patients with rhinitis and/or asthma are urgently needed. Although some biologic biomarkers exist in specialist care for asthma, they cannot be largely used in primary care. There are no validated biomarkers in rhinitis or allergen immunotherapy (AIT) that can be used in clinical practice. The digital transformation of health and health care (including mHealth) places the patient at the centre of the health system and is likely to optimise the practice of allergy. ARIA (Allergic Rhinitis and its Impact on Asthma) and EAACI (European Academy of Allergy and Clinical Immunology) developed a Task Force aimed at proposing patient-reported outcome measures (PROMs) as digital biomarkers that can be easily used for different purposes in rhinitis and asthma. It first defined control digital biomarkers that should make a bridge between clinical practice, randomised controlled trials, observational real-life studies and allergen challenges. Using the MASK-air app as a model, a daily electronic combined symptom-medication score for allergic diseases (CSMS) or for asthma (e-DASTHMA), combined with a monthly control questionnaire, were embedded in a strategy similar to the diabetes approach for disease control. To mimic real-life, it secondly proposed quality-of-life digital biomarkers including daily EQ-5D visual analogue scales and the bi-weekly RhinAsthma Patient Perspective (RAAP). The potential implications for the management of allergic respiratory diseases were proposed.

Keywords: ARIA; EAACI; apps; asthma; digital health; rhinitis.

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. 2023 Apr 11;258024231169230.

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Thunder storm mortality: Issues of medicolegal concern

Roger W Byard^{1,2}

Affiliations expand

- PMID: 37041741
- DOI: [10.1177/00258024231169230](https://doi.org/10.1177/00258024231169230)

Abstract

Thunderstorms refer to atmospheric disturbances that are associated with electrical discharges in the form of lightning, with acoustic effects from thunder. They involve the rapid upward movement of warm, moist air which then cools and condenses creating typical cumulonimbus clouds with precipitation. Thunderstorms range in severity but are usually associated with heavy rains, winds and sometimes sleet, hail and snow. If the intensity of a storm increases there may be tornadoes or cyclones. In cases with lightning strikes and minimal or no rain there is an associated risk for the development of quite devastating wild (bush) fires. Lightning strikes may also be associated with the development, or an exacerbation, of potentially lethal natural cardiac or respiratory diseases.

Keywords: Thunder storms; asthma; cyclones; death; lightning; wildfires.

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. 2023 Apr 11;13(1):5893.

doi: [10.1038/s41598-023-32485-9](https://doi.org/10.1038/s41598-023-32485-9).

Most patients with COPD are unaware of their health threats and are not

diagnosed: a national-level study using pulmonary function test

Myung-Bae Park¹, Tae Sic Lee², Ji-Ho Lee³, Jinhee Lee⁴

Affiliations expand

- PMID: 37041257
- PMCID: [PMC10090160](#)
- DOI: [10.1038/s41598-023-32485-9](#)

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Abstract

This study aimed to investigate national-level prevalence of COPD, proportion of patients diagnosed with and without COPD. We performed pulmonary function test (PFT) in 24,454 adults aged > 40 years for 8 years (2010-2017). The annual COPD prevalence increased from 13.1% in 2010 to 14.6% in 2012, followed by 13.3% in 2017. However, patients diagnosed with COPD ranged between 0.5 and 1.0% in the last 8 years, which means that only 5% of all COPD patients were diagnosed with COPD by doctors. We defined potential high-risk individuals as those with a FEV₁/FVC ratio of < 0.70, who have not been diagnosed with COPD and other respiratory diseases tuberculosis, asthma, lung cancer. The proportion of this group was 80.8% in 2010 and 78.1% in 2017. The older age group, women, low-educated group, and current smokers who have been smoking for a long time are more likely to be in the high-risk group having a higher possibility to develop COPD but are not diagnosed with COPD appropriately. Although COPD prevalence was high in the ever, current, and heavy smokers, only the diagnosis rate of COPD in ever smokers was 2.38 times higher than never smokers, indicating that a system is needed to screen and intervention for these groups.

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Conflict of interest statement

The authors declare no competing interests.

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

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MeSH terms, Grant support expand
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"rhinitis"[MeSH Terms] OR rhinitis[Text Word]

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Review

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doi: 10.1007/s11882-023-01076-z. Online ahead of print.

Diagnostics and Prevention of Occupational Allergy in Hairdressers

Wolfgang Uter¹, Jeanne D Johansen², Jelena Macan³, Cara Symanzik^{4,5}, Swen M John^{4,5}

Affiliations expand

- PMID: 37043158
- DOI: [10.1007/s11882-023-01076-z](https://doi.org/10.1007/s11882-023-01076-z)

Abstract

Purpose of review: This study aims to provide an overview on current knowledge on occupational allergic diseases in hairdressers and up-to-date perspectives of prevention.

Recent findings: Hand eczema (dermatitis) is common in hairdressers, often caused by contact allergy to one or multiple small molecules (haptens) used, e.g., for dyeing, bleaching, and waving/relaxing or by ancillary substances such as preservatives. Hairdressers, compared to other patch-tested patients, have an up to fivefold increased risk to be found sensitized, e.g., against p-phenylenediamine, ammonium persulfate, and glyceryl thioglycolate. Some of these small molecules may induce respiratory sensitization causing allergic rhinitis and/or asthma, notably persulfate salts. Occupational hazards in hairdressing are well described. This knowledge needs to be put into use for risk reduction, mainly by substitution of allergenic ingredients by less allergenic ones, education, and use of ventilation and suitable single-use gloves.

Keywords: Asthma; Hair cosmetics; Hairdressers; Occupational diseases; Skin diseases; Workers' health.

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. 2023 Apr 12;1-12.

doi: [10.1080/02770903.2023.2200844](https://doi.org/10.1080/02770903.2023.2200844). Online ahead of print.

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[Gennaro Liccardi](#)¹, [Matteo Martini](#)^{2,3}, [Maria Beatrice Bilò](#)^{3,4}, [Manlio Milanese](#)⁵, [Luigino Calzetta](#)⁶, [Rossella Laitano](#)⁷, [Paola Rogliani](#)^{1,7}

[Affiliations expand](#)

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- DOI: [10.1080/02770903.2023.2200844](https://doi.org/10.1080/02770903.2023.2200844)

Abstract

Objective: Among animals defined as "pests", cockroaches and rodents (mouse and rat) represent the most common cause of airway allergic sensitization and bronchial asthma worldwide. Their frequency of sensitization has been widely assessed in US and other countries but poorly in Western Europe. This narrative review aims to provide a synthesis of data resulting in MEDLINE concerning allergic sensitization/asthma to pests as well as their related environmental/social risk factors, specifically in the European area.**Data**

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Conclusion: Further research should be done on many aspects of pest allergy such as a better characterization of allergens and epidemiological aspects. Relevant social actions should be carried out against poverty, healthcare disparities, psycho-social stress, poor compliance to therapy, with economic contributions to improve private and public living environments. Allergic sensitization to pests and pest-allergic respiratory diseases like asthma are "paradoxical" conditions, as they typically affect the poorest communities but can only be corrected by high-cost (diagnostic and preventive) interventions. We hope that progress can be made in this direction in the future.

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. 2023 Apr 11.

doi: 10.1111/all.15740. Online ahead of print.

Patient-centred digital biomarkers for allergic respiratory diseases and asthma: the ARIA-EAACI approach

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Affiliations expand

- PMID: 37042071
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Abstract

Biomarkers for the diagnosis, treatment and follow-up of patients with rhinitis and/or asthma are urgently needed. Although some biologic biomarkers exist in specialist care for asthma, they cannot be largely used in primary care. There are no validated biomarkers in rhinitis or allergen immunotherapy (AIT) that can be used in clinical practice. The digital transformation of health and health care (including mHealth) places the patient at the centre of the health system and is likely to optimise the practice of allergy. ARIA (Allergic Rhinitis and its Impact on Asthma) and EAACI (European Academy of Allergy and Clinical Immunology) developed a Task Force aimed at proposing patient-reported outcome measures (PROMs) as digital biomarkers that can be easily used for different purposes in rhinitis and asthma. It first defined control digital biomarkers that should make a bridge between clinical practice, randomised controlled trials, observational real-life studies and allergen challenges. Using the MASK-air app as a model, a daily electronic combined symptom-medication score for allergic diseases (CSMS) or for asthma (e-DASTHMA), combined with a monthly control questionnaire, were embedded in a strategy similar to the diabetes approach for disease control. To mimic real-life, it secondly proposed quality-

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Keywords: ARIA; EAACI; apps; asthma; digital health; rhinitis.

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. 2023 Apr 11.

doi: 10.1080/1744666X.2023.2200165. Online ahead of print.

Intranasal corticosteroid and antihistamine combinations in the treatment of allergic rhinitis: the role of the novel formulation olopatadine/mometasone furoate

Erminia Ridolo¹, Alessandro Barone¹, Francesca Nicoletta¹, Giovanni Paoletti^{2,3}, Enrico Hefler^{2,3}, Luca Malvezzi⁴, Giorgio Walter Canonica^{2,3}

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- PMID: 37038974
- DOI: [10.1080/1744666X.2023.2200165](https://doi.org/10.1080/1744666X.2023.2200165)

Abstract

Introduction: Allergic rhinitis (AR) is a common disease with an important impact on the quality of life and very high management costs. In many patients, the poor control of

rhinitis symptoms often requires the use of different drugs, and polytherapy tends to reduce therapeutic adherence. According to the latest version of ARIA guidelines, the currently recommended drugs for the treatment of moderate to severe AR are second-generation anti-histamines, intranasal corticosteroids, and their combination, even in a single nasal spray device. A single medication with a rapid onset of action, acting on breakthrough symptoms too, would be advantageous, also in terms of patient compliance.

Areas covered: GSP301 (olopatadine 600 mcg-mometasone furoate 25 mcg) is a novel intranasal formulation, combining the second-generation antihistamine olopatadine hydrochloride with mometasone furoate. Here, we review the evidence for GSP301, especially concerning the efficacy and safety profile of this intranasal combination in the treatment of AR.

Expert opinion: The evidence provided in the current review clearly supports the use of GSP301 as a novel INCS/INAH with a well-documented efficacy and safety profile in terms of rapid symptom relief and good tolerability.

Keywords: allergic rhinitis; anti-histamine; corticosteroid; intranasal combinations.; mometasone furoate; olopatadine hydrochloride.

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

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. 2023 Apr 14;7:e44036.
doi: 10.2196/44036.

A New Questionnaire to Assess Respiratory Symptoms (The Respiratory Symptom Experience Scale): Quantitative Psychometric Assessment and Validation Study

Saul Shiffman^{#1}, Stacey A McCaffrey^{#2}, Michael J Hannon^{#1}, Nicholas I Goldenson^{#2}, Ryan A Black^{#2}

Affiliations expand

- PMID: 37058347
- DOI: [10.2196/44036](https://doi.org/10.2196/44036)

Abstract

Background: Smokers often experience respiratory symptoms (eg, morning cough), and those who stop smoking, including those who do so by switching completely to electronic nicotine delivery systems (ENDS), may experience reductions in symptoms. Existing respiratory symptom questionnaires may not be suitable for studying these changes, as they are intended for patient populations, such as those with chronic obstructive pulmonary disease (COPD).

Objective: This study aimed to develop a respiratory symptom questionnaire appropriate for current smokers and for assessing changes when smokers stop smoking.

Methods: The Respiratory Symptom Experience Scale (RSES) was derived from existing instruments and subject matter expert input and refined through cognitive debriefing interviews (n=49). Next, for purposes of the quantitative psychometric evaluation, the RSES was administered to smokers (n=202), former smokers (no tobacco use in >6 months; n=200), and switchers (n=208, smokers who switched to ENDS for >6 months), all of whom had smoked for at least 10 years (mean age 33 years). Participants, who averaged 62 (SD 12) years of age, included 28% (173/610) with respiratory allergy symptoms and 17% (104/610) with COPD. Test-retest reliability was assessed by repeat assessment after 1 week in 128 participants.

Results: A generalized partial credit model confirmed that the response options were ordered, and a parallel analysis using principal components confirmed that the scale was unidimensional. With allowance for 2 sets of correlated errors between pairs of items, a 1-factor graded response model fit the data. Discrimination parameters were approximately 1 or greater for all items. Scale reliability was 0.80 or higher across a broad range of severity (standardized scores -0.40 to 3.00). Test-retest reliability (absolute intraclass correlation) was good, at 0.89. RSES convergent validity was supported by substantial differences (Cohen d=0.74) between those with and without a diagnosis of respiratory disease (averaging 0.57 points, indicating that differences of this size or smaller represent meaningful differences). RSES scores also strongly differentiated those with and without COPD (d=1.52). Smokers' RSES scores were significantly higher than former smokers' scores (P<.001). Switchers' RSES scores were significantly lower than smokers' scores (P<.001) and no different from former smokers' scores (P=.34).

Conclusions: The RSES fills an important gap in the existing toolkit of respiratory symptom questionnaires; it is a reliable and valid tool to assess respiratory symptoms in adult current and former smokers, including those who have switched to noncombusted nicotine products. This suggests that the scale is sensitive to respiratory symptoms that develop in smokers and to their remission when smokers quit or switch to noncombusted nicotine

products intended to reduce the harm of smoking. The findings also suggest that switching from cigarettes to ENDS may improve respiratory health.

Keywords: COPD; ENDS; development; e-cigarettes; electronic nicotine delivery system; health intervention; lung; measure development; pulmonary; questionnaire; respiratory; respiratory disease; respiratory health; respiratory symptoms; smoker; smoking; validate; validation.

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. 2023 Apr 11;9(2):00007-2023.

doi: 10.1183/23120541.00007-2023. eCollection 2023 Mar.

Variability in P2X receptor composition in human taste nerves: implications for treatment of chronic cough

Brigit High¹, Marie E Jetté², Mei Li¹, Vijay R Ramakrishnan², Matthew Clary², Jeremy Prager³, Julia Draf⁴, Thomas Hummel⁴, Thomas E Finger¹

Affiliations expand

- PMID: 37057093
- PMID: [PMC10086694](#)
- DOI: [10.1183/23120541.00007-2023](https://doi.org/10.1183/23120541.00007-2023)

Abstract

Background: Antagonists to the P2X purinergic receptors on airway sensory nerves relieve refractory or unexplained chronic cough (RCC/UCC) but can evoke unwanted dysgeusias because the gustatory nerves innervating taste buds express this same family of receptors. However, the subunit composition of the P2X receptors in these systems may differ, with implications for pharmacological intervention of RCC/UCC. In most species, the extrapulmonary airway nerves involved in cough predominantly express P2X3 subunits that form homotrimeric P2X3 receptors. In contrast, most sensory nerves innervating taste buds in mice express both P2X2 and P2X3 subunits, so the majority of receptors in that system are likely P2X2/P2X3 heteromers.

Methods: Since neural P2X subunit composition can differ across species, we used immunohistochemistry to test whether taste nerves in humans and rhesus macaque monkeys express both P2X2 and P2X3 as in mice.

Results: In taste bud samples of fungiform papillae and larynx from humans and monkeys, all taste bud samples exhibited P2X3⁺ nerve fibres, but the majority lacked substantial P2X2⁺. Of the 35 human subjects, only four (one laryngeal and three fungiform) showed strong P2X2 immunoreactivity in taste nerves; none of the rhesus monkey samples showed immunoreactivity for P2X2.

Conclusions: These findings suggest that for most humans, unlike mice, taste buds are innervated by nerve fibres predominantly expressing only P2X3 homomeric receptors and not P2X2/P2X3 heteromers. Thus, antagonists specific for P2X3 homomeric receptors might not be spared from affecting taste function in RCC/UCC patients.

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Conflict of interest statement

Conflict of interest: Since 2018, T. Hummel has performed research together with and received funding from Sony, Stuttgart, Germany; Smell and Taste Lab, Geneva, Switzerland; Takasago, Paris, France; Aspuraclip, Berlin, Germany; Baia Foods, Madrid, Spain; Frequency Therapeutics, Farmington, CT, USA; and Bayer Healthcare, Berlin, Germany. The remaining authors do not have conflicts of interests to disclose.

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. 2023 Apr 11;9(2):00678-2022.

doi: 10.1183/23120541.00678-2022. eCollection 2023 Mar.

Efficacy and tolerability of zinc acetate for treatment of chronic refractory cough: pilot randomised futility trial

Aparna Balasubramanian¹, Janet T Holbrook², Brendan J Canning¹, Loretta G Que³, Mario Castro⁴, Barry J Make⁵, Linda Rogers⁶, Michael F Busk⁷, Alexis Rea², Ashley A McCook-Veal², Jiaxian He², Meredith C McCormack¹, Robert A Wise¹

Affiliations expand

- PMID: 37057088
- PMCID: [PMC10086688](#)
- DOI: [10.1183/23120541.00678-2022](#)

Abstract

Background: Cough is the most reported symptom in the United States, with chronic refractory cough representing significant morbidity to patients. Zinc acetate may have beneficial effects in the cough reflex pathway. We sought to assess the safety and efficacy of zinc acetate in the management of chronic refractory cough.

Study design and methods: This was a randomised, placebo-controlled, parallel-design pilot trial of individuals with chronic refractory cough. The effects of 6 weeks of zinc acetate *versus* placebo on quality of life and symptoms as measured by the Cough Quality-of-Life Questionnaire (CQLQ), Leicester Cough Questionnaire (LCQ), cough visual analogue score (C-VAS) and Global Assessment of Change in Cough (GACC) scores were evaluated. A futility analysis plan with a one-sided 80% confidence interval was used to compare treatment effect to published minimum clinically important differences (MCID) for each outcome.

Results: 34 participants, 17 in each group, were enrolled and randomised. Participants were primarily white females with moderate-severe cough. Participants assigned to zinc acetate had a significant increase in serum zinc levels after 6 weeks, while those assigned to placebo did not. Both groups showed improvement in CQLQ, LCQ, C-VAS and GACC scores, but the treatment effects of zinc acetate *versus* placebo were small with confidence intervals that did not include the MCIDs.

Interpretation: We observed no benefit of zinc therapy over placebo on cough symptoms or quality of life and conclude that larger trials of zinc for chronic cough are not warranted.

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Conflict of interest statement

Conflict of interest: M. Castro reports grant funding from the National Institutes of Health, American Lung Association and the Patient-Centered Outcomes Research Institute, pharmaceutical grant funding from AstraZeneca, GSK, Novartis, Pulmatrix, Sanofi-Aventis, Shionogi, is a consultant for Genentech, Teva, Sanofi-Aventis, Merck, Novartis, a speaker for for Amgen, AstraZeneca, Genentech, GSK, Regeneron, Sanofi-Aventis, Teva, and receives royalties from Elsevier. Conflict of interest: Authors A. Balasubramanian, J.T. Holbrook, B.J. Canning, L.G. Que, B.J. Make, L. Rogers, M.F. Busk, A. Rea, A.A. McCook-Veal, J. He, M.C. McCormack report no conflicts of interest related to this manuscript. Conflict of interest: R.A. Wise reports personal fees for consultation from Merck relevant to the content of this manuscript.

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The P2X3 receptor antagonist filapixant in patients with refractory chronic cough: a randomized controlled trial

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Abstract

Background: P2X3 receptor antagonists seem to have a promising potential for treating patients with refractory chronic cough. In this double-blind, randomized, placebo-controlled study, we investigated the efficacy, safety, and tolerability of the novel selective P2X3 receptor antagonist filapixant (BAY1902607) in patients with refractory chronic cough.

Methods: Following a crossover design, 23 patients with refractory chronic cough (age: 60.4 ± 9.1 years) received ascending doses of filapixant in one period (20, 80, 150, and 250 mg, twice daily, 4-days-on/3-days-off) and placebo in the other. The primary efficacy endpoint was the 24-h cough frequency on Day 4 of each dosing step. Further, subjective cough severity and health-related quality of life were assessed.

Results: Filapixant at doses ≥ 80 mg significantly reduced cough frequency and severity and improved cough health-related quality of life. Reductions in 24-h cough frequency over placebo ranged from 17% (80 mg dose) to 37% (250 mg dose), reductions over baseline from 23% (80 mg) to 41% (250 mg) (placebo: 6%). Reductions in cough severity ratings on a 100-mm visual analog scale ranged from 8 mm (80 mg) to 21 mm (250 mg). No serious or severe adverse events or adverse events leading to discontinuation of treatment were reported. Taste-related adverse events occurred in 4%, 13%, 43%, and 57% of patients treated with filapixant 20, 80, 150, and 250 mg, respectively, and in 12% treated with placebo.

Conclusions: Filapixant proved to be efficacious, safe, and—apart from the occurrence of taste disturbances, especially at higher dosages—well tolerated during the short therapeutic intervention. Clinical trial registration EudraCT, [eudract.ema.europa.eu](#), 2018-000129-29; ClinicalTrials.gov, [NCT03535168](#).

Keywords: Airway hyperreactivity; Airway hyperresponsiveness; Cough reflex sensitivity; P2X3 receptor antagonist; Proof of concept; Receptor pharmacology; Refractory chronic cough; Taste disturbances.

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Conflict of interest statement

CF, KF, and SK are employees of Bayer AG, the company that developed the study drug and sponsored the study and the preparation of this manuscript. IG was employed by Bayer AG when the study was planned and conducted. AHM has received grant funding and personal fees from Merck, Shionogi, Bellus, and Bayer. PAM has received industry-sponsored research funding. AMT, JWKvdB, LMcG, PW, and SSB have no potential conflicts of interest to declare.

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Principal stratification analysis to determine health benefit of indoor air pollution reduction in a randomized environmental intervention in COPD: Results from the CLEAN AIR study

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Abstract

Background: Indoor air quality represents a modifiable exposure to Chronic Obstructive Pulmonary Disease (COPD) health. In a randomized controlled trial (CLEAN AIR study), air cleaner assignment had causal effect in improving COPD outcomes. It is unclear, however, what is the treatment effect among those for whom intervention reduced air pollution and whether it was reduction in fine particulate matter (PM_{2.5}) or nitrogen dioxide (NO₂) that contributed to such improvement. Because pollution is a posttreatment variable, treatment effect cannot be assessed while controlling for pollution using intention-to-treat (ITT) analysis.

Objective: Using principal stratification method, we assess indoor pollutants as the intermediate variable, and determine the causal effect of reducing indoor air pollution on COPD health.

Method: In randomized controlled trial, former smokers with COPD received either active or placebo HEPA air cleaners and were followed for 6 months. Saint George's Respiratory Questionnaire (SGRQ) was the primary outcome and secondary measures included SGRQ subscales, COPD assessment test (CAT), dyspnea (mMRC), and breathlessness, cough, and sputum scale (BCSS). Indoor PM_{2.5} and NO₂ were measured. Principal stratification analysis was performed to assess the treatment effect while controlling for pollution reduction.

Results: Among those showing at least 40 % PM_{2.5} reduction through air cleaners, the intervention showed improvement in respiratory symptoms for the active (vs. placebo), and the size of treatment effect shown for this subgroup was larger than that for the overall sample. In this subgroup, those with active air cleaners (vs. placebo) showed 7.7 points better SGRQ (95%CI: -14.3, -1.1), better CAT ($\beta = -5.5$; 95%CI: -9.8, -1.2), mMRC ($\beta = -0.6$; 95%CI: -1.1, -0.1), and BCSS ($\beta = -1.8$; 95%CI: -3.0, -0.5). Among those showing at least 40 % NO₂ reduction through air cleaners, there was no intervention difference in outcomes.

Conclusion: Air cleaners caused clinically significant improvement in respiratory health for individuals with COPD through reduction in indoor PM_{2.5}.

Trial registration: ClinicalTrials.gov: [NCT02236858](https://clinicaltrials.gov/ct2/show/study/NCT02236858).

Keywords: Air cleaners; COPD; Environment; Particulate matter; Principal stratification; Randomized controlled trial.

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Conflict of interest statement

Declaration of competing interest Meredith McCormack reports financial support was provided by Aridis. Meredith McCormack reports financial support was provided by GlaxoSmithKline. Meredith McCormack reports financial support was provided by Celgene.

Roger Peng reports financial support was provided by Health Effects Institute. Nadia Hansel reports financial support was provided by COPD Foundation. Nadia Hansel reports financial support was provided by AstraZeneca. Nadia Hansel reports financial support was provided by GlaxoSmithKline. Nadia Hansel reports financial support was provided by Boehringer Ingelheim. Nadia Hansel reports financial support was provided by Mylan. supplementary info

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Sputum pathogen spectrum and clinical outcomes of upper respiratory tract infection in bronchiectasis exacerbation: A prospective cohort study

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Abstract

Upper respiratory tract infection (URTI) is common in humans. We sought to profile sputum pathogen spectrum and impact of URTI on acute exacerbation of bronchiectasis (AE). Between March 2017 and December 2021, we prospectively collected sputum from adults with bronchiectasis. We stratified AEs into events related (URTI-AE) and unrelated to URTI (non-URTI-AE). We captured URTI without onset of AE (URTI-non-AE). We did bacterial culture and viral detection with polymerase chain reaction, and explored the pathogen spectrum and clinical impacts of URTI-AE via longitudinal follow-up. Finally, we collected 479 clinically stable samples, 170 AE samples (89 collected at URTI-AE) and 113 URTI-non-AE samples. The viral detection rate was significantly higher in URTI-AE (46.1%) than in non-URTI-AE (4.9%) and URTI-non-AE (11.5%) (both $P < 0.01$). Rhinovirus [odds ratio (OR): 5.00, 95% confidence interval (95% CI): 1.06-23.56, $P = 0.03$] detection was independently associated with URTI-AE compared with non-URTI-AE. URTI-AE tended to yield higher viral load and detection rate of rhinovirus, metapneumovirus and bacterial shifting compared with URTI-non-AE. URTI-AE was associated with higher initial viral loads (esp. rhinovirus, metapneumovirus), greater symptom burden (consistently higher scores of three validated questionnaires) and prolonged recovery compared to those without. Having experienced URTI-AE predicted greater risk of future URTI-AE (OR: 10.90, 95% CI: 3.60-33.05). In summary, URTI is associated with a distinct pathogen spectrum and aggravates bronchiectasis exacerbation, providing the scientific rationale for the prevention of URTI to hinder bronchiectasis progression.

Keywords: Upper respiratory tract infections; bronchiectasis; exacerbation; symptom burden; virus.