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

1

J Electrocardiol

. 2023 Apr 3;79:100-107.
doi: 10.1016/j.jelectrocard.2023.03.085. Online ahead of print.

Relationship between abnormal P-wave axis, chronic obstructive pulmonary disease and mortality in the general population

Richard Kazibwe[1], Muhammad Imtiaz Ahmad[2], T K Luqman-Arafat[3], Haiying Chen[4], Joseph Yeboah[5], Elsayed Z Soliman[6]
Affiliations expand

- PMID: 37030109

- DOI: 10.1016/j.jelectrocard.2023.03.085

Abstract

Background: It is unclear whether the presence of a vertical P-wave axis on electrocardiogram modifies the association of COPD with mortality.

Objective: To examine the association and interaction of abnormal P-wave axis and COPD with mortality.

Study design and methods: The analysis included 7359 with ECG data from the Third National Health and Nutrition Examination Survey (NHANES-III) who were free of cardiovascular disease (CVD) at enrollment. Abnormal P-wave axis (aPWA) was defined as values above 75°. COPD was self-reported as either a diagnosis of emphysema or chronic bronchitis. National Death Index was used to identify the date of death and cause of death. Using multivariable Cox proportional hazard analysis, we examined the association of COPD with all-cause mortality by aPWA status.

Results: Over a median follow-up of 14 years, 2435 deaths occurred. Participants with concomitant presence of aPWA and COPD experienced higher death rates (73.9 per 1000 person-years (PY)) compared to either COPD or aPWA alone (36.4 per 1000 PY and 31.1 per 1000 PY), respectively. In multivariable-adjusted models, a stronger association between COPD and mortality was noted in the presence compared to the absence of aPWA (HR 95% CI): 1.71 (1.37-2.13) vs. 1.22(1.00-1.49), respectively (interaction P-value = 0.02). Similarly, a stronger association between aPWA and mortality was observed in the presence compared to the absence of COPD (HR 95% CI): 1.66(1.26-2.19) vs. 1.18(1.06-1.31), respectively (interaction P-value = 0.02). Similar higher death rates and mortality risk was observed when spirometry-confirmed COPD and aPWA were present together than in isolation.

Conclusion: The concomitant presence of aPWA and COPD leads to a significantly higher mortality rate compared to the presence either COPD or aPWA alone as a clinical variable. P-wave axis, reported routinely on ECG printout, can potentially identify patients with COPD who need intensive control of risk factors and disease management.

Keywords: And nutrition examination survey; COPD; Mortality; P-wave axis; The third National Health.

Respir Res

. 2023 Apr 7;24(1):102.

doi: 10.1186/s12931-023-02393-7.

Pulmonary rehabilitation after severe exacerbation of COPD: a nationwide population study

Marina Guecamburu[1], Anaëlle Coquelin[2], Amandine Rapin[3 4], Nelly Le Guen[2], Agnès Solomiac[2], Pauline Henrot[1 4], Marie Erbault[2], Sandrine Morin[2], Maéva Zysman[5 6]
Affiliations expand

- PMID: 37029390
- PMCID: PMC10082500
- DOI: 10.1186/s12931-023-02393-7

Abstract

Background: Acute exacerbations of chronic obstructive pulmonary disease (COPD) lead to a significant reduction in quality of life and an increased mortality risk. Current guidelines strongly recommend pulmonary rehabilitation (PR) after a severe exacerbation. Studies reporting referral for PR are scarce, with no report to date in Europe. Therefore, we assessed the proportion of French patients receiving PR after hospitalization for COPD exacerbation and factors associated with referral.

Methods: This was a national retrospective study based on the French health insurance database. Patients hospitalized in 2017 with COPD exacerbation were identified from the exhaustive French medico-administrative database of hospitalizations. In France, referral to PR has required as a stay in a specialized PR center or unit accredited to provide multidisciplinary care (exercise training, education, etc.) and admission within 90 days after discharge was assessed. Multivariate logistic regression was used to assess the association between patients' characteristics, comorbidities according to the Charlson index, treatment, and PR uptake.

Results: Among 48,638 patients aged ≥ 40 years admitted for a COPD exacerbation, 4,182 (8.6%) received PR within 90 days after discharge. General practitioner's (GP) density (number of GPs for the population at regional level) and PR center facilities (number of beds for the population at regional level) were significantly correlated with PR uptake (respectively r = 0.64 and r = 0.71). In multivariate analysis, variables independently associated with PR uptake were female gender (aOR 1.36 [1.28-1.45], p < 0.0001), age (p < 0.0001), comorbidities (p = 0.0013), use of non-invasive ventilation and/or oxygen therapy (aOR 1.52 [1.41-1.64], p < 0.0001) and administration of long-acting bronchodilators (p = 0.0038).

Conclusion: This study using the French nationally exhaustive health insurance database shows that PR uptake after a severe COPD exacerbation is dramatically low and must become a high-priority management strategy.

Keywords: Acute exacerbation of COPD; Health inequalities; Medical density; Pulmonary rehabilitation.

Conflict of interest statement

MG, AC, AR, NLG, AS, ME, SM have no conflicts of interest to disclose. PH reports grants from Avad outside the submitted work. MZ reports grants and personal fees from Boehringer Ingelheim, personal fees from Novartis, personal fees from Chiesi, personal fees from AstraZeneca, personal fees from CSLBehring and personal fees from GSK outside the submitted work, grants from AVAD, grants from FRM.

- 40 references
- 3 figures

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Sci Rep

. 2023 Apr 7;13(1):5715.
doi: 10.1038/s41598-023-32901-0.

Lung microbiome and cytokine profiles in different disease states of COPD: a cohort study

Qing Xue[#1], Yu Xie[#2 3], Yukun He[#2], Yan Yu[#2], Guiju Fang[1], Wenyi Yu[2], Jianhui Wu[1], Jiwei Li[4], Lili Zhao[2], Xinyu Deng[1], Ran Li[2], Fang Wang[2], Yali Zheng[5 6], Zhancheng Gao[7]
Affiliations expand

- PMID: 37029178
- PMCID: PMC10080507

- DOI: 10.1038/s41598-023-32901-0

Abstract

Increasing evidence indicates that respiratory tract microecological disorders may play a role in the pathogenesis of chronic obstructive pulmonary disease (COPD). Understanding the composition of the respiratory microbiome in COPD and its relevance to respiratory immunity will help develop microbiome-based diagnostic and therapeutic approaches. One hundred longitudinal sputum samples from 35 subjects with acute exacerbation of COPD (AECOPD) were analysed for respiratory bacterial microbiome using 16S ribosomal RNA amplicon sequencing technology, and the sputum supernatant was analysed for 12 cytokines using a Luminex liquid suspension chip. Unsupervised hierarchical clustering was employed to evaluate the existence of distinct microbial clusters. In AECOPD, the respiratory microbial diversity decreased, and the community composition changed significantly. The abundances of Haemophilus, Moraxella, Klebsiella, and Pseudomonas increased significantly. Significant positive correlations between the abundance of Pseudomonas and TNF-α, abundance of Klebsiella and the percentage of eosinophils were observed. Furthermore, COPD can be divided into four clusters based on the respiratory microbiome. AECOPD-related cluster was characterized by the enrichment of Pseudomonas and Haemophilus and a high level of TNF-α. Lactobacillus and Veillonella are enriched in therapy-related phenotypes and may play potential probiotic roles. There are two inflammatory endotypes in the stable state: Gemella is associated with the Th2 inflammatory endotypes, whereas Prevotella is associated with the Th17 inflammatory endotypes. Nevertheless, no differences in clinical manifestations were found between these two endotypes. The sputum microbiome is associated with the disease status of COPD, allowing us to distinguish different inflammatory endotypes. Targeted anti-inflammatory and anti-infective therapies may improve the long-term prognosis of COPD.

Conflict of interest statement

The authors declare no competing interests.

- 34 references
- 5 figures

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Review

Adv Ther

. 2023 Apr 7;1-18.
doi: 10.1007/s12325-023-02479-0. Online ahead of print.

A Charter to Fundamentally Change the Role of Oral Corticosteroids in the Management of Asthma

John Haughney[1], Tonya Winders[2,3], Steve Holmes[4], Pascal Chanez[5], Andrew Menzies-Gow[6], Janwillem Kocks[7,8,9,10], Adel H Mansur[11], Christopher McPherson[12], Giorgio Walter Canonica[13,14]
Affiliations expand

- PMID: 37027115
- PMCID: PMC10080509
- DOI: 10.1007/s12325-023-02479-0

Abstract

Asthma affects 339 million people worldwide, with an estimated 5-10% experiencing severe asthma. In emergency settings, oral corticosteroids (OCS) can be lifesaving, but acute and long-term treatment can produce clinically important adverse outcomes and increase the risk of mortality. Therefore, global guidelines recommend limiting the use of OCS. Despite the risks, research indicates that 40-60% of people with severe asthma are receiving or have received long-term OCS treatment. Although often perceived as a low-cost option, long-term OCS use can result in significant health impairments and costs owing to adverse outcomes and increased utilization of healthcare resources. Alternative treatment methods, such as biologics, may produce cost-saving benefits with a better safety profile. A comprehensive and concerted effort is necessary to tackle the continued reliance on OCS. Accordingly, a threshold for OCS use should be established to help identify patients at risk of OCS-related adverse outcomes. Receiving a total dose of more than 500 mg per year should trigger a review and specialist referral. Changes to national and local policies, following examples from other chronic diseases, will be crucial to achieving this goal. Globally, multiple barriers to change still exist, but specific steps have

been identified to help clinicians reduce reliance on OCS. Implementing these changes will result in positive health outcomes for patients and social and economic benefits for societies.

Keywords: Asthma; Long-term; Oral corticosteroids.

- 81 references
- 1 figure

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Medicine (Baltimore)

. 2023 Apr 7;102(14):e33466.
doi: 10.1097/MD.0000000000033466.

The function of S100A4 in pulmonary disease: A review

Ting Wang[1]
Affiliations expand

- PMID: 37026957
- PMCID: PMC10082230
- DOI: 10.1097/MD.0000000000033466

Abstract

S100 protein family, which represents 25 relatively small calcium binding proteins, is involved in many intracellular and/or extracellular processes, including differentiation,

apoptosis, migration/invasion, Ca2+ homeostasis, inflammation, and tissue repair. As an important member, S100A4 was reported to have an abnormal expression in several lung diseases, such as lung cancer, pulmonary hypertension, idiopathic pulmonary fibrosis (IPF), etc. For example, in lung cancer, S100A4 was demonstrated to be associated to metastatic tumor progression and epithelial to mesenchymal transition (EMT). In IPF, S100A4 was considered as a promising serum biomarker predicting disease progression. Various studies in recent years focused on the S100A4 function in lung diseases, showing researchers' interests on this protein. It is necessary to focuses on relative studies, and make a comprehensive understanding of S100A4 in common pulmonary diseases. By doing this, this paper provides a review of the evidence for S100A4 in lung cancer, chronic obstructive pulmonary disease (COPD), asthma, IPF and pulmonary hypertension.

Conflict of interest statement

The authors have no conflicts of interest to disclose.

- 60 references
- 1 figure

6
Respir Med
.
. 2023 Apr 4;107236.
doi: 10.1016/j.rmed.2023.107236. Online ahead of print.

Change in physical activity related to admission for exacerbation in COPD patients

Cristóbal Esteban[1], Ane Antón-Ladislao[2], Amaia Aramburu[3], Leyre Chasco[3], Miren Orive[4], Eva Tabernero[5], Monica Rayón[6], José Joaquín Cebrián[7], José Terán[8], Ignacio García-Talavera[9], José M Quintana[10]; ReEPOC-REDISSEC group
Collaborators, Affiliations expand

- PMID: 37023870

- DOI: 10.1016/j.rmed.2023.107236

Abstract

Introduction: The aim of this study was to determine the impact of hospitalizations on levels of physical activity (PA) and whether other factors were associated with subsequent changes in PA.

Methods: Prospective observational cohort study with a nested case-control study, with follow-up 60 days from the index hospital admission. Nine hospitals participated in the study. Patients were recruited consecutively. Several variables and questionnaires of the clinical baseline status of the patients were recorded including: the COPD Assessment Test (CAT), the Hospital Anxiety-Depression scale (HADS), comorbidities and the Yale Physical Activity Survey. Patients' data related to admission and up to two months after discharge were also recorded.

Results: 883 patients were studied: 79.7% male; FEV1 48%; Charlson index 2; 28.7% active smokers. The baseline PA level for the total sample was 23 points. A statistically significant difference in PA was found between patients readmitted up to 2 months after the index admission and those not readmitted (17vs. 27, $p < 0.0001$). Multivariable linear regression analysis identified the following as predictors of the decrease of PA from baseline (index admission) up to 2 months follow-up: admission for COPD exacerbation in the two months prior to the index admission; readmission up to 2 months after the index admission; baseline HAD depressive symptoms, worse CAT score, and patient-reported "need for help".

Conclusions: In a cohort of admitted COPD patients, we identified a strong relationship between hospitalization for exacerbation and PA. In addition, some other potentially modifiable factors were found associated with the change in PA level after an admission.

Keywords: COPD; Exacerbation; Physical activity.

Conflict of interest statement

Declaration of competing interest The study protocol was approved by the Basque Ethics Committee (reference PI2015124). Ninguno de los autores de este original presenta conflicto de interés alguno (directo o indirecto) en relación al mismo.

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Respir Med
.
. 2023 Apr 4;107221.
doi: 10.1016/j.rmed.2023.107221. Online ahead of print.

COPD and 20-year hearing decline: The HUNT cohort study

Lisa Aarhus[1], Morten Sand[2], Bo Engdahl[3]
Affiliations expand

- PMID: 37023869
- DOI: 10.1016/j.rmed.2023.107221

Abstract

Background: We aimed to assess the association between chronic obstructive pulmonary disease (COPD) and long-term hearing decline. A further aim was to study sex differences.

Methods: Population-based cohort study in Norway (the HUNT study) with baseline measurements in 1996-1998 and follow-up in 2017-2019. The sample included 12,082 participants (43% men, mean age at follow-up 64 years). We used multiple linear regression to assess the association between COPD (minimum one registered ICD-10 code with emphysema or other COPDs during follow-up) and 20-year hearing decline in the low/mid/high frequency area (0.25-0.5/1-2/3-8 kHz). We adjusted for age, sex, education, smoking, noise exposure, ear infections, hypertension and diabetes.

Results: Persons registered with COPD (N = 403) had larger 20-year hearing decline at low frequencies (1.5 dB, 95% confidence interval (CI) 0.6-2.3) and mid frequencies (1.2 dB, 95% CI 0.4-2.1), but not at high frequencies. At high frequencies, the association was stronger and statistically significant only among women (1.9 dB, 95% CI 0.6-3.2). Persons registered with both COPD and respiratory failure (N = 19) had larger 20-year hearing decline at low and mid frequencies: 7.4 dB (95% CI 3.6-11.2) and 4.5 dB (95% CI 0.7-8.4), respectively.

Conclusion: Our large cohort study shows an association between COPD and increased long-term hearing decline. Women seem to be more susceptible to COPD-related hearing loss at high frequencies. The findings support that COPD can affect the cochlear function.

Conflict of interest statement

Declaration of competing interest None.

PLoS One

. 2023 Apr 6;18(4):e0283949.
doi: 10.1371/journal.pone.0283949. eCollection 2023.

Identification of male COPD patients with exertional hypoxemia who may benefit from long-term oxygen therapy

Brian J Garnet[1,2], Elie Jean[3], Rodrigo Diaz Lankenau[3], Michael A Campos[1,2]
Affiliations expand

- PMID: 37023024
- PMCID: PMC10079074
- DOI: 10.1371/journal.pone.0283949

Free PMC article

Abstract

Several studies have documented increased exercise capacity with supplemental oxygen therapy in patients with COPD and exertional hypoxemia, but a large trial failed to demonstrate a survival benefit in this population. Due to the heterogeneity observed in therapeutic responses, we sought to retrospectively evaluate survival in male COPD patients with exertional hypoxemia who had a clinically meaningful improvement in exercise capacity while using supplemental oxygen compared to their 6-minute walk test distance (6MWD) while walking on room air. We defined them as responders or non-responders based on a change in 6MWD of greater or less than 54m. We compared their clinical and physiologic characteristics, and their survival over time. From 817 COPD subjects who underwent an assessment for home oxygen during the study period, 140 met inclusion criteria, with 70 (50%) qualifying as responders. There were no significant differences in demographics, lung function, or baseline oxygenation between the groups.

The only difference noted was in the baseline 6MWD on room air, with responders to oxygen therapy having significantly lower values (137 ± 74m, 27 ± 15% predicted) compared to non-responders (244 ± 108, 49 ± 23% predicted). Despite their poorer functional capacity, mortality was significantly lower in responders after adjusting for age, comorbidities, and FEV1 (HR 0.51; CI 0.31-0.83; p = 0.007) compared to non-responders after a median follow-up time of 3 years. We conclude that assessing the immediate effects of oxygen on exercise capacity may be an important way to identify individuals with exertional hypoxemia who may benefit in the long-term from ambulatory oxygen. Prospective long-term studies in this subset of patients with exercise induced hypoxemia are warranted.

Conflict of interest statement

The authors have declared that no competing interests exist.

- 21 references
- 2 figures

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Minerva Med

. 2023 Apr 6.
doi: 10.23736/S0026-4806.22.08266-0. Online ahead of print.

Comparison among populations with severe and intermediate alpha1-

antitrypsin deficiency and chronic obstructive pulmonary disease

Davide Piloni[1,2], Stefania Ottaviani[1,2], Laura Saderi[3], Luciano Corda[4], Paolo Baderna[5], Valentina Barzon[2], Alice M Balderacchi[2], Christine Seebacher[6], Bruno Balbi[7], Federica Albicini[1], Alessandra Corino[1], Maria C Mennitti[1], Claudio Tirelli[1], Fabio Spreafico[4], Matteo Bosio[1], Francesca Mariani[1,2], Giovanni Sotgiu[3], Angelo G Corsico[1,2,8], Ilaria Ferrarotti[9,8]
Affiliations expand

- PMID: 37021471

- DOI: 10.23736/S0026-4806.22.08266-0

Abstract

Background: Severe alpha1-antitrypsin (AAT) deficiency (AATD) is associated with a high risk of airflow obstruction and emphysema. The risk of lung disease in those with intermediate AAT deficiency is unclear. Our aims were to compare pulmonary function, time of onset of symptoms, and indicators of quality of life among patients with severe AATD (PI*ZZ), patients with intermediate AATD (PI*MZ) from the Italian Registry of AATD with a chronic obstructive pulmonary disease (COPD) cohort of patients without AATD (PI*MM).

Methods: We considered a total of 613 patients: 330 with the PI*ZZ genotype, 183 with the PI*MZ genotype and 100 with the PI*MM genotype. Radiological exams, pulmonary function test, and measurement of quality of life have been performed on all cohorts of patients.

Results: The three populations differ significantly in terms of age at COPD/AATD diagnosis (P=0.00001), respiratory function (FEV1, FVC, DLCO P<0.001), quality of life (P=0.0001) and smoking history (P<0.0001). PI*ZZ genotype had 24.9 times a higher likelihood of developing airflow obstruction. The MZ genotype is not associated with a significant early risk of airflow obstruction.

Conclusions: The comparison of populations with PI*ZZ, MZ and MM genotypes allows to delineate the role of alpha1-antitrypsin deficiency on respiratory function and on the impact on quality of life, in relation to other risk factors. These results highlight the crucial role of primary and secondary prevention on smoking habits in PI*MZ subjects and the importance of an early diagnosis.

ERJ Open Res

. 2023 Apr 3;9(2):00344-2022.
doi: 10.1183/23120541.00344-2022. eCollection 2023 Mar.

Functional imaging in asthma and COPD: design of the NOVELTY ADPro substudy

Helen Marshall[1], Jim M Wild[1], Laurie J Smith[1], Latife Hardaker[2], Titti Fihn-Wikander[3], Hana Müllerová[4], Rod Hughes[5]
Affiliations expand

- PMID: 37020837
- PMCID: PMC10068571
- DOI: 10.1183/23120541.00344-2022

Free PMC article

Abstract

The NOVEL observational longiTudinal studY (NOVELTY; ClinicalTrials.gov identifier NCT02760329) is a global, prospective, observational study of ~12 000 patients with a diagnosis of asthma and/or COPD. Here, we describe the design of the Advanced Diagnostic Profiling (ADPro) substudy of NOVELTY being conducted in a subset of ~180 patients recruited from two primary care sites in York, UK. ADPro is employing a combination of novel functional imaging and physiological and metabolic modalities to explore structural and functional changes in the lungs, and their association with different phenotypes and endotypes. Patients participating in the ADPro substudy will attend two visits at the University of Sheffield, UK, 12±2 months apart, at which they will undergo imaging and physiological lung function testing. The primary end-points are the distributions of whole lung functional and morphological measurements assessed with xenon-129 magnetic resonance imaging, including ventilation, gas transfer and airway microstructural indices. Physiological assessments of pulmonary function include spirometry, bronchodilator reversibility, static lung volumes *via* body plethysmography, transfer factor of the lung for carbon monoxide, multiple-breath nitrogen washout and airway oscillometry. Fractional exhaled nitric oxide will be measured as a marker of type-2 airways inflammation. Regional and global assessment of lung function using these

techniques will enable more precise phenotyping of patients with physician-assigned asthma and/or COPD. These techniques will be assessed for their sensitivity to markers of early disease progression.

Conflict of interest statement

Conflict of interest: H. Marshall, J. Wild and L. Smith are employees of the University of Sheffield, who received funding to conduct the study. H. Marshall has received support for attending meetings from AstraZeneca. T. Fihn-Wikander and H. Müllerová are employees of AstraZeneca. R. Hughes has received personal fees from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline and Novartis outside of the submitted work, and is an employee of AstraZeneca. L. Hardaker has no conflicts to disclose.

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Published Erratum

Eur Respir Rev

-
-
-

. 2023 Apr 5;32(168):225144.

doi: 10.1183/16000617.5144-2022. Print 2023 Jun 30.

"Targeting interleukin-33 and thymic stromal lymphopoietin pathways for novel pulmonary therapeutics in asthma and COPD". Ariel A. Calderon, Colin Dimond, David F. Choy, Rajita Pappu, Michele A.

Grimbaldeston, Divya Mohan and Kian Fan Chung. *Eur Respir Rev* 2023; 32: 220144

No authors listed

- PMID: 37019459
- PMCID: PMC10074163
- DOI: 10.1183/16000617.5144-2022

Free PMC article

No abstract available

Erratum for

- Targeting interleukin-33 and thymic stromal lymphopoietin pathways for novel pulmonary therapeutics in asthma and COPD.
  Calderon AA, Dimond C, Choy DF, Pappu R, Grimbaldeston MA, Mohan D, Chung KF.Eur Respir Rev. 2023 Jan 25;32(167):220144. doi: 10.1183/16000617.0144-2022. Print 2023 Mar 31.PMID: 36697211 **Free PMC article.** Review.

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Review

Eur Respir Rev

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-
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. 2023 Apr 5;32(168):220207.
doi: 10.1183/16000617.0207-2022. Print 2023 Jun 30.

The role of telemonitoring in patients on home mechanical ventilation

Ries van den Biggelaar[1], Anda Hazenberg[2 3], Marieke L Duiverman[4 3]
Affiliations expand

- PMID: 37019457
- PMCID: PMC10074164
- DOI: 10.1183/16000617.0207-2022

Free PMC article

Abstract

There is a growing number of patients being treated with long-term home mechanical ventilation (HMV). This poses a challenge for the healthcare system because in-hospital resources are decreasing. The application of digital health to assist HMV care might help. In this narrative review we discuss the evidence for using telemonitoring to assist in initiation and follow-up of patients on long-term HMV. We also give an overview of available technology and discuss which parameters can be measured and how often this should be done. To get a telemonitoring solution implemented in clinical practice is often complex; we discuss which factors contribute to that. We discuss patients' opinions regarding the use of telemonitoring in HMV. Finally, future perspectives for this rapidly growing and evolving field will be discussed.

Conflict of interest statement

Conflict of interest: M.L. Duiverman has received research grants from RESMED, Philips, Lowenstein, Vivisol, Sencure and Fisher & Paykel and speaking fees from Chiesi and Breas, outside the submitted work. The remaining authors have nothing to disclose.

Comment in

- New insights into acute and chronic respiratory failure: highlights from the Respiratory Failure and Mechanical Ventilation Conference 2022.
  Heunks L, Duiverman ML. Eur Respir Rev. 2023 Apr 5;32(168):230027. doi: 10.1183/16000617.0027-2023. Print 2023 Jun 30. PMID: 37019460 **Free PMC article.**

- 55 references
- 1 figure

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Publication types, MeSH termsexpand
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Biomed Pharmacother
.
. 2023 Apr 3;162:114628.
doi: 10.1016/j.biopha.2023.114628. Online ahead of print.

Ivacaftor therapy post myocardial infarction augments systemic inflammation and evokes contrasting effects with respect to tissue inflammation in brain and lung

Lotte Vanherle [1], Frank Matthes [2], Franziska E Uhl [3], Anja Meissner [4]
Affiliations expand

- PMID: 37018991

- DOI: 10.1016/j.biopha.2023.114628

Abstract

Acquired cystic fibrosis transmembrane regulator (CFTR) dysfunctions have been associated with several conditions, including myocardial infarction (MI). Here, CFTR is downregulated in brain, heart, and lung tissue and associates with inflammation and degenerative processes. Therapeutically increasing CFTR expression attenuates these effects. Whether potentiating CFTR function yields similar beneficial effects post-MI is unknown. The CFTR potentiator ivacaftor is currently in clinical trials for treatment of acquired CFTR dysfunction associated with chronic obstructive pulmonary disease and chronic bronchitis. Thus, we tested ivacaftor as therapeutic strategy for MI-associated target tissue inflammation that is characterized by CFTR alterations. MI was induced in male C57Bl/6 mice by ligation of the left anterior descending coronary artery. Mice were treated with ivacaftor starting ten weeks post-MI for two consecutive weeks. Systemic ivacaftor treatment ameliorates hippocampal neuron dendritic atrophy and spine loss and attenuates hippocampus-dependent memory deficits occurring post-MI. Similarly, ivacaftor therapy mitigates MI-associated neuroinflammation (i.e., reduces higher proportions of activated microglia). Systemically, ivacaftor leads to higher frequencies of circulating $Ly6C^{+}$ and $Ly6C^{hi}$ cells compared to vehicle-treated MI mice. Likewise, an ivacaftor-mediated augmentation of MI-associated pro-inflammatory macrophage phenotype

characterized by higher CD80-positivity is observed in the MI lung. In vitro, ivacaftor does not alter LPS-induced CD80 and tumor necrosis factor alpha mRNA increases in BV2 microglial cells, while augmenting mRNA levels of these markers in mouse macrophages and differentiated human THP-1-derived macrophages. Our results suggest that ivacaftor promotes contrasting effects depending on target tissue post-MI, which may be largely dependent on its effects on different myeloid cell types.

Keywords: Cystic fibrosis transmembrane regulator; Inflammation; Ivacaftor; Myocardial infarction; Target tissue damage.

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.

Expert Opin Investig Drugs

. 2023 Apr 5.

doi: 10.1080/13543784.2023.2199920. Online ahead of print.

Navafenterol for chronic obstructive pulmonary disease therapy

Sabina Antonela Antoniu[1], Claudia Mariana Handra[2], Agripina Rascu[2], Bogdan Alexandru Barbu[2], Ioan Chirap Mitulschi[1]

Affiliations expand

- PMID: 37017626

- DOI: 10.1080/13543784.2023.2199920

Abstract

Introduction: Chronic obstructive pulmonary disease (COPD) is a prevalent disease of the airways in which inhaled bronchodilators can be given as monotherapy or fixed dose combination, in order to better control disease symptoms and to reduce its morbidity. A novel bronchodilator approach is represented by bifunctional molecules such as navafenterol which exert dual synergic bronchodilator effects as a monotherapy. Navafenterol is currently investigated for COPD.

Areas covered: this review summarizes the preclinical data regarding navafenterol synthesis and in vitro and in vivo testing. Clinical data coming from phase I and II studies are also discussed. Navafenterol was found to improve lung function, dyspnea and cough severity and was well tolerated, and its effect was comparable with that of fixed dose combinations in patients with moderate to severe COPD.

Expert opinion: despite clinical evidence of efficacy for navafenterol is still limited the existing data prompts further clinical evaluation and also consideration of other inhalation approaches such as pressure metered dose inhalers (pMDIs) or nebulization. Other interesting approach would be combination with another bifunctional molecule such as ensifentrine.

Keywords: aclidinium; formoterol- bronchodilators-chronic obstructive pulmonary disease-glycopyrrolate; formoterol-indacaterol; glycopyrrolate-muscarinic antagonist beta 2 agonist (MABA)-navafenterol- tiotropium; olodaterol.

Br J Community Nurs

. 2023 Apr 2;28(4):172-178.
doi: 10.12968/bjcn.2023.28.4.172.

Early experiences of telehealth monitoring for patients with COPD and implementation of person-centred care plans

Jacqueline Eeles[1], Sarah Ellison[2], Caroline Jones[3], Claire Huntington[4]

Affiliations expand

- PMID: 36989197

- DOI: 10.12968/bjcn.2023.28.4.172

Abstract

Aims: The authors share their early experiences of developing and implementing a telehealth service for patients with chronic obstructive pulmonary disease (COPD), through a collaborative approach. The article will explore the process of implementing telehealth service in a local care community team, identifying opportunities for improving care delivery and person-centred care. **Discussion:** The initial feedback and thoughts of both patients and healthcare professionals were obtained. Such feedback included patient's health insights, which helped improve risk assessment and personalised parameter settings. **Conclusions:** To-date, there has been a lack of robust evidence for the clinical benefits of telehealth. However, the feedback from staff and patients using telehealth was positive in several areas. Person-centred care plans also helped provide greater insight into patient's health goals, thereby streamlining care.

Keywords: Long-term plan; chronic obstructive pulmonary disease; community respiratory team; person-centred care plans; telehealth.

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Respir Res
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. 2023 Apr 8;24(1):106.
doi: 10.1186/s12931-023-02394-6.

Chronic Airways Assessment Test: psychometric properties in patients with asthma and/or COPD

Erin L Tomaszewski[1], Mark J Atkinson[2], Christer Janson[3], Niklas Karlsson[4], Barry Make[5], David Price[6,7], Helen K Reddel[8], Claus F Vogelmeier[9], Hana Müllerová[10], Paul W Jones[11]; NOVELTY Scientific Community; and the NOVELTY study investigators
Collaborators, Affiliations expand

- PMID: 37031164

- DOI: 10.1186/s12931-023-02394-6

Abstract

Background: No short patient-reported outcome (PRO) instruments assess overall health status across different obstructive lung diseases. Thus, the wording of the introduction to the Chronic Obstructive Pulmonary Disease (COPD) Assessment Test (CAT) was modified to permit use in asthma and/or COPD. This tool is called the Chronic Airways Assessment Test (CAAT).

Methods: The psychometric properties of the CAAT were evaluated using baseline data from the NOVELTY study (NCT02760329) in patients with physician-assigned asthma, asthma + COPD or COPD. Analyses included exploratory/confirmatory factor analyses, differential item functioning and analysis of construct validity. Responses to the CAAT and CAT were compared in patients with asthma + COPD and those with COPD.

Results: CAAT items were internally consistent (Cronbach's alpha: > 0.7) within each diagnostic group (n = 510). Models for structural and measurement invariance were strong. Tests of differential item functioning showed small differences between asthma and COPD in individual items, but these were not consistent in direction and had minimal overall impact on the total score. The CAAT and CAT were highly consistent when assessed in all NOVELTY patients who completed both (N = 277, Pearson's correlation coefficient: 0.90). Like the CAT itself, CAAT scores correlated moderately (0.4-0.7) to strongly (> 0.7) with other PRO measures and weakly (< 0.4) with spirometry measures.

Conclusions: CAAT scores appear to reflect the same health impairment across asthma and COPD, making the CAAT an appropriate PRO instrument for patients with asthma and/or COPD. Its brevity makes it suitable for use in clinical studies and routine clinical practice.

Trial registration: NCT02760329.

Keywords: Asthma; COPD; COPD Assessment Test; Chronic Airways Assessment Test; Patient-reported; Psychometrics.

- 31 references

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Pulmonology
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. 2023 Apr 6;S2531-0437(23)00054-5.
doi: 10.1016/j.pulmoe.2023.03.002. Online ahead of print.

Mepolizumab in severe asthma exacerbation in a respiratory ICU-a successful off-label use

H C Rodrigues[1], C Martins[2], E Fragoso[2], C Lopes[3], P Azevedo[2]
Affiliations expand

- PMID: 37031002

- DOI: 10.1016/j.pulmoe.2023.03.002

No abstract available

Conflict of interest statement

Conflicts of interest The authors declare to have no conflict of interest directly or indirectly related to the manuscript contents.

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3
Ann Allergy Asthma Immunol
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. 2023 Apr 6;S1081-1206(23)00248-X.
doi: 10.1016/j.anai.2023.03.032. Online ahead of print.

Tiotropium for refractory cough in asthma via cough reflex sensitivity: a randomized, parallel, open-label, trial

Kensuke Fukumitsu[1], Yoshihiro Kanemitsu[2], Ryota Kurokawa[1], Norihisa Takeda[1], Tomoko Tajiri[1], Hirono Nishiyama[1], Keima Ito[1], Yoshitsugu Inoue[1], Sayaka Yamamoto[1], Yuta Mori[1], Satoshi Fukuda[1], Takehiro Uemura[1], Hirotsugu Ohkubo[1], Ken Maeno[1], Yutaka Ito[1], Tetsuya Oguri[1], Masaya Takemura[1], Akio Niimi[1]
Affiliations expand

- PMID: 37030486
- DOI: 10.1016/j.anai.2023.03.032

Abstract

Background: We previously reported in an uncontrolled study that tiotropium alleviated chronic cough in asthma refractory to inhaled corticosteroids and long-acting β2 agonists (ICS/LABA) by modulating capsaicin cough reflex sensitivity (C-CRS).

Objective: We sought to demonstrate the antitussive effects of tiotropium for refractory cough in asthma in a randomized, parallel, open-label, trial.

Methods: Fifty-eight asthmatics with chronic cough refractory to ICS/LABA were randomized in a 2:1 ratio to add tiotropium 5 μg (39 patients) or theophylline 400 mg (19 patients) for 4 weeks. Patients underwent workup, including capsaicin cough challenge test and subjective measures such as cough severity visual analog scales (VAS). We adopted C5, the lowest capsaicin concentration to induce at least 5 coughs, as an index of C-CRS. We also performed a post hoc analysis to identify factors predicting tiotropium responders, who showed an improvement of ≥15 mm in cough severity VAS.

Results: Fifty-two patients (tiotropium; 38, theophylline; 14) completed the study. Both tiotropium and theophylline significantly improved cough severity VAS and cough-specific quality of life. Tiotropium, but not theophylline, significantly increased C5 values, whereas pulmonary function did not change in either group. Additionally, changes in cough severity VAS correlated with changes in C5 values in the tiotropium group. A post hoc analysis

revealed that heightened C-CRS (C5 ≤1.22 μM) before the addition of tiotropium was an independent predictor for tiotropium responders.

Conclusion: Tiotropium may alleviate chronic cough in asthma refractory to ICS/LABA by modulating C-CRS. Heightened C-CRS may predict responsiveness to tiotropium for refractory cough in asthma.

Keywords: Asthma control; Capsaicin cough reflex sensitivity; Cough severity; Cough-specific quality of life; Neuronal dysfunction; Refractory cough; Tiotropium.

Review

Adv Ther

. 2023 Apr 7;1-18.
doi: 10.1007/s12325-023-02479-0. Online ahead of print.

A Charter to Fundamentally Change the Role of Oral Corticosteroids in the Management of Asthma

John Haughney[1], Tonya Winders[2,3], Steve Holmes[4], Pascal Chanez[5], Andrew Menzies-Gow[6], Janwillem Kocks[7,8,9,10], Adel H Mansur[11], Christopher McPherson[12], Giorgio Walter Canonica[13,14]
Affiliations expand

- PMID: 37027115
- PMCID: PMC10080509
- DOI: 10.1007/s12325-023-02479-0

Abstract

Asthma affects 339 million people worldwide, with an estimated 5-10% experiencing severe asthma. In emergency settings, oral corticosteroids (OCS) can be lifesaving, but acute and long-term treatment can produce clinically important adverse outcomes and increase the risk of mortality. Therefore, global guidelines recommend limiting the use of OCS. Despite the risks, research indicates that 40-60% of people with severe asthma are receiving or have received long-term OCS treatment. Although often perceived as a low-cost option, long-term OCS use can result in significant health impairments and costs owing to adverse outcomes and increased utilization of healthcare resources. Alternative treatment methods, such as biologics, may produce cost-saving benefits with a better safety profile. A comprehensive and concerted effort is necessary to tackle the continued reliance on OCS. Accordingly, a threshold for OCS use should be established to help identify patients at risk of OCS-related adverse outcomes. Receiving a total dose of more than 500 mg per year should trigger a review and specialist referral. Changes to national and local policies, following examples from other chronic diseases, will be crucial to achieving this goal. Globally, multiple barriers to change still exist, but specific steps have been identified to help clinicians reduce reliance on OCS. Implementing these changes will result in positive health outcomes for patients and social and economic benefits for societies.

Keywords: Asthma; Long-term; Oral corticosteroids.

- 81 references
- 1 figure

J Asthma

. 2023 Apr 7;1-15.

doi: 10.1080/02770903.2023.2200842. Online ahead of print.

Assessing asthma self-management education among US children with current asthma, Asthma Call-back Survey (ACBS) 2015-2017

Priyadarshini Pattath [1,2], Cheryl R Cornwell [1], Kanta Sircar [1], Xiaoting Qin [1]
Affiliations expand

- PMID: 37026680

- DOI: 10.1080/02770903.2023.2200842

Abstract

Objective: Asthma self-management education (AS-ME) is an effective strategy to help children with asthma achieve better asthma control and outcome. The objective of this study is to assess the association between the prevalence of receiving AS-ME curriculum components and sociodemographic characteristics among children with current asthma.

Methods: Behavioral Risk Factor Surveillance System, child Asthma Call-back Survey 2015-2017 aggregated data were used. Multivariable logistic regression models were used to assess associations of each AS-ME component question and sociodemographic characteristic, adjusting for sample weighting.

Results: Among 3,213 children with current asthma, 52% of children reported ever being given an asthma action plan by a doctor or other healthcare professional. After adjusting for other variables, boys and Non-Hispanic Black children were more likely to report being given an action plan (APR= 1.15[95% CI 1.00-1.32] and APR= 1.28[95% CI 1.07-1.54] respectively). Non-Hispanic Black (APR = 2.15 [95% CI 1.30-3.55]), non-Hispanic, other race (APR = 1.95 [95% CI1.04-3.66]), and Hispanic children (APR = 1.84 [95% CI 1.18-2.89]) were more likely to report taking a course to learn how to manage asthma than non-Hispanic White children. Hispanic children (40.8%) were more likely to report being advised to change home environment compared to non-Hispanic Whites (31.5%) (APR =1.28 [95% CI 1.01-1.63).

Conclusion: The prevalence of some elements of asthma-self management education was relatively low and there were differences observed in the prevalence of receiving AS-ME by race/ethnicity, parental education, and income. Targeted implementation of asthma self-management components and interventions may improve asthma control and reduce asthma morbidity.

Keywords: Asthma; asthma attack; children; education; self-management.

J Asthma
.
. 2023 Apr 6;1-17.
doi: 10.1080/02770903.2023.2200824. Online ahead of print.

Do improvements in clinical practice guidelines alter pregnancy outcomes in asthmatic women? A single-center retrospective cohort study

J L Robinson[1,2], K L Gatford[1], C P Hurst[3], V L Clifton[4], J L Morrison[2], M J Stark[1,5]
Affiliations expand

- PMID: 37021838

- DOI: 10.1080/02770903.2023.2200824

Abstract

Objective: Asthma occurs in ~17% of Australian pregnancies and is associated with adverse perinatal outcomes, which worsen with poor asthma control . Consequently, the South Australian 'Asthma in Pregnancy' perinatal guidelines were revised in 2012 to address management according to severity. This study investigated if these revised guidelines reduced the impact of maternal asthma on risks of adverse perinatal outcomes before (Epoch 1, 2006-2011) and after the revision (Epoch 2, 2013-2018).

Methods: Routinely collected perinatal and neonatal datasets from the Women's and Children's Hospital (Adelaide, Australia) were linked. Maternal asthma (prevalence:7.5%) was defined as asthma medication use or symptoms described to midwives. In imputation (n = 59131) and complete case datasets (n = 49594), analyses were conducted by inverse proportional weighting and multivariate logistic regression, accounting for confounders.

Results: Overall, maternal asthma was associated with increased risks of any antenatal corticosteroid treatment for threatened preterm birth (aOR 1.319, 95% CI 1.078-1.614), any Caesarean section (aOR 1.196, 95% CI 1.059-1.351), Caesarean section without labor (aOR 1.241, 95% CI 1.067-1.444), intrauterine growth restriction (IUGR, aOR 1.285, 95% CI 1.026-

1.61), and small for gestational age (aOR 1.324, 95% CI 1.136-1.542). After guideline revision, asthma-associated risks of any Caesarean section ($p < 0.001$), any antenatal corticosteroids ($p = 0.041$), and small for gestational age ($p = 0.050$), but not IUGR and Caesarean section without labour, were reduced.

Conclusions: Clinical practice guidelines based on the latest evidence do not guarantee clinical efficacy. Since adverse perinatal outcomes did not all improve, this work highlights the need to evaluate the ongoing impact of guidelines on clinical outcomes.

Keywords: clinical guidelines; maternal asthma; obstetrics; perinatal medicine; pregnancy.

ERJ Open Res

. 2023 Apr 3;9(2):00745-2022.
doi: 10.1183/23120541.00745-2022. eCollection 2023 Mar.

Evaluation of real-world mepolizumab use in severe asthma across Europe: the SHARP experience with privacy-preserving federated analysis

Johannes A Kroes[1], Rafael Alfonso-Cristancho[2], Aruna T Bansal[3], Emmanuelle Berret[4], Kristina Bieksiene[5], Arnaud Bourdin[6], Luisa Brussino[7], Diogo Canhoto[8], Cristina Cardini[9], Gulfem Celik[10], Zsuzsanna Csoma[11], Barbro Dahlén[12], Ebru Damadoglu[13], Katrien Eger[14], Lisa Gauquelin[15], Bilun Gemicioglu[16], Ozlem Goksel[17], Sophie Graff[18], Enrico Heffler[19 20], Hendrik B Hofstee[21], Peter Howarth[22], Rupert W Jakes[22], Fabienne Jaun[23], Virginija Kalinauskaite-Zukauske[5], Peter Kopač[24 25], Namhee Kwon[22], Claudia C Loureiro[26], Victor Lozoya García[27], Matthew Masoli[28], Mariana Paula Rezelj[24], Luis Pérez De Llano[29], Sanja Popović-Grle[30], David Ramos-Barbón[31], Ana Sà Sousa[32], Konstantinos Samitas[33], Florence Schleich[18 34], Concetta Sirena[9], Sabina Skrgat[25 35], Eleftherios Zervas[33], George Zichnalis[36], Elisabeth H Bel[14], Jacob K Sont[21], Simone Hashimoto[14], Anneke Ten Brinke[1]
Affiliations expand

- PMID: 37020841

- PMCID: PMC10068512

- DOI: 10.1183/23120541.00745-2022

Free PMC article

Abstract

Background: An objective of the Severe Heterogeneous Asthma Registry, Patient-centered (SHARP) is to produce real-world evidence on a pan-European scale by linking nonstandardised, patient-level registry data. Mepolizumab has shown clinical efficacy in randomised controlled trials and prospective real-world studies and could therefore serve as a proof of principle for this novel approach. The aim of the present study was to harmonise data from 10 national severe asthma registries and characterise patients receiving mepolizumab, assess its effectiveness on annual exacerbations and maintenance oral glucocorticoid (OCS) use, and evaluate treatment patterns.

Methods: In this observational cohort study, registry data (5871 patients) were extracted for harmonisation. Where harmonisation was possible, patients who initiated mepolizumab between 1 January 2016 and 31 December 2021 were examined. Changes of a 12-month (range 11-18 months) period in frequent (two or more) exacerbations, maintenance OCS use and dose were analysed in a privacy-preserving manner using meta-analysis of generalised estimating equation parameters. Periods before and during the coronavirus disease 2019 pandemic were analysed separately.

Results: In 912 patients who fulfilled selection criteria, mepolizumab significantly reduced frequent exacerbations (OR 0.18, 95% CI 0.13-0.25), maintenance OCS use (OR 0.75, 95% CI 0.61-0.92) and dose (mean -3.93 mg·day^{-1}, 95% CI -5.24-2.62 mg·day^{-1}) in the pre-pandemic group, with similar trends in the pandemic group. Marked heterogeneity was observed between registries in patient characteristics and mepolizumab treatment patterns.

Conclusions: By harmonising patient-level registry data and applying federated analysis, SHARP demonstrated the real-world effectiveness of mepolizumab on asthma exacerbations and maintenance OCS use in severe asthma patients across Europe, consistent with previous evidence. This paves the way for future pan-European real-world severe asthma studies using patient-level data in a privacy-proof manner.

Conflict of interest statement

Conflict of interest: Z. Csoma reports lecture honoraria from AstraZenca, Sanofi, Teva and GSK outside the submitted work. A. ten Brinke reports grants and payment for expert testimony from GlaxoSmithKline, AstraZeneca, TEVA and Sanofi-Genzyme Regeneron outside the submitted work. B. Gemicioglu reports support for the present work from GSK; lecture honoraria from GSK, Novartis, Deva, Chiesi, Abdi İbrahim and Sandoz; travel

support from GSK, AstraZeneca and Novartis; and leadership positions with SHARP (Turkey Coordinator), GARD (Turkey Coordinator) and Turkish Board of Pulmonology (Chair), outside the submitted work. C.C. Loureiro reports grants from GSK; consulting fees from AstraZeneca, GSK, Novartis and Sanofi; lecture honoraria from AstraZeneca, GSK, Novartis, Sanofi and Teva; and travel support from AstraZeneca, Novartis and Sanofi, outside the submitted work. D. Ramos-Barbón reports honoraria and institutional research funding from GSK, outside the submitted work. E.H. Bel reports grants from GlaxoSmithKline and TEVA; lecture honoraria from GlaxoSmithKline, TEVA, AstraZeneca, Sanofi-Genzyme, Regeneron, Chiesi and Sterna, outside the submitted work. J.A. Kroes reports grants from AstraZeneca, outside the submitted work. K. Samitas reports lecture honoraria from MSD, GSK, Chiesi, Novartis, AstraZeneca, ELPEN, Menarini, BMS, Specialty Therapeutics, Boehringer and Rontis; travel support from Boehringer; advisory board participation with AstraZeneca, GSK and Specialty Therapeutics; and a leadership position with the Hellenic Thoracic Society, outside the submitted work. L. Pérez de Llano reports support for the present work from AstraZeneca; grants from AstraZeneca, Faes, TEVA and Sanofi; lecture honoraria from AstraZeneca, TEVA, Sanofi, MSD, Leo Pharma, Gebro, GSK, Novartis, Chiesi, Techdow Pharma and Gilead; patents from AstraZeneca, Novartis, Faes, TEVA, GSK, Sanofi and Chiesi; and advisory board participation with AstraZeneca, outside the submitted work. R.W. Jakes reports support for the present work from GSK, as an employee and shareholder. S. Škrgat reports honoraria for lectures and educational events, supported by AstraZeneca, Sanofi, Chiesi, Pliva Teva and Medis; and participation on advisory boards of AstraZeneca, Chiesi and Sanofi, outside the submitted work. A. Bourdin reports support for the present work from GSK; grants from AstraZeneca, GSK and Boehringer Ingelheim; lecture honoraria, nonfinancial support and other support from AstraZeneca, GSK, Boehringer Ingelheim, Novartis, TEVA, Chiesi Farmaceuticals, Actelion, Gilead, Roche and Regeneron, outside the submitted work. B. Dahlén reports grants from Novartis and GSK; and consulting fees from AstraZeneca, Teva and Sanofi, outside the submitted work. E. Zervas reports advisory board fees from Astra, Chiesi, Elpen, GSK, Menarini, MSD and Novartis; honoraria and fees for lectures from Astra, Boehringer, Bristol-Myers, Chiesi, Elpen, GSK, Menarini, MSD and Novartis; travel accommodations and meeting expenses from Astra, Boehringer, Chiezi, Galenica, GSK, Elpen, MSD, Novartis and Roche; and holds a leadership role as Secretary General of Hellenic Thoracic Society, outside the submitted work. E. Heffler reports consulting fees and lecture honoraria from AstraZeneca, Sanofi, Regeneron, Novartis, GSK, Stallergenes-Greer and Circassia outside the submitted work. F. Schleich reports grants from GSK and AstraZeneca; and consulting fees and lecture honoraria from GSK, AstraZeneca and Chiesi, outside the submitted work. K. Eger reports that TEVA sponsored printing their PhD thesis, outside the submitted work. K. Bieksiene reports lecture honoraria from AstraZeneca and Berlin Chemie, outside the submitted work. M. Paula Rezelj reports lecture honoraria from AstraZeneca, Novartis, GSK and Stallergenes, outside the submitted work. M. Masoli reports an investigator-led nonpromotional grant from GlakoSmithKline and an advisory board fee from AstraZeneca outside the submitted work. N. Kwon reports support for the present work from GSK, as an employee and shareholder. P. Howarth reports support for the present work from GSK, as an employee and shareholder. P. Kopač reports lecture honoraria and advisory board

participation from AstraZeneca, GSK and Berlin-Chemie outside the submitted work. R. Alfonso-Cristancho reports support for the present work from GSK, as an employee and shareholder. G. Celik reports consulting fees and lecture honoraria from Novartis and GSK outside the submitted work. J.K. Sont reports grants from AstraZeneca; outside the submitted work. All other authors have nothing to disclose.

- 33 references
- 4 figures

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ERJ Open Res

. 2023 Apr 3;9(2):00344-2022.
doi: 10.1183/23120541.00344-2022. eCollection 2023 Mar.

Functional imaging in asthma and COPD: design of the NOVELTY ADPro substudy

Helen Marshall[1], Jim M Wild[1], Laurie J Smith[1], Latife Hardaker[2], Titti Fihn-Wikander[3], Hana Müllerová[4], Rod Hughes[5]

Affiliations expand

- PMID: 37020837
- PMCID: PMC10068571
- DOI: 10.1183/23120541.00344-2022

Free PMC article

Abstract

The NOVEL observational longiTudinal studY (NOVELTY; ClinicalTrials.gov identifier NCT02760329) is a global, prospective, observational study of ~12 000 patients with a diagnosis of asthma and/or COPD. Here, we describe the design of the Advanced Diagnostic Profiling (ADPro) substudy of NOVELTY being conducted in a subset of ~180 patients recruited from two primary care sites in York, UK. ADPro is employing a

combination of novel functional imaging and physiological and metabolic modalities to explore structural and functional changes in the lungs, and their association with different phenotypes and endotypes. Patients participating in the ADPro substudy will attend two visits at the University of Sheffield, UK, 12±2 months apart, at which they will undergo imaging and physiological lung function testing. The primary end-points are the distributions of whole lung functional and morphological measurements assessed with xenon-129 magnetic resonance imaging, including ventilation, gas transfer and airway microstructural indices. Physiological assessments of pulmonary function include spirometry, bronchodilator reversibility, static lung volumes *via* body plethysmography, transfer factor of the lung for carbon monoxide, multiple-breath nitrogen washout and airway oscillometry. Fractional exhaled nitric oxide will be measured as a marker of type-2 airways inflammation. Regional and global assessment of lung function using these techniques will enable more precise phenotyping of patients with physician-assigned asthma and/or COPD. These techniques will be assessed for their sensitivity to markers of early disease progression.

Conflict of interest statement

Conflict of interest: H. Marshall, J. Wild and L. Smith are employees of the University of Sheffield, who received funding to conduct the study. H. Marshall has received support for attending meetings from AstraZeneca. T. Fihn-Wikander and H. Müllerová are employees of AstraZeneca. R. Hughes has received personal fees from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline and Novartis outside of the submitted work, and is an employee of AstraZeneca. L. Hardaker has no conflicts to disclose.

- 50 references
- 2 figures

ERJ Open Res

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. 2023 Apr 3;9(2):00413-2022.

doi: 10.1183/23120541.00413-2022. eCollection 2023 Mar.

Airway wall splice quantitative trait locus analysis reveals novel downstream mechanisms for known asthma single-nucleotide polymorphisms

Tessa M Kole[1,2], Simon D Pouwels[1,2,3], Rene Bults[1,2], Marlies E Ketelaar[1,3,4], Victor Guryev[1,5], Lisanne Koll[1,3], Huib A M Kerstjens[1,2], Martijn C Nawijn[1,3], Alen Faiz[1,2,6,7], Maarten van den Berge[1,2,7]
Affiliations expand

- PMID: 37020836
- PMCID: PMC10068516
- DOI: 10.1183/23120541.00413-2022

Free PMC article

Abstract

Studying the effects of asthma SNPs on alternative splicing can lead to new insights into asthma pathophysiology. More specifically, a 17q12 SNP is associated to alternative splicing of *GSDMB*. https://bit.ly/3W49oTs.

Conflict of interest statement

Conflict of interest: T.M. Kole has nothing to disclose. Conflict of interest: S.D. Pouwels has nothing to disclose. Conflict of interest: R. Bults has nothing to disclose. Conflict of interest: M.E. Ketelaar has nothing to disclose. Conflict of interest: V. Guryev has nothing to disclose. Conflict of interest: L. Koll has nothing to disclose. Conflict of interest: H.A.M. Kerstjens has nothing to disclose. Conflict of interest: M.C. Nawijn has nothing to disclose. Conflict of interest: A. Faiz is a member of a TSANZ Special Interest Group. Conflict of interest: M. van den Berge reports research grants paid to their institution by GlaxoSmithKline, Novartis, AstraZeneca, Roche and Genentech. The submitted work is co-financed by the Dutch Ministry of Economic Affairs and Climate Policy by means of the PPP.

- 15 references
- 1 figure

full text links

ERJ Open Res
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. 2023 Apr 3;9(2):00687-2022.
doi: 10.1183/23120541.00687-2022. eCollection 2023 Mar.

Prevalence and management of severe asthma in the Nordic countries: findings from the NORDSTAR cohort

Susanne Hansen[1 2 3], Anna von Bülow[1 3], Patrik Sandin[4], Olivia Ernstsson[4 5], Christer Janson[6], Lauri Lehtimäki[7 8], Hannu Kankaanranta[8 9 10], Charlotte Ulrik[11], Bernt Bøgvald Aarli[12 13], Hanna Fues Wahl[4], Kirk Geale[4 14], Sheila Tuyet Tang[15], Maija Wolf[16], Tom Larsen[17], Alan Altraja[18 19], Helena Backman[20], Maritta Kilpeläinen[21 22], Arja Viinanen[21 22], Dora Ludviksdottir[23], Paula Kauppi[24], Asger Sverrild[1], Sverre Lehmann[12 13], Vibeke Backer[25], Valentyna Yasinska[26 27], Tina Skjold[28], Jussi Karjalainen[7 8], Apostolos Bossios[26 27 29], Celeste Porsbjerg[1]
Affiliations expand

- PMID: 37020835
- PMCID: PMC10068510
- DOI: 10.1183/23120541.00687-2022

Free PMC article

Abstract

Background: Real-life evidence on prevalence and management of severe asthma is limited. Nationwide population registries across the Nordic countries provide unique opportunities to describe prevalence and management patterns of severe asthma at population level. In nationwide register data from Sweden, Norway and Finland, we examined the prevalence of severe asthma and the proportion of severe asthma patients being managed in specialist care.

Methods: This is a cross-sectional study based on the Nordic Dataset for Asthma Research (NORDSTAR) research collaboration platform. We identified patients with severe asthma in adults (aged ≥18 years) and in children (aged 6-17 years) in 2018 according to the

European Respiratory Society/American Thoracic Society definition. Patients managed in specialist care were those with an asthma-related specialist outpatient contact (only available in Sweden and Finland).

Results: Overall, we identified 598 242 patients with current asthma in Sweden, Norway and Finland in 2018. Among those, the prevalence of severe asthma was 3.5%, 5.4% and 5.2% in adults and 0.4%, 1.0%, and 0.3% in children in Sweden, Norway and Finland, respectively. In Sweden and Finland, 37% and 40% of adult patients with severe asthma and two or more exacerbations, respectively, were managed in specialist care; in children the numbers were 56% and 41%, respectively.

Conclusion: In three Nordic countries, population-based nationwide data demonstrated similar prevalence of severe asthma. In children, severe asthma was a rare condition. Notably, a large proportion of patients with severe asthma were not managed by a respiratory specialist, suggesting the need for increased recognition of severe asthma in primary care.

Conflict of interest statement

Conflict of interest: The work was financially supported by Novartis and Sanofi & Regeneron Pharmaceuticals. S. Hansen reports no conflicts of interest. A. von Bülow reports consulting fees from Novartis, speaker fees from Novartis, GSK and AstraZeneca, travel grants from AstraZeneca, and participation in advisory boards with AstraZeneca and Novartis. P. Sandin has no conflicts of interest. O. Ernstsson has no conflicts of interest. C. Janson reports speaker fees from AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Novartis, Orion Pharma and Sanofi, and expert testimony payments from AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Novartis, Orion Pharma and Sanofi. L. Lehtimäki reports consulting fees from AstraZeneca and GSK, and speaker fees from AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Novartis, Orion Pharma and Sanofi. H. Kankaanranta reports consulting fees from AstraZeneca, GSK, Chiesi, MSD, Orion Pharma, Novartis and Sanofi Genzyme, and speaker fees from AstraZeneca, GSK, Chiesi, Mundipharma, Orion Pharma and Sanofi Genzyme. C. Ulrik reports grants from Sanofi, Boehringer Ingelheim, AstraZeneca and Novartis, consulting fees from Orion Pharma, AstraZeneca and Teva, and participation in advisory boards with Novartis, GSK, AstraZeneca, Sanofi, Chiesi and Boehringer Ingelheim. B.B. Aarli reports consulting fees from GSK and AstraZeneca, lecture fees from GSK, AstraZeneca, Sanofi-Aventis Norge, Novartis and Boehringer Ingelheim, and participation in advisory boards with GSK, Astra Zeneca and Sanofi-Aventis Norge. H. Fues Wahl has no conflicts of interest. K. Geale is a board member of Quantify Research AB, Quantify Research ApS, Quantify Research AS and Quantify HEOR Private Limited, is CEO of Quantify Research AB, Quantify Research ApS and Quantify Research AS, and has stock and stock options in Quantify Research AB. S.T. Tang is an employee at Sanofi and holds stocks in Sanofi. M. Wolf is an employee at Novartis Finland. T. Larsen is an employee at Novartis Norway. A. Altraja reports consulting fees from AstraZeneca, Boehringer Ingelheim, GSK and Sanofi, speaker fees from AstraZeneca, Berlin-Chemie Menarini, Boehringer Ingelheim,

Norameda (Chiesi), GSK, Sanofi, Teva and Zentiva, expert testimony for AstraZeneca, Boehringer Ingelheim, GSK and Sanofi, travel grants from AstraZeneca, Berlin-Chemie Menarini, Boehringer Ingelheim and Norameda (Chiesi), participation in advisory boards with AstraZeneca, Boehringer Ingelheim, GSK and Sanofi, and receipt of equipment from Berlin-Chemie Menarini. H. Backman reports speaker fees from AstraZeneca, Boehringer Ingelheim, GSK and Sanofi. M. Kilpeläinen reports no conflicts of interest. A. Viinanen reports consulting fees from GSK, speaker fees from AstraZeneca, ALK, GSK, Boehringer Ingelheim and Chiesi, and travel grants from AstraZeneca, Sanofi and Boehringer Ingelheim. D. Ludviksdottir reports travel grants from GSK and AstraZeneca. P. Kauppi reports no conflicts of interest. A. Sverrild reports grants from AstraZeneca, consulting fees from Novartis, speaker fees from AstraZeneca and Chiesi, travel grants from Teva, and participation in advisory boards with Chiesi and Sanofi-Genzyme. S. Lehmann reports no conflicts of interest. V. Backer reports no conflicts of interest. V. Yasinska reports lecture fees from GSK and Sanofi, and participation in advisory boards with AstraZeneca, Chiesi and GSK. T. Skjold reports no conflicts of interest. J. Karjalainen reports consulting fees from AstraZeneca, GSK, MSD and Novartis, and lecture fees from AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, MSD, MundiPharma, Novartis and Orion Pharma. A. Bossios reports lecture fees from GSK, AstraZeneca, Teva and Novartis, travel grants from AstraZeneca and Novartis, and participation in advisory boards with GSK, AstraZeneca, Teva, Novartis and Sanofi, and is a member of the steering committee of SHARP, Secretary of Assembly 5 (Airway diseases, asthma, COPD and chronic cough) of the European Respiratory Society and the vice-president of the Nordic Severe Asthma Network. C. Porsbjerg reports grants from AstraZeneca, GSK, Novartis, Teva, Sanofi, Chiesi and ALK, consulting fees from AZ, GSK, Novartis, TEVA, Sanofi, Chiesi and ALK, lecture fees from AZ, GSK, Novartis, TEVA, Sanofi, Chiesi and ALK, and participation in advisory boards with AstraZeneca, Novartis, TEVA, Sanofi and ALK.

- 35 references
- 3 figures

Published Erratum

Eur Respir Rev

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. 2023 Apr 5;32(168):225144.

doi: 10.1183/16000617.5144-2022. Print 2023 Jun 30.

"Targeting interleukin-33 and thymic stromal lymphopoietin pathways for novel pulmonary therapeutics in asthma and COPD". Ariel A. Calderon, Colin Dimond, David F. Choy, Rajita Pappu, Michele A. Grimbaldeston, Divya Mohan and Kian Fan Chung. *Eur Respir Rev* 2023; 32: 220144

No authors listed

- PMID: 37019459
- PMCID: PMC10074163
- DOI: 10.1183/16000617.5144-2022

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No abstract available

Erratum for

- Targeting interleukin-33 and thymic stromal lymphopoietin pathways for novel pulmonary therapeutics in asthma and COPD.
  Calderon AA, Dimond C, Choy DF, Pappu R, Grimbaldeston MA, Mohan D, Chung KF.Eur Respir Rev. 2023 Jan 25;32(167):220144. doi: 10.1183/16000617.0144-2022. Print 2023 Mar 31.PMID: 36697211 **Free PMC article.** Review.

supplementary info

Publication typesexpand

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. 2023 Apr 3;S0091-6749(23)00371-8.
doi: 10.1016/j.jaci.2023.03.019. Online ahead of print.

OPTIMIZATION OF THE ALLERGENS CLASSIFICATION TO THE INTERNATIONAL CLASSIFICATION OF DISEASES (ICD)-11

Luciana Kase Tanno[1], Yann Briand[2], Mélissa Mary[3], David A Khan[4], James L Sublett[5], Mark L Corbett[6], Ruby Pawankar[7], Stefano Del Giacco[8], Maria Jose Torres[9], Ignacio J Ansontegui[10], Motohiro Ebisawa[11], Bryan Martin[12], Pascal Demoly[13]; American Academy of Allergy Asthma & Immunology (AAAAI); American College of Allergy Asthma and Immunology (ACAAI); Asia Pacific Association of Allergy Asthma and Clinical Immunology (APAAACI); European Academy of Allergy and Clinical Immunology (EAACI); World Allergy Organization (WAO)
Affiliations expand

- PMID: 37019392

- DOI: 10.1016/j.jaci.2023.03.019

Abstract

Background: Accurate diagnosis of triggers or causative allergens is essential for appropriate risk assessment, providing correct advice to allergic patients and caregivers and personalized treatment. However, allergens have never been represented in the World Health Organization International Classification of Diseases (ICD). In this manuscript, we present the process of selection of allergens to better fit the ICD-11 structure and the outcomes of this process.

Methods: The Logical Observation Identifiers Names and Codes (LOINC) database, containing 1 444 allergens was used as the basis for the selection process. Two independent experts were responsible for the first selection of the allergens according to specific technical criteria. Second step of the selection process was based on real-life relevance of allergens according to the frequency of requests of each allergen.

Results: We selected 1 109 allergens (76.8%) from all 1 444 present in the LOINC database, with a considerable agreement between experts (Cohen kappa: 8.6). After assessing real-life data, 297 more relevant allergens worldwide were selected. Grouped as plants (36.4%), drugs (32.6%), animal proteins (21%), mold and other microorganisms (1.5%), occupational allergens (0.4%) and miscellaneous (0.5%).

Conclusion: The stepwise approach allowed us to select the most relevant allergens in practice which is the first step to build a classification of allergens to the WHO ICD-11. Aligned with the achievement in the construction of the pioneer section addressed to the allergic and hypersensitivity conditions in the ICD-11, the introduction of a classification for allergens can be considered timely and much needed in clinical practice.

Keywords: International Classification of Diseases; World Health Organization; allergens; allergy; classification; coding; epidemiology; hypersensitivity.

Review

ORL J Otorhinolaryngol Relat Spec

. 2023 Apr 5;1-13.
doi: 10.1159/000529918. Online ahead of print.

Chinese Expert Consensus on the Use of Biologics in Patients with Chronic Rhinosinusitis (2022, Zhuhai)

Hai-Yu Hong[1], Teng-Yu Chen[2], Qin-Tai Yang[3 4], Yue-Qi Sun[5], Feng-Hong Chen[6], Hong-Fei Lou[7], Hong-Tian Wang[8], Rui-Li Yu[8], Yun-Fang An[9], Feng Liu[10], Tian-Sheng Wang[11], Mei-Ping Lu[12], Qian-Hui Qiu[13], Xiang-Dong Wang[14], Jian-Jun Chen[15], Cui-da Meng[16], Zhi-Hai Xie[17], Juan Meng[10], Ming Zeng[18], Cheng-Li Xu[19], Ying Wang[20], Yu-Cheng Yang[21], Wei-Tian Zhang[22], Jun Tang[23], Yan-Li Yang[24], Rui Xu[6], Guo-Dong Yu[25], Zhao-Hui Shi[26], Xin Wei[27], Hui-Ping Ye[28], Ya-Nan Sun[29], Shao-Qing Yu[30], Tian-Hong Zhang[31], Jun Yong[32], Wei Hang[33], Yuan-Teng Xu[34], Yu Xu[35], Guo-Lin Tan[11], Na Sun[36], Gui Yang[37], You-Jin Li[38], Jing Ye[39], Ke-Jun Zuo[6], Li-Qiang Zhang[40], Xue-Yan Wang[8], An-Ni Yang[1], Ying-Xiang Xu[1], Wei Liao[1], Yun-Ping Fan[5], Hua-Bin Li[7]
Affiliations expand

- PMID: 37019094

- DOI: 10.1159/000529918

Free article

Abstract

Background: Chronic rhinosinusitis (CRS) is a common inflammatory disease in otolaryngology, mainly manifested as nasal congestion, nasal discharge, facial pain/pressure, and smell disorder. CRS with nasal polyps (CRSwNP), an important phenotype of CRS, has a high recurrence rate even after receiving corticosteroids and/or functional endoscopic sinus surgery. In recent years, clinicians have focused on the application of biological agents in CRSwNP. However, it has not reached a consensus on the timing and selection of biologics for the treatment of CRS so far.

Summary: We reviewed the previous studies of biologics in CRS and summarized the indications, contraindications, efficacy assessment, prognosis, and adverse effects of biologics. Also, we evaluated the treatment response and adverse reactions of dupilumab, omalizumab, and mepolizumab in the management of CRS and made recommendations.

Key messages: Dupilumab, omalizumab, and mepolizumab have been approved for the treatment of CRSwNP by the US Food and Drug Administration. Type 2 and eosinophilic inflammation, need for systemic steroids or contraindication to systemic steroids, significantly impaired quality of life, anosmia, and comorbid asthma are required for the use of biologics. Based on current evidence, dupilumab has the prominent advantage in improving quality of life and reducing the risk of comorbid asthma in CRSwNP among the approved monoclonal antibodies. Most patients tolerate biological agents well in general with few major or severe adverse effects. Biologics have provided more options for severe uncontrolled CRSwNP patients or patients who refuse to have surgery. In the future, more novel biologics will be assessed in high-quality clinical trials and applied clinically.

Keywords: Biologics; Dupilumab; Mepolizumab; Omalizumab; Rhinosinusitis.

. 2023 Apr 3;256:114868.
doi: 10.1016/j.ecoenv.2023.114868. Online ahead of print.

Higher greenspace exposure is associated with a decreased risk of childhood asthma in Shanghai - A megacity in China

Yabin Hu[1], Yiting Chen[2], Shijian Liu[1], Jianguo Tan[3], Guangjun Yu[4], Chonghuai Yan[5], Yong Yin[6], Shenghui Li[2], Shilu Tong[7]
Affiliations expand

- PMID: 37018854

- DOI: 10.1016/j.ecoenv.2023.114868

Abstract

Inconsistent evidence exists about whether exposure to greenspace benefits childhood asthma. Previous studies have only focused on residential or school greenspace, and no research has combined greenspace exposures at both homes and schools to determine their link with childhood asthma. A population-based cross-sectional study was conducted among 16,605 children during 2019 in Shanghai, China. Self-reported questionnaires were used to collect information on childhood asthma and demographic, socioeconomic and behavioural factors. Environmental data including ambient temperature, particulate matter with aerodynamic diameter less than 1 μm (PM_1), enhanced vegetation index (EVI), and normalized difference vegetation index (NDVI) were collected from satellite data. Binomial generalized linear models with a logit link were carried out to evaluate the association between greenspace exposure and children's asthma, as well as the effect modifiers. An interquartile range increment of whole greenspace ($NDVI_{500}$, $NDVI_{250}$, EVI_{500}, and EVI_{250}) exposure was associated with a reduced odds ratio of children's asthma (0.88, 95% CI: 0.78, 0.99; 0.89, 95% CI: 0.79, 1.01; 0.87, 95% CI: 0.77, 0.99; and 0.88, 95% CI: 0.78, 0.99, respectively) after controlling potential confounders. Low temperature, low PM_1, males, vaginal delivery, suburban/rural area, and without family history of allergy appeared to enhance the greenspace-asthma association. Increased greenspace exposure was associated with a lower risk of childhood asthma, and the association was modified by a range of socio-environmental factors. These findings add to the body of evidence on the benefits of biodiversity and supporting the promotion of urban greenspace to protect children's health.

Keywords: Asthma; Children; EVI; Greenspace; NDVI.

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.

Sci Rep

. 2023 Apr 4;13(1):5468.
doi: 10.1038/s41598-023-32246-8.

Real-world efficacy of anti-IL-5 treatment in patients with allergic bronchopulmonary aspergillosis

Katsuyoshi Tomomatsu[1], Hirotaka Yasuba[2], Takashi Ishiguro[3], Shiro Imokawa[4], Johsuke Hara[5], Seiko Soeda[6], Norihiro Harada[7], Naomi Tsurikisawa[8], Naohiro Oda[9], Shigeki Katoh[10], Takanori Numata[11], Yasuteru Sugino[12], Mitsuhiro Yamada[13], Mitsuhiro Kamimura[14], Takeshi Terashima[15], Naoki Okada[1], Jun Tanaka[1], Tsuyoshi Oguma[1], Koichiro Asano[16]

Affiliations expand

- PMID: 37015988
- PMCID: PMC10073186
- DOI: 10.1038/s41598-023-32246-8

Free PMC article

Abstract

Despite standard treatment with systemic corticosteroids and/or antifungal triazoles, a substantial proportion of patients with allergic bronchopulmonary aspergillosis (ABPA)

experience frequent relapses and require long-term treatment despite unfavorable adverse effects. We investigated the efficacy and safety of anti-interleukin (IL)-5/IL-5 receptor α chain (Rα) monoclonal antibodies (mAbs) in patients with ABPA complicated by asthma. ABPA cases treated with anti-IL-5/IL-5Rα mAbs were collected from 132 medical institutes in 2018 and published case reports in Japan. Clinical outcomes, laboratory and physiological data, and radiographic findings during 32 weeks before and after treatment were retrospectively evaluated. We analyzed 29 cases of ABPA: 20 treated with mepolizumab and nine with benralizumab. Treatment with anti-IL-5/IL-5Rα mAbs reduced the frequency of exacerbations ($p = 0.03$), decreased the dose of oral corticosteroids ($p < 0.01$), and improved pulmonary function ($p = 0.01$). Mucus plugs in the bronchi shrank or diminished in 18 patients (82%). Despite the clinical/radiographical improvement, serum levels of total IgE, the key biomarker for the pharmacological response in ABPA, were unchanged. Anti-IL-5/IL-5Rα mAbs that directly target eosinophils are promising candidates for the treatment of patients with ABPA, especially those with mucus plugs in the bronchi.

Conflict of interest statement

KA received lecture fees from GlaxoSmithKline plc and AstraZeneca K.K., Novartis, Sanofi. KT received lecture fees from AstraZeneca K.K. NH received personal fees from AstraZeneca K.K, GlaxoSmithKline plc, Novartis, Sanofi and grants from AstraZeneca K.K. JT received a research grant from GlaxoSmithKline plc. Other authors declare no competing interests.

- 59 references
- 2 figures

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J Infect Dis

. 2023 Apr 5;jiad093.
doi: 10.1093/infdis/jiad093. Online ahead of print.

Bronchiolitis, regardless of its aetiology and severity, is associated with an increased risk of asthma: a population-based study

Cintia Muñoz-Quiles[1], Mónica López-Lacort[1], Javier Díez-Domingo[1,2], Alejandro Orrico-Sánchez[1,2,3]
Affiliations expand

- PMID: 37015894

- DOI: 10.1093/infdis/jiad093

Abstract

An association exists between severe Respiratory Syncytial Virus (RSV)-bronchiolitis and a subsequent increased risk of recurrent wheezing (RW) and asthma. However, a causal relationship remains unproven. Using a retrospective population-based cohort study (339,814 children), bronchiolitis during the first two years (regardless of aetiology and severity) was associated with at least a threefold increased risk of RW/asthma at 2-4 years and an increased prevalence of asthma at ≥5 years of age. The risk was similar in children with mild bronchiolitis as in those with hospitalised-RSV-bronchiolitis and was higher in children with hospitalized-non-RSV-bronchiolitis. The rate of RW/asthma was higher when bronchiolitis occurred after the first 6 months of life. Our results seem to support the hypothesis of a shared predisposition to bronchiolitis (irrespective of aetiology) and RW/asthma. However, 60% of hospitalized bronchiolitis in our setting are due to RSV, which should be paramount in decision-making on imminent RSV prevention strategies.

Keywords: Bronchiolitis; RSV; aetiology; asthma; laboratory-confirmation; primary care; recurrent wheezing; respiratory syncytial virus; retrospective cohort study; severity.

. 2023 Apr 4;13(4):e067271.
doi: 10.1136/bmjopen-2022-067271.

Investigating the effect of early life antibiotic use on asthma and allergy risk in over 600 000 Canadian children: a protocol for a retrospective cohort study in British Columbia and Manitoba

Hannah Lishman[1,2], Nathan C Nickel[3,4,5], Hind Sbihi[6,2], Max Xie[2], Abdullah Mamun[2], Bei Yuan Zhang[7], Caren Rose[6,2], Patricia Janssen[6], Ashley Roberts[8,9], Meghan B Azad[3,5,10], Stuart Turvey[8,9], David M Patrick[6,2]
Affiliations expand

- PMID: 37015798

- DOI: 10.1136/bmjopen-2022-067271

Free article

Abstract

Introduction: Allergic conditions, such as asthma, hay fever and eczema, are some of the most common conditions impacting children globally. There is a strong incentive to study their determinants to improve their prevention. Asthma, hay fever and eczema are influenced through the same immunological pathway and often copresent in children ('the atopic march'). Increasing evidence shows a link between infant antibiotic use and the risk of childhood atopic conditions, mediated through gut microbial dysbiosis during immune system maturation, however, the potential for confounding remains. This study will investigate the relationship between infant antibiotic use and risk of allergic conditions in British Columbian and Manitoban children born over 10 years, adjusting for relevant confounders.

Methods and analysis: Provincial administrative datasets will be linked to perform comparable retrospective cohort analyses, using Population Data BC and the Manitoba Population Research Data Repository. All infants born between 2001 and 2011 in BC and Manitoba will be included (approximately 460 000 and 162 500 infants, respectively), following up to age 7. Multivariable logistic regression will determine the outcome risk by the fifth birthday among children who did and did not receive antibiotics before their first birthday. Clinical, demographic and environmental covariates will be explored, and sensitivity analyses performed to reduce confounding by indication.

Ethics and dissemination: The University of British Columbia Research Ethics Board (H19-03255) and University of Manitoba Ethics Board (HS25156 (H2021:328)) have approved this study. Data stewardship committees for all administrative datasets have granted permissions, facilitated by Population Data BC and the Manitoba Centre for Health Policy. Permissions from the Canadian Health Infant Longitudinal Development Study are being sought for breastfeeding data (CP185). Findings will be published in scientific journals and presented at infectious disease and respiratory health conferences. A stakeholder committee will guide and enhance sensitive and impactful communication of the findings to new parents.

Keywords: Allergy; Asthma; Community child health; EPIDEMIOLOGY; THERAPEUTICS.

Conflict of interest statement

Competing interests: None declared.

supplementary info

Publication types, MeSH terms, Substancesexpand

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Am J Respir Crit Care Med

. 2023 Apr 4.

doi: 10.1164/rccm.202210-2005OC. Online ahead of print.

Efficacy of Tezepelumab in Severe, Uncontrolled Asthma: Pooled Analysis of PATHWAY and NAVIGATOR Studies

Jonathan Corren[1], Andrew Menzies-Gow[2], Geoffrey Chupp[3], Elliot Israel[4], Stephanie Korn[5,6], Bill Cook[7], Christopher S Ambrose[7], Åsa Hellqvist[8], Stephanie L Roseti[9], Nestor A Molfino[10], Jean-Pierre Llanos[11], Neil Martin[12,13], Karin Bowen[14], Janet M Griffiths[15], Jane R Parnes[16], Gene Colice[17]

Affiliations expand

- PMID: 37015033

- DOI: 10.1164/rccm.202210-2005OC

Abstract

Rationale: Tezepelumab reduced exacerbations in patients with severe, uncontrolled asthma across a range of baseline blood eosinophil counts (BECs) and fractional exhaled nitric oxide (FeNO) levels, and irrespective of allergy status, in the phase 2b PATHWAY (NCT02054130) and phase 3 NAVIGATOR (NCT03347279) studies.

Objectives: To examine the efficacy and safety of tezepelumab in additional clinically relevant subgroups using pooled data from PATHWAY and NAVIGATOR.

Methods: PATHWAY and NAVIGATOR were randomized, double-blind, placebo-controlled studies with similar designs. This pooled analysis included patients with severe, uncontrolled asthma (PATHWAY, 18-75 years old; NAVIGATOR, 12-80 years old) who received tezepelumab 210 mg or placebo subcutaneously every 4 weeks for 52 weeks. The annualized asthma exacerbation rate (AAER) over 52 weeks and secondary outcomes were calculated in the overall population and in subgroups defined by inflammatory biomarker levels or clinical characteristics.

Measurements and main results: Overall, 1,334 patients were included (tezepelumab, n=665; placebo, n=669). Tezepelumab reduced the AAER (rate ratios; 95% confidence intervals) versus placebo by 60% (0.40; 0.34, 0.48) in the overall population, and clinically meaningful reductions in exacerbations were observed in tezepelumab-treated patients with type 2-high and type 2-low disease by multiple definitions. Tezepelumab reduced exacerbation-related hospitalization or emergency department visits and improved secondary outcomes compared with placebo overall and across subgroups. The incidence of adverse events was similar between treatment groups.

Conclusions: Tezepelumab resulted in clinically meaningful reductions in exacerbations and improvements in other outcomes in patients with severe, uncontrolled asthma, across clinically relevant subgroups.

Keywords: asthma; biomarkers; eosinophil; thymic stromal lymphopoietin.

Trials
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. 2023 Apr 3;24(1):252.
doi: 10.1186/s13063-023-07253-9.

IMPlementing IMProved Asthma self-management as RouTine (IMP²ART) in primary care: study protocol for a cluster randomised controlled implementation trial

Kirstie McClatchey[1], Vicky Hammersley[1], Liz Steed[2], Jessica Sheringham[3], Viv Marsh[1], Atena Barat[2], Brigitte Delaney[4], Thomas Hamborg[2], Deborah Fitzsimmons[5], Steve Holmes[6,7], Tracy Jackson[1], Elisabeth Ehrlich[1], Noelle Morgan[1], Ann Saxon[8], Megan Preston[9], David Price[10,11], Stephanie J C Taylor[2], Hilary Pinnock[12]; IMP2 ART Programme Group
Affiliations expand

- PMID: 37013577
- PMCID: PMC10068707
- DOI: 10.1186/s13063-023-07253-9

Free PMC article

Abstract

Background: Asthma is a common long-term condition and major public health problem. Supported self-management for asthma that includes a written personalised asthma action plan, supported by regular professional review, reduces unscheduled consultations and improves asthma outcomes and quality of life. However, despite unequivocal inter/national guideline recommendations, supported self-management is poorly implemented in practice. The IMPlementing IMProved Asthma self-management as RouTine (IMP²ART) implementation strategy has been developed to address this challenge. The aim of this implementation trial is to determine whether facilitated delivery of the IMP²ART strategy increases the provision of asthma action plans and reduces unscheduled care in the context of routine UK primary care.

Methods: IMP²ART is a parallel group, cluster randomised controlled hybrid II implementation trial. One hundred forty-four general practices will be randomly assigned to either the IMP²ART implementation strategy or control group. Following a facilitation workshop, implementation group practices will receive organisational resources to help them prioritise supported self-management (including audit and feedback; an IMP²ART asthma review template), training for professionals and resources to support patients to self-manage their asthma. The control group will continue with usual asthma care. The primary clinical outcome is the between-group difference in unscheduled care in the second year after randomisation (i.e. between 12 and 24 months post-randomisation) assessed from routine data. Additionally, a primary implementation outcome of asthma action plan ownership at 12 months will be assessed by questionnaire to a random sub-group of people with asthma. Secondary outcomes include the number of asthma reviews conducted, prescribing outcomes (reliever medication and oral steroids), asthma symptom control, patients' confidence in self-management and professional support and resource use. A health economic analysis will assess cost-effectiveness, and a mixed methods process evaluation will explore implementation, fidelity and adaptation.

Discussion: The evidence for supported asthma self-management is overwhelming. This study will add to the literature regarding strategies that can effectively implement supported self-management in primary care to reduce unscheduled consultations and improve asthma outcomes and quality of life.

Trial registration: ISRCTN15448074. Registered on 2 December 2019.

Keywords: Asthma; IMP2ART; Primary care; Protocol; Randomised controlled implementation trial; Self-management.

Conflict of interest statement

The authors declare that they have no competing interests.

- 78 references
- 2 figures

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Randomized Controlled Trial

BMC Public Health

. 2023 Apr 3;23(1):629.
doi: 10.1186/s12889-023-15465-6.

The ADEM2 project: early pathogenic mechanisms of preschool wheeze and a randomised controlled trial assessing the gain in health and cost-effectiveness by application of the breath test for the diagnosis of asthma in wheezing preschool children

Sophie Kienhorst[1], Moniek H D van Aarle[2], Quirijn Jöbsis[2], Michiel A G E Bannier[2], Elin T G Kersten[3], Jan Damoiseaux[4], Onno C P van Schayck[5], Peter J F M Merkus[6], Gerard H Koppelman[3], Frederik-Jan van Schooten[7]; ADEM2 Consortium; Agnieszka Smolinska[7], Edward Dompeling[2]
Collaborators, Affiliations expand

- PMID: 37013496
- PMCID: PMC10068201
- DOI: 10.1186/s12889-023-15465-6

Free PMC article

Abstract

Background: The prevalence of asthma-like symptoms in preschool children is high. Despite numerous efforts, there still is no clinically available diagnostic tool to discriminate asthmatic children from children with transient wheeze at preschool age. This leads to potential overtreatment of children outgrowing their symptoms, and to potential undertreatment of children who turn out to have asthma. Our research group developed a breath test (using GC-tof-MS for VOC-analysis in exhaled breath) that is able to predict a diagnosis of asthma at preschool age. The ADEM2 study assesses the improvement in health gain and costs of care with the application of this breath test in wheezing preschool children.

Methods: This study is a combination of a multi-centre, parallel group, two arm, randomised controlled trial and a multi-centre longitudinal observational cohort study. The preschool children randomised into the treatment arm of the RCT receive a probability diagnosis (and corresponding treatment recommendations) of either asthma or transient wheeze based on the exhaled breath test. Children in the usual care arm do not receive a probability diagnosis. Participants are longitudinally followed up until the age of 6 years. The primary outcome is disease control after 1 and 2 years of follow-up. Participants of the RCT, together with a group of healthy preschool children, also contribute to the parallel observational cohort study developed to assess the validity of alternative VOC-sensing techniques and to explore numerous other potential discriminating biological parameters (such as allergic sensitisation, immunological markers, epigenetics, transcriptomics, microbiomics) and the subsequent identification of underlying disease pathways and relation to the discriminative VOCs in exhaled breath.

Discussion: The potential societal and clinical impact of the diagnostic tool for wheezing preschool children is substantial. By means of the breath test, it will become possible to deliver customized and high qualitative care to the large group of vulnerable preschool children with asthma-like symptoms. By applying a multi-omics approach to an extensive set of biological parameters we aim to explore (new) pathogenic mechanisms in the early development of asthma, creating potentially interesting targets for the development of new therapies.

Trial registration: Netherlands Trial Register, NL7336, Date registered 11-10-2018.

Keywords: Asthma; Biomarkers; Breath test; Diagnosis; Exhaled VOC; Pathogenesis; Preschool; Wheeze.

- 40 references

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Editorial

Eur Respir J
-

. 2023 Apr 3;61(4):2202058.
doi: 10.1183/13993003.02058-2022. Print 2023 Apr.

Defining the questions to be asked in severe asthma trials: data from the COMSA working group

Thomas Eiwegger[1234], Sarah A Bendien[5]
Affiliations expand

- PMID: 37012083
- DOI: 10.1183/13993003.02058-2022

No abstract available

Conflict of interest statement

Conflict of interest: T. Eiwegger reports to act/recently acted as local PI for company sponsored trials by DBV Therapeutics and Greer Stallergens, and as sub-investigator for Regeneron and ALK-Abelló. He/his lab received unconditional/in-kind contributions from Macro Array Diagnostics and ALK-Abelló and he is co-investigator in an investigator-initiated trial with in-kind support from Novartis. He holds advisory board roles for ALK-Abelló, and Aimmune, and reports lecture fees from Novartis, ThermoFisher, Nutricia/Danone, Aimmune, ALK-Abelló and Novartis. S.A. Bendien reports lecture fees from AstraZeneca, GSK, Teva and Sanofi.

Comment on

- Development of Core Outcome Measures sets for paediatric and adult Severe Asthma (COMSA).
  Khaleva E, Rattu A, Brightling C, Bush A, Bossios A, Bourdin A, Chung KF, Chaudhuri R, Coleman C, Dahlén SE, Djukanovic R, Deschildre A, Fleming L, Fowler SJ, Gupta A, Hamelmann E, Hashimoto S, Hedlin G, Koppelman GH, Melén E, Murray CS, Pilette C, Porsbjerg C, Pike KC, Rusconi F, Williams C, Ahrens B, Alter P, Anckers F, van den Berge M, Blumchen K, Brusselle G, Clarke GW, Cunoosamy D, Dahlén B, Dixey P, Exley A, Frey U, Gaillard EA, Giovannini-Chami L, Grigg J, Hartenstein D, Heaney LG, Karadag B, Kaul S, Kull I, Licari A, Maitland-van der Zee AH, Mahler V, Schoos AM, Nagakumar P, Negus J, Nielsen H, Paton J, Pijnenburg M, Ramiconi V, Romagosa Vilarnau S, Principe S, Rutjes N, Saglani S, Seddon P, Singer F, Staudinger H, Turner S, Vijverberg S, Winders T, Yasinska V, Roberts G; COMSA Working Group in the 3TR Consortium.Eur Respir J. 2023 Apr 3;61(4):2200606. doi: 10.1183/13993003.00606-2022. Print 2023 Apr.PMID: 36229046 **Free PMC article.** Review.

supplementary info

Ann Hum Genet
.
. 2023 Apr 3.
doi: 10.1111/ahg.12506. Online ahead of print.

The impact of obesity on lung function measurements and respiratory disease: A Mendelian randomization study

Jiayan Liu[1], Hanfei Xu[2], L Adrienne Cupples[2], George T O' Connor[3,4], Ching-Ti Liu[2]
Affiliations expand

- PMID: 37009668
- DOI: 10.1111/ahg.12506

Abstract

Introduction: Observational studies have shown that body mass index (BMI) and waist-to-hip ratio (WHR) are both inversely associated with lung function, as assessed by forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV1). However, observational data are susceptible to confounding and reverse causation.

Methods: We selected genetic instruments based on their relevant large-scale genome-wide association studies. Summary statistics of lung function and asthma came from the UK Biobank and SpiroMeta Consortium meta-analysis (n = 400,102). After examining pleiotropy and removing outliers, we applied inverse-variance weighting to estimate the causal association of BMI and BMI-adjusted WHR (WHRadjBMI) with FVC, FEV1, FEV1/FVC, and asthma. Sensitivity analyses were performed using weighted median, MR-Egger, and MRlap methods.

Results: We found that BMI was inversely associated with FVC (effect estimate, -0.167; 95% confidence interval (CI), -0.203 to -0.130) and FEV1 (effect estimate, -0.111; 95%CI, -0.149 to -0.074). Higher BMI was associated with higher FEV1/FVC (effect estimate, 0.079; 95%CI,

0.049 to 0.110) but was not significantly associated with asthma. WHRadjBMI was inversely associated with FVC (effect estimate, -0.132; 95%CI, -0.180 to -0.084) but has no significant association with FEV1. Higher WHR was associated with higher FEV1/FVC (effect estimate, 0.181; 95%CI, 0.130 to 0.232) and with increased risk of asthma (effect estimate, 0.027; 95%CI, 0.001 to 0.053).

Conclusion: We found significant evidence that increased BMI is suggested to be causally related to decreased FVC and FEV1, and increased BMI-adjusted WHR could lead to lower FVC value and higher risk of asthma. Higher BMI and BMI-adjusted WHR were suggested to be causally associated with higher FEV1/FVC.

- 38 references

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. 2023 Apr 7;212(1):14-28.
doi: 10.1093/cei/uxad031.

Clinical and experimental treatment of allergic asthma with an emphasis on allergen immunotherapy and its mechanisms

Scott Fiala[1], Howard B Fleit[1]

Affiliations expand

- PMID: 36879430

- PMCID: PMC10081111 (available on 2024-03-05)

- DOI: 10.1093/cei/uxad031

Abstract

Allergen immunotherapy (AIT) is currently the only form of treatment that modifies allergic asthma. Pharmacotherapy alone seeks to control the symptoms of allergic asthma, allergic rhinitis, and other atopic conditions. In contrast, AIT can induce long-term physiological modifications through the immune system. AIT enables individuals to live improved lives many years after treatment ends, where they are desensitized to the allergen(s) used or no longer have significant allergic reactions upon allergen provocation. The leading forms of treatment with AIT involve injections of allergen extracts with increasing doses via the subcutaneous route or drops/tablets via the sublingual route for several years. Since the initial attempts at this treatment as early as 1911 by Leonard Noon, the mechanisms by which AIT operates remain unclear. This literature-based review provides the primary care practitioner with a current understanding of the mechanisms of AIT, including its treatment safety, protocols, and long-term efficacy. The primary mechanisms underlying AIT include changes in immunoglobulin classes (IgA, IgE, and IgG), immunosuppressive regulatory T-cell induction, helper T cell type 2 to helper T cell type 1 cell/cytokine profile shifts, decreased early-phase reaction activity and mediators, and increased production of IL-10, IL-35, TGF-β, and IFN-γ. Using the databases PubMed and Embase, a selective literature search was conducted searching for English, full-text, reviews published between 2015 and 2022 using the keywords (with wildcards) "allerg*," "immunotherap*," "mechanis*," and "asthma." Among the cited references, additional references were identified using a manual search.

Keywords: allergen immunotherapy (AIT); allergic asthma; regulatory T (Treg) cell; subcutaneous allergen immunotherapy (SCIT); sublingual allergen immunotherapy (SLIT).

Conflict of interest statement

The authors declare no conflicts of interest to report.

. 2023 Apr 3;36(2):356-359.
doi: 10.3122/jabfm.2022.220292R2. Epub 2023 Feb 17.

Thinking "Green" When Treating "Pink Puffers" and "Blue Bloaters"-Reducing Carbon Footprint When Prescribing Inhalers

Harland T Holman[1], Michael J Bouthillier[2], Frank Müller[2]
Affiliations expand

- PMID: 36801847

- DOI: 10.3122/jabfm.2022.220292R2

Free article

Abstract

The impact of man-made climate change is already affecting millions of people worldwide. The health care sector in the US is a relevant contributor, accounting for about 8 to 10% of national greenhouse gas emissions. This special communication describes the harmful impact of propellant gases in metered dose inhalers (MDI) on the climate and summarizes and discusses current knowledge and recommendations from European countries. Dry powder inhalers (DPI) are a good alternative to MDIs and are available for all inhaler drug classes recommended in current asthma and COPD guidelines. Changing an MDI to PDI can significantly reduce carbon footprints. The majority of the US population is willing to do more to protect the climate. Primary care providers can engage in this by addressing the impacts of drug therapy on climate change in medical decision making.

Keywords: Asthma; COPD; Carbon Dioxide; Carbon Footprint; Climate Change; Drug Prescriptions; Dry Powder Inhalers; Environmental Medicine; Family Medicine; Global Warming; Greenhouse Gases; Metered Dose Inhalers; Norflurane.

Conflict of interest statement

Conflict of interest: None.

supplementary info

MeSH termsexpand

full text links

Review

Med Clin (Barc)
. 2023 Apr 6;160(7):310-317.
doi: 10.1016/j.medcli.2023.01.003. Epub 2023 Feb 9.

Eosinophilic granulomatosis with polyangiitis

[Article in English, Spanish]

Carlos Romero Gómez [1], Halbert Hernández Negrín [2], María Del Mar Ayala Gutiérrez [2]
Affiliations expand

- PMID: 36774291
- DOI: 10.1016/j.medcli.2023.01.003

Abstract

Eosinophilic granulomatosis with polyangiitis (EGPA) is a systemic vasculitis characterized by the presence of asthma associated with eosinophilia, eosinophilic infiltration of different organs, and vasculitis of small and medium-sized vessels. Although classified as anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis, it occurs in less than half of the patients. The disease is infrequent, typically appearing in patients with asthma and affecting multiple organs such as lung, skin and peripheral nervous system. Treatment has been based on the use of glucocorticoids and immunosuppressants. In recent years, progress has been made in the knowledge of the pathophysiology, in treatment with the inclusion of biologic agents, the classification criteria have been revised and new therapeutic recommendations have been published.

Keywords: Eosinofilia; Eosinophilia; Eosinophilic granulomatosis with polyangiitis; Granulomatosis eosinofílica con poliangeítis; Systemic vasculitis; Vasculitis sistémica.

supplementary info

Transl Behav Med

. 2023 Apr 3;13(3):149-155.
doi: 10.1093/tbm/ibac093.

Adapting adaptive design methods to accelerate adoption of a digital asthma management intervention

Bruce G Bender[1], Peter J Cvietusa[2 3], Glenn K Goodrich[2], Diane K King[4], Jo Ann Shoup[2]
Affiliations expand

- PMID: 36689336
- PMCID: PMC10068903 (available on 2024-01-23)
- DOI: 10.1093/tbm/ibac093

Abstract

Investigators conducting translational research in real-world settings may experience changes that create challenges to the successful completion of the trial as well as post-trial adoption and implementation. Adaptive designs support translational research by systematically adapting content and methods to meet the needs of target populations, settings and contexts. This manuscript describes an adaptive implementation research model that provides strategies for changing content, delivery processes, and research methods to correct course when anticipated and unanticipated circumstances occur during a pragmatic trial. The Breathewell Program included two large pragmatic trials of the effectiveness of a digital communication technology intervention to improve symptom management and medication adherence in asthma care. The first trial targeted parents of children with asthma; the second targeted adults with asthma. Adaptations were made iteratively to adjust to dynamic conditions within the healthcare setting, informed by

prospectively collected stakeholder input, and were categorized retrospectively by the authors as proactive or reactive. Study outcomes demonstrated improved treatment adherence and clinical efficiency. Kaiser Permanente Colorado, the setting for both studies, adopted the speech recognition intervention into routine care, however, both interventions required numerous adaptations, including changes to target population, intervention content, and internal workflows. Proactive and reactive adaptations assured that both trials were successfully completed. Adaptive research designs will continue to provide an important pathway to move healthcare delivery research into practice while conducting ongoing effectiveness evaluation.

Trial registration: ClinicalTrials.gov NCT00958932 NCT02761837.

Keywords: Adaptive implementation research; Asthma; Pragmatic trials.

Plain language summary

Health care research often moves slowly and consequently important results may take a long time to reach the patients they are intended to help. Implementation studies conducted in routine clinical practice are intended to accelerate the process of delivering new discoveries into settings where they can be more quickly put to use. However, conducting research in real-world settings can be challenging if changes occur in those settings during the course of the study. Therefore, an adaptive implementation approach that allows researchers to make changes during the course of a study can facilitate study completion and improve likelihood of intervention adoption into routine care. This report demonstrates the use of an adaptive implementation model in two large studies of asthma in children and adults. In both studies, communication technology including computerized phone calls, texts, and email helped improve treatment consistency and efficiency.

. 2023 Apr 3;61(4):2201231.
doi: 10.1183/13993003.01231-2022. Print 2023 Apr.

Identifying and appraising outcome measures for severe asthma: a systematic review

Anna Rattu[1], Ekaterina Khaleva[1], Chris Brightling[2], Sven-Erik Dahlén[3,4], Apostolos Bossios[4], Louise Fleming[5], Kian Fan Chung[5], Erik Melén[6], Ratko Djukanovic[1,7], Rekha Chaudhuri[8], Andrew Exley[9], Gerard H Koppelman[10,11], Arnaud Bourdin[12], Franca Rusconi[13], Celeste Porsbjerg[13], Courtney Coleman[14], Clare Williams[14], Hanna Nielsen[15,16], Elizabeth Davin[16], Phil Taverner[16], Sofia Romagosa Vilarnau[17], Graham Roberts[18,7,19]; 3TR Consortium Respiratory Work Package
Affiliations expand

- PMID: 36549712

- DOI: 10.1183/13993003.01231-2022

Abstract

Background: Valid outcome measures are imperative to evaluate treatment response, yet the suitability of existing end-points for severe asthma is unclear. This review aimed to identify outcome measures for severe asthma and appraise the quality of their measurement properties.

Methods: A literature search was performed to identify "candidate" outcome measures published between 2018 and 2020. A modified Delphi exercise was conducted to select "key" outcome measures within healthcare professional, patient, pharmaceutical and regulatory stakeholder groups. Initial validation studies for "key" measures were rated against modified quality criteria from COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN). The evidence was discussed at multi-stakeholder meetings to ratify "priority" outcome measures. Subsequently, four bibliographic databases were searched from inception to 20 July 2020 to identify development and validation studies for these end-points. Two reviewers screened records, extracted data, assessed their methodological quality and graded the evidence according to COSMIN.

Results: 96 outcome measures were identified as "candidates", 55 as "key" and 24 as "priority" for severe asthma, including clinical, healthcare utilisation, quality of life, asthma control and composite. 32 studies reported measurement properties of 17 "priority" end-points from the latter three domains. Only the Severe Asthma Questionnaire and Childhood Asthma Control Test were developed with input from severe asthma patients.

The certainty of evidence was "low" to "very low" for most "priority" end-points across all measurement properties and none fulfilled all quality standards.

Conclusions: Only two outcome measures had robust developmental data for severe asthma. This review informed development of core outcome measures sets for severe asthma.

Conflict of interest statement

Conflict of interest: A. Rattu and E. Khaleva declare funding from the European Commission's Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement number 831434 (3TR) for this manuscript. C. Brightling declares grants from GlaxoSmithKline, AstraZeneca, Novartis, Chiesi, Boehringer Ingelheim, Genentech, Roche, Sanofi, Mologic and 4DPharma, consulting fees from GlaxoSmithKline, AstraZeneca, Novartis, Chiesi, Boehringer Ingelheim, Genentech, Roche, Sanofi, Mologic, 4DPharma and Teva, and support from the 3TR project. S-E. Dahlén declares a 3TR IMI grant, consulting fees from AstraZeneca, Cayman Co., GlaxoSmithKline, Novartis, Regeneron, Sanofi and Teva, and payment for lectures from AstraZeneca and Sanofi. A. Bossios declares honoraria for lectures from GlaxoSmithKline, AstraZeneca, Teva and Novartis, support for attending meetings from AstraZeneca and Novartis, honoraria for advisory board meetings from GlaxoSmithKline, AstraZeneca, Teva, Novartis and Sanofi, and being a member of the Steering Committee of SHARP, Secretary of Assembly 5 (Airway Diseases, Asthma, COPD and Chronic Cough) of the European Respiratory Society, and Vice-chair of the Nordic Severe Asthma Network (NSAN). L. Fleming declares participation in advisory boards and honoraria for lectures from Sanofi, Respiri UK, AstraZeneca, Novartis and Teva, outside the submitted work; all payments were made to her institution. K.F. Chung has received honoraria for participating in advisory board meetings of GlaxoSmithKline, AstraZeneca, Roche, Novartis, Merck and Shionogi regarding treatments for asthma, COPD and chronic cough, and has also been remunerated for speaking engagements for Novartis and AstraZeneca; has received an MRC grant on precision medicine for severe asthma, an EPSRC grant on air pollution and asthma, and a GlaxoSmithKline grant on mepolizumab and eosinophils in asthma. E. Melén declares consulting fees from AstraZeneca, Chiesi, Novartis and Sanofi, outside the submitted work. R. Chaudhuri has received lecture fees from GlaxoSmithKline, AstraZeneca, Teva, Chiesi, Sanofi and Novartis, honoraria for advisory board meetings from GlaxoSmithKline, AstraZeneca, Teva, Chiesi and Novartis, sponsorship to attend international scientific meetings from Chiesi, Napp, Sanofi and GlaxoSmithKline, and a research grant to her institute from AstraZeneca for a UK multicentre study. R. Djukanovic declares funding from the European Respiratory Society, Teva, GlaxoSmithKline, Novartis, Sanofi and Chiesi for the SHARP CRC, consulting fees for Synairgen, honorarium for a lecture from GlaxoSmithKline, participation on a data safety monitoring board or advisory board for Kymab (Cambridge), and shares in Synairgen, outside the submitted work. A. Exley declares being a minority shareholder in GlaxoSmithKline PLC. G.H. Koppelman reports receiving research grants from the Lung

Foundation of the Netherlands, Ubbo Emmius Foundation, H2020 European Union, Teva, GlaxoSmithKline and Vertex, outside this work (money to institution); he reports memberships of advisory boards to GlaxoSmithKline and PURE-IMS, outside this work (money to institution). A. Bourdin declares unrestricted grants from AstraZeneca and Boehringer Ingelheim to his institute; consulting fees, honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events, and support for attending meetings and travel from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Novartis and Sanofi; participation on a data safety monitoring board or advisory board for AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Novartis, Sanofi and Abs science. C. Porsbjerg declares grants (paid to institution), consulting fees (paid to institution and personal honoraria) and honoraria for lectures (paid to institution and personal honoraria) from AstraZeneca, GlaxoSmithKline, Novartis, Teva, Sanofi, Chiesi and ALK; participation on an advisory board (paid to institution and personal honoraria) for AstraZeneca, Novartis, Teva, Sanofi and ALK. C. Coleman and C. Williams declare funding received to support this work by the European Lung Foundation (ELF) from the European Commission's Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement number 831434 (3TR), and are employees of the ELF. E. Davin bought and sold shares on the public market during 2021–2022 in Regeneron, Roche and ICON Plc, and declares no current holdings. P. Taverner declares honorarium for being a lay member of Asthma and Lung UK's research funding panel, and chairing a Patient and Community Oversight Group for two NIHR health protection research units on environmental and chemical hazards; and payment for chairing a NICE guideline committee on advocacy services. S. Romagosa Vilarnau declares unrestricted educational grants paid to the organisation from Novartis, Pfizer, AstraZeneca, Chiesi Farmaceutici, GlaxoSmithKline, AbbVie, LeoPharma, Boehringer Ingelheim, Sanofi, Regeneron, OM Pharma, MSD, Roche and DBV Technologies. G. Roberts declares EU IMI funding and consulting fees from AstraZeneca paid to his institution. No other author has any conflict of interest to declare.

. 2023 Apr 3;61(4):2200606.
doi: 10.1183/13993003.00606-2022. Print 2023 Apr.

Development of Core Outcome Measures sets for paediatric and adult Severe Asthma (COMSA)

Ekaterina Khaleva[1], Anna Rattu[1], Chris Brightling[2], Andrew Bush[3], Apostolos Bossios[4], Arnaud Bourdin[5], Kian Fan Chung[6], Rekha Chaudhuri[7], Courtney Coleman[8], Sven-Erik Dahlén[4], Ratko Djukanovic[1 9], Antoine Deschildre[10 11], Louise Fleming[6], Stephen J Fowler[12], Atul Gupta[13], Eckard Hamelmann[14], Simone Hashimoto[15 16], Gunilla Hedlin[17], Gerard H Koppelman[18 19], Erik Melén[20], Clare S Murray[12], Charles Pilette[21], Celeste Porsbjerg[22], Katharine C Pike[23], Franca Rusconi[24], Clare Williams[8], Birgit Ahrens[25], Peter Alter[26], Freja Anckers[27], Maarten van den Berge[19 28], Katharina Blumchen[29], Guy Brusselle[30], Graham W Clarke[31], Danen Cunoosamy[32], Barbro Dahlén[4], Piers Dixey[6 33], Andrew Exley[34], Urs Frey[35], Erol A Gaillard[36], Lisa Giovannini-Chami[37 38], Jonathan Grigg[39], Diana Hartenstein[25], Liam G Heaney[40], Bülent Karadag[41], Susanne Kaul[25], Inger Kull[20], Amelia Licari[42], Anke H Maitland-van der Zee[15 16], Vera Mahler[25], Ann-Marie M Schoos[43 44], Prasad Nagakumar[45 46], Jenny Negus[27], Hanna Nielsen[27 47], James Paton[48], Mariëlle Pijnenburg[49], Valeria Ramiconi[50], Sofia Romagosa Vilarnau[50], Stefania Principe[16 51], Niels Rutjes[15], Sejal Saglani[6], Paul Seddon[52], Florian Singer[53 54], Heribert Staudinger[55], Steve Turner[56 57], Susanne Vijverberg[15 16], Tonya Winders[58 59], Valentyna Yasinska[4], Graham Roberts[1 9 60]; COMSA Working Group in the 3TR Consortium

Affiliations expand

- PMID: 36229046

- PMCID: PMC10069873

- DOI: 10.1183/13993003.00606-2022

Free PMC article

Abstract

Background: Effectiveness studies with biological therapies for asthma lack standardised outcome measures. The COMSA (Core Outcome Measures sets for paediatric and adult Severe Asthma) Working Group sought to develop Core Outcome Measures (COM) sets to facilitate better synthesis of data and appraisal of biologics in paediatric and adult asthma clinical studies.

Methods: COMSA utilised a multi-stakeholder consensus process among patients with severe asthma, adult and paediatric clinicians, pharmaceutical representatives, and health

regulators from across Europe. Evidence included a systematic review of development, validity and reliability of selected outcome measures plus a narrative review and a pan-European survey to better understand patients' and carers' views about outcome measures. It was discussed using a modified GRADE (Grading of Recommendations Assessment, Development and Evaluation) Evidence to Decision framework. Anonymous voting was conducted using predefined consensus criteria.

Results: Both adult and paediatric COM sets include forced expiratory volume in 1 s (FEV_1) as z-scores, annual frequency of severe exacerbations and maintenance oral corticosteroid use. Additionally, the paediatric COM set includes the Paediatric Asthma Quality of Life Questionnaire and Asthma Control Test or Childhood Asthma Control Test, while the adult COM set includes the Severe Asthma Questionnaire and Asthma Control Questionnaire-6 (symptoms and rescue medication use reported separately).

Conclusions: This patient-centred collaboration has produced two COM sets for paediatric and adult severe asthma. It is expected that they will inform the methodology of future clinical trials, enhance comparability of efficacy and effectiveness of biological therapies, and help assess their socioeconomic value. COMSA will inform definitions of non-response and response to biological therapy for severe asthma.

Conflict of interest statement

Conflict of interest: E. Khaleva and A. Rattu declare funding from 3TR European Union Innovative Medicines Initiative 2 to their institution for the present manuscript. C. Brightling declares grants from GlaxoSmithKline, AstraZeneca, Novartis, Chiesi, Boehringer Ingelheim, Genentech, Roche, Sanofi, Mologic and 4DPharma; consulting fees from GlaxoSmithKline, AstraZeneca, Novartis, Chiesi, Boehringer Ingelheim, Genentech, Roche, Sanofi, Mologic, 4DPharma and Teva; and support from the 3TR project. G.W. Clarke declares that he is an employee of AstraZeneca; and that he holds stock or stock options in AstraZeneca. M. van den Berge declares grants from GlaxoSmithKline, AstraZeneca, Roche, Genentech and Novartis paid to the university. A. Bossios declares honoraria for lectures from GlaxoSmithKline, AstraZeneca, Teva and Novartis; support for attending meetings from AstraZeneca and Novartis; honoraria for advisory board meetings from GlaxoSmithKline, AstraZeneca, Teva, Novartis and Sanofi; being a member of the Steering Committee of SHARP, Secretary of Assembly 5 (Airway Diseases, Asthma, COPD and Chronic Cough) of the European Respiratory Society; Vice-chair of the Nordic Severe Asthma Network (NSAN). V. Ramiconi and S. Romagosa Vilarnau declare unrestricted educational grants paid to the organisation from Novartis, Pfizer, AstraZeneca, Chiesi Farmaceutici, GlaxoSmithKline, AbbVie, LeoPharma, Boehringer Ingelheim, Sanofi, Regeneron, OM Pharma, MSD, Roche and DBV Technologies; support for attending meetings from Novartis. S-E. Dahlén declares a 3TR Innovative Medicines Initiative grant; consulting fees for AstraZeneca, Cayman Co., GlaxoSmithKline, Novartis, Regeneron, Sanofi and Teva; payment for lectures from AstraZeneca and Sanofi. S. Principe declares support for provision of study materials and medical writing. G. Hedlin declares participation in

advisory boards of AstraZeneca and Sanofi. F. Singer reports grants from Lung League Bern, grants from the Swiss Cystic Fibrosis Society (CFCH), personal fees from Vertex Pharmaceuticals, personal fees from Novartis, outside the submitted work. A. Deschildre reports personal consulting fees from Sanofi-Regeneron, ALK, Novartis and GlaxoSmithKline; honoraria for lectures from ALK, Boehringer Ingelheim and Novartis; support for attending meetings from AstraZeneca, Stallergènes-Greer, MEDA, Nutricia, Sanofi and Novartis, outside the submitted work; and being on the scientific committee of SFA (Société Française d'Allergologie). L.J. Fleming declares participation in advisory boards and honoraria for lectures from Sanofi, Respiri UK, AstraZeneca, Novartis and Teva, outside of the scope of this publication; all payments were made to her institution. H. Staudinger reports that he is a salaried employee of Sanofi Genzyme and owns company stock of Sanofi and Merck & Co. K.C. Pike declares consultancy fees from Novartis, Adherium and Respiri, and honoraria for a lecture from Novartis. J. Grigg declares payments from GlaxoSmithKline, OM Pharma, Omron and Novartis (advisory boards), Sanofi (for lectures) and AstraZeneca (CI clinical trial). N. Rutjes reports personal fees for advisory board work from Sanofi. G.H. Koppelman reports receiving research grants from the Lung Foundation of the Netherlands, Ubbo Emmius Foundation, H2020 European Union, Teva, GlaxoSmithKline and Vertex, outside this work (money to institution); he reports memberships of advisory boards to GlaxoSmithKline and PURE-IMS, outside this work (money to institution). D. Cunoosamy holds shares in AstraZeneca and Sanofi. A.H. Maitland-van der Zee has received research grants outside the submitted work from GlaxoSmithKline, Boehringer Ingelheim and Vertex, she is the PI of a P4O2 (Precision Medicine for more Oxygen) public private partnership sponsored by Health Holland involving many private partners that contribute in cash and/or in kind (Boehringer Ingelheim, Breathomix, Fluidda, Ortec Logiqcare, Philips, Quantib-U, Roche, Smartfish, SODAQ, Thirona, TopMD and Novartis), and she has served in advisory boards for AstraZeneca, GlaxoSmithKline and Boehringer Ingelheim with money paid to her institution. K.F. Chung has received honoraria for participating in advisory board meetings of GlaxoSmithKline, AstraZeneca, Roche, Novartis, Merck and Shionogi, regarding treatments for asthma, COPD and chronic cough, and has also been remunerated for speaking engagements for Novartis and AstraZeneca; received a MRC grant on Precision Medicine for severe asthma, EPSRC grant on air pollution and asthma, and a GlaxoSmithKline grant on mepolizumab and eosinophils in asthma. P. Nagakumar received speaker fees for talks on severe asthma from GlaxoSmithKline and Novartis. G. Brusselle declares payments from AstraZeneca, Novartis, Boehringer Ingelheim, Chiesi, Sanofi, GlaxoSmithKline and MSD, outside the submitted work. E. Hamelmann declares support from the German Ministry of Education and Research (BMBF) and German Asthma Net (GAN) eV; funding for research in severe asthma in children (CHAMP-01GL1742D) and for Severe Asthma Register. S. Vijverberg is PI of the PERMEABLE consortium. The PERMEABLE consortium is a research consortium focused on severe asthma and allergy and supported by ZonMW (456008004), the Swedish Research Council (2018-05619), the Ministry of Education, Science and Sport of the Republic of Slovenia (C3330-19-252012), and the German Ministry of Education and Research (BMBF) FKZ01KU1909A), under the frame of the ERA PerMed JTC 2018 Call. In addition, S. Vijverberg has received research funding for

a project on severe paediatric asthma from the Lung Foundation Netherlands (6.2.18.244JO). A-M.M. Schoos has participated on an advisory board for ALK. B. Dahlén reports personal fees for lectures from AstraZeneca, Novartis and Sanofi; and grants from Novartis and GlaxoSmithKline, outside the submitted work; participation on an advisory board for AstraZeneca and Sanofi. A. Exley declares being a minority shareholder in GlaxoSmithKline Plc. E.A. Gaillard reports consultancy work for Boehringer Ingelheim with money paid to the institution (University of Leicester); investigator-led research grants from Circassia Group, Gilead Sciences, Chiesi Limited and Propeller Health; and has a research collaboration with Medimmune. M. Pijnenburg declares payments to her institution from Sanofi Genzyme (advisory work) and Novartis (speakers fee). E. Melén declares consulting fees from AstraZeneca, Chiesi, Novartis and Sanofi, outside the submitted work. R. Chaudhuri has received lecture fees from GlaxoSmithKline, AstraZeneca, Teva, Chiesi, Sanofi and Novartis; honoraria for advisory board meetings from GlaxoSmithKline, AstraZeneca, Teva, Chiesi and Novartis; sponsorship to attend international scientific meetings from Chiesi, Napp, Sanofi and GlaxoSmithKline, and a research grant to her institute from AstraZeneca for a UK multi-centre study. C. Pilette declares grants, consulting fees and honoraria for lectures (paid to institution) from AstraZeneca, Chiesi, GlaxoSmithKline, Novartis, Mundipharma, Teva, Sanofi and ALK. C. Porsbjerg declares grants (paid to institution), consulting fees (paid to institution and personal honoraria) and honoraria for lectures (paid to institution and personal honoraria) from AstraZeneca, GlaxoSmithKline, Novartis, Teva, Sanofi, Chiesi and ALK; participation on an advisory board (paid to institution and personal honoraria) for AstraZeneca, Novartis, Teva, Sanofi and ALK. C. Coleman and C. Williams declare funding received to support this work by the European Lung Foundation (ELF) from the European Commission's Innovative Medicines Initiative 2 Joint Undertaking under grant agreement number 831434 (3TR), and are employees of the ELF. B. Ahrens, S. Kaul, D. Hartenstein and V. Mahler declare no conflict of interest for this article and state that the views expressed in this review are the personal views of the author and may not be understood or quoted as being made on behalf of or reflecting the position of the respective national competent authorities, the European Medicines Agency or one of its committees or working parties. L.G. Heaney declares support from the 3TR; grants from industrial pharma partners Amgen, AstraZeneca, Medimmune, Janssen, Novartis, Roche/Genentech, GlaxoSmithKline and Boehringer Ingelheim; project grant funding from Medimmune, Novartis UK, Roche/Genentech and GlaxoSmithKline, outside the submitted work; payments for lectures by AstraZeneca, Novartis, Roche/Genentech, GlaxoSmithKline, Chiesi and Teva, outside the submitted work; travel funding support to international respiratory meetings by AstraZeneca, Chiesi, Novartis, Boehringer Ingelheim, Teva and GlaxoSmithKline, outside the submitted work; advisory boards for AstraZeneca, Novartis, GlaxoSmithKline, Chiesi, Teva, Theravance and Vectura, outside the submitted work. R. Djukanovic declares funding from the European Respiratory Society, Teva, GlaxoSmithKline, Novartis, Sanofi and Chiesi for the SHARP Clinical Research Collaboration; consulting fees for Synairgen; honorarium for a lecture from GlaxoSmithKline; participation on a data safety monitoring board or advisory board for Kymab (Cambridge) and shares in Synairgen outside of the submitted work. A. Bourdin declares grants from Boehringer and AstraZeneca; consulting fees and payments

from Boehringer, AstraZeneca, GlaxoSmithKline, Novartis, Chiesi, Regeneron, Sanofi and Amgen outside of the submitted work. B. Karadag declares participation in a trial conducted by Sanofi (payment to institution) and attending advisory board meetings for GlaxoSmithKline (personal fees). K. Blumchen declares grants from Aimmune Therapeutics, DBV Technologies and Hipp GmbH; consulting fees from Aimmune Therapeutics, DBV Technologies and Allergy Therapeutics; payments for lectures from Aimmune Therapeutics, DBV Technologies, Novartis, Allergy Therapeutics, HAL, ALK, Allergopharma, Nutricia, Thermo Fisher Scientific, and Bausch and Lomb; personal fees for expert discussions from Novartis and Nestle; fees for attending meetings from Aimmune Therapeutics and DBV Technologies; being on data safety monitoring board of Charité, IIT. A. Gupta received speaker/advisory board fees from GlaxoSmithKline, Novartis, AstraZeneca and Boehringer Ingelheim; received research grants from GlaxoSmithKline, Novartis, AstraZeneca and Boehringer Ingelheim, paid to institution. L. Giovannini-Chami declares consulting fees from ALK, AstraZeneca and Novartis; honoraria for lectures, presentations from Novartis, ALK, Stallergènes, Sanofi and AstraZeneca; support for attending meetings from Stallergènes; participation on a data safety monitoring board or advisory board for Sanofi; being head of the Scientific Committee of the French Pediatric Pulmonology and Allergology Society. C.S. Murray has received lecture fees from GlaxoSmithKline and Novartis; received grants from Asthma UK and National Institute for Health Research; and has participated on an advisory board for Boehringer Ingelheim. G. Roberts declares European Union Innovative Medicines Initiative funding and AstraZeneca paid to the institution. Other co-authors declare no conflicts of interest for this article.

Comment in

- Defining the questions to be asked in severe asthma trials: data from the COMSA working group.
  Eiwegger T, Bendien SA.Eur Respir J. 2023 Apr 3;61(4):2202058. doi: 10.1183/13993003.02058-2022. Print 2023 Apr.PMID: 37012083 No abstract available.
- Cited by 1 article
- 76 references
- 5 figures

supplementary info

Publication types, MeSH terms, Substances, Grant supportexpand

full text links

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

Eur Arch Otorhinolaryngol
.
. 2023 Apr 5.
doi: 10.1007/s00405-023-07955-5. Online ahead of print.

Therapeutic management of allergic rhinitis: a survey of otolaryngology and allergology specialists

Carlos Colás[1], María Elena Álvarez-Suárez[2], Laura Benedito-Palos[3], Isam Alobid[4]
Affiliations expand

- PMID: 37020046
- DOI: 10.1007/s00405-023-07955-5

Abstract

Purpose: To describe the current management of allergic rhinitis (AR) in Spain's specialized care according to the next-generation ARIA guidelines.

Methods: An ad hoc online survey was distributed to AR specialists to appraise their perceptions of pathology management, knowledge of next-generation ARIA guidelines (including four case clinics), and their views on the principal barriers and the actions to proper AR management.

Results: one hundred nine specialists (38.5% allergists and 61.5% otolaryngologists) completed the study survey. Most respondents (87.2%) had read all or part of the Next-Generation ARIA Guidelines, and 81.6% stated that they considered the patient's treatment choice preferences. However, only 20.2% of specialists answered according to the recommendations in at least three of the four case clinics. Most participants failed to fulfill the treatment duration according to the guidelines. They regarded the lack of multidisciplinary teams (21.7%) and the lack of patients' AR treatment adherence (30.6%) as the most critical healthcare system- and patient-related barriers to the correct management of AR, respectively. Promoting patients' education was considered the most crucial action to improve it.

Conclusion: Despite specialists' awareness, there is a gap between the evidence-based guidelines' recommendations and their implementation in clinical practice.

Keywords: Adherence; Allergic rhinitis; Clinical practice; Next-generation ARIA guidelines.

2
Rev Med Suisse
.
. 2023 Apr 5;19(821):658-662.
doi: 10.53738/REVMED.2023.19.821.658.

[Update on allergenic immunotherapy for asthma and rhinoconjunctivitis]

[Article in French]

Camille Beniada[1], Sophie Vandenberghe-Dürr[1]
Affiliations expand

- PMID: 37017346

- DOI: 10.53738/REVMED.2023.19.821.658

Abstract

in English, French

Allergenic immunotherapy consists of repeated administration of allergenic extracts to which an individual is allergic. It is currently the only treatment that modifies the course of allergic disease and induces short- as well as long-term remission of symptoms. Two formulations are currently available: subcutaneous immunotherapy (SCIT) or sublingual immunotherapy (SLIT), with comparable efficacy. In specific situations, it can be used in combination with the new approved biologic therapies for asthma to improve tolerance of immunotherapy.

Conflict of interest statement

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

Laryngoscope
.
. 2023 Apr 5.
doi: 10.1002/lary.30685. Online ahead of print.

The Long-Term Implications of Rhinitis and Chronic Rhinosinusitis in Young Adults

Yoni Shopen[1,2], Nir Tsur[1,2,3], Ethan Soudry[1,2]
Affiliations expand

- PMID: 37017253
- DOI: 10.1002/lary.30685

Abstract

Background: The long-term impact of rhinitis and chronic rhinosinusitis (CRS) on general health and medical services utilization in young adults have been limitedly studied.

Methods: A case-control study in the Israeli Defense Forces, between the years 2005 and 2019, of all individuals with either rhinitis or CRS and a matched cohort of healthy individuals with a minimum of 5 years of consecutive follow-up.

Results: The study groups included 617 patients with rhinitis and 296 patients with CRS and 2739 healthy controls with an average age of 28 years. During a mean follow-up of 8 years, a significant fraction of patients in both study groups were diagnosed with asthma compared to the control group, (26.1% and 23.3% vs. 3.7%, respectively; CI 95%: 12.1%-14.9%, $p < 0.0001$). 7.6% of patients with rhinitis developed CRS. Significantly increased loss of productivity and medical system utilization were noted in the study groups compared to controls ($p < 0.0001$). Moreover, deterioration in general health, manifested as loss of physical fitness for combative service was observed in a third of patients during follow-up.

Conclusions: Rhinitis and CRS significantly impact productivity and medical service utilization in young adults, as well as general health associated with development of asthma and impairment of physical fitness. A minority of rhinitis patients develop CRS overtime, further affecting this patient group. These patients should be followed up and managed to improve disease control and associated outcomes.

Level of evidence: 3 Laryngoscope, 2023.

Keywords: asthma; chronic rhinitis; chronic rhinosinusitis; health-care burden; productivity; young adults.

- 16 references

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Clin Respir J

. 2023 Apr 4.
doi: 10.1111/crj.13608. Online ahead of print.

Health-related quality of life in asthma measured by the World Health Organization brief questionnaire (WHO-BREF) and the effect of concomitant allergic rhinitis-A population-based study

Obianuju B Ozoh[1,2], Sunday A Aderibigbe[3], Adaeze C Ayuk[4,5], Sandra K Dede[2], Eruke Egbagbe[6], Musa Babashani[7]
Affiliations expand

- PMID: 37016072

- DOI: 10.1111/crj.13608

Abstract

Background and objective: The impact of allergic rhinitis (AR), a common comorbidity in asthma, on global quality of life (QoL) using generic QoL questionnaires has not been extensively evaluated.

Methods: This was a cross-sectional population-based study among adults ≥18 years old. Generic QoL was measured using the World Health Organization (WHO) questionnaire (WHOQOL-BREF), and asthma control was assessed using the Asthma Control Test. Participants were categorized into four groups: Group 1 (No asthma, no AR), Group 2 (Asthma only), Group 3 (AR only) and Group 4 (Concomitant asthma and AR). The student t-test or the ANOVA was used for comparison between groups and based on the level of asthma control. Linear regression was used to

assess the association between the level of asthma control and QoL scores, adjusted for age and sex. A p-value of less than 0.05 was considered significant for all associations.

Results: There were 9115 participants; 906 (9.9%) had asthma, and 1998 (21.9%) had AR. The lowest QoL scores were in the environment domain. Mean QoL scores were significantly lower in asthma compared to 'no asthma' and in AR compared to 'no AR'. Either asthma or rhinitis (Group 2 or 3) had significantly lower scores compared to no disease (Group 1) only in the environment domain, but the concomitant disease (Group 4) had lower scores across all categories and domains. Scores were significantly lower for uncontrolled asthma compared to controlled asthma and for 'concomitant asthma and AR' compared to 'asthma only'. Increasing age and uncontrolled asthma predicted worse health-related quality of life (HRQoL) consistently.

Conclusion: Although asthma and AR negatively impact HRQoL independently, concomitant asthma and AR are worse. Uncontrolled asthma underpins poor QoL in asthma because QoL is not impaired in controlled disease. This underscores the need for recognition and treatment of AR in asthma and reinforces the benefits of achieving asthma control as a priority in asthma treatment.

Keywords: WHO-BREF; allergic rhinitis; asthma; quality of life.

- 34 references

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BMJ Open

. 2023 Apr 4;13(4):e067271.
doi: 10.1136/bmjopen-2022-067271.

Investigating the effect of early life antibiotic use on asthma and allergy risk in over 600 000 Canadian children: a protocol for a retrospective cohort study in British Columbia and Manitoba

Hannah Lishman[1,2], Nathan C Nickel[3,4,5], Hind Sbihi[6,2], Max Xie[2], Abdullah Mamun[2], Bei Yuan Zhang[7], Caren Rose[6,2], Patricia Janssen[6], Ashley Roberts[8,9], Meghan B Azad[3,5,10], Stuart Turvey[8,9], David M Patrick[6,2]
Affiliations expand

- PMID: 37015798

- DOI: 10.1136/bmjopen-2022-067271

Free article

Abstract

Introduction: Allergic conditions, such as asthma, hay fever and eczema, are some of the most common conditions impacting children globally. There is a strong incentive to study their determinants to improve their prevention. Asthma, hay fever and eczema are influenced through the same immunological pathway and often copresent in children ('the atopic march'). Increasing evidence shows a link between infant antibiotic use and the risk of childhood atopic conditions, mediated through gut microbial dysbiosis during immune system maturation, however, the potential for confounding remains. This study will investigate the relationship between infant antibiotic use and risk of allergic conditions in British Columbian and Manitoban children born over 10 years, adjusting for relevant confounders.

Methods and analysis: Provincial administrative datasets will be linked to perform comparable retrospective cohort analyses, using Population Data BC and the Manitoba Population Research Data Repository. All infants born between 2001 and 2011 in BC and Manitoba will be included (approximately 460 000 and 162 500 infants, respectively), following up to age 7. Multivariable logistic regression will determine the outcome risk by the fifth birthday among children who did and did not receive antibiotics before their first birthday. Clinical, demographic and environmental covariates will be explored, and sensitivity analyses performed to reduce confounding by indication.

Ethics and dissemination: The University of British Columbia Research Ethics Board (H19-03255) and University of Manitoba Ethics Board (HS25156 (H2021:328)) have approved this study. Data stewardship committees for all administrative datasets have granted permissions, facilitated by Population Data BC and the Manitoba Centre for Health Policy. Permissions from the Canadian Health Infant Longitudinal Development Study are being sought for breastfeeding data (CP185). Findings will be published in scientific journals and presented at infectious disease and respiratory health conferences. A stakeholder committee will guide and enhance sensitive and impactful communication of the findings to new parents.

Keywords: Allergy; Asthma; Community child health; EPIDEMIOLOGY; THERAPEUTICS.

Conflict of interest statement

Competing interests: None declared.

supplementary info

Publication types, MeSH terms, Substancesexpand

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Clin Exp Allergy
.
2023 Apr 4.
doi: 10.1111/cea.14307. Online ahead of print.

Intralymphatic immunotherapy with birch and grass pollen extracts. A randomized double-blind placebo-controlled clinical trial

Lars Ahlbeck[1,2], Emelie Ahlberg[2], Linn Stuivers[2], Janne Björkander[3], Ulla Nyström[1], Pavlos Retsas[1], Dhanapal Govindaraj[2], Maria C Jenmalm[2], Karel Duchén[1,4]
Affiliations expand

- PMID: 37013723

- DOI: 10.1111/cea.14307

Abstract

Introduction: There is a need to evaluate the safety and efficacy of intralymphatic immunotherapy (ILIT) for inducing tolerance in patients with allergic rhinitis.

Methods: Thirty-seven patients with seasonal allergic symptoms to birch and grass pollen and skin prick test >3 mm and/or IgE to birch and timothy >0.35 kU/L were randomized to either ILIT, with three doses of 0.1 mL of birch pollen and 5-grass pollen allergen extracts on aluminium hydroxide (10,000 SQ-U/ml; ALK-Abelló) or placebo using ultrasound-guided intralymphatic injections at monthly intervals. Daily combined symptom medical score and rhinoconjunctivitis total symptom score were recorded during the peak pollen seasons the year before and after treatment. Rhinoconjunctivitis total symptom score, medication score and rhinoconjunctivitis quality of life questionnaire were recorded annually starting 2 years after treatment. Circulating proportions of T helper cell subsets and allergen-induced cytokine and chemokine production were analysed using flow cytometry and ELISA.

Results: There were no differences between the groups related to daily combined symptom medical score the year before and after treatment. Two years after ILIT (after unblinding), the actively treated group reported significantly fewer symptoms, lower medication use and improved quality of life than did the placebo group. After the pollen seasons the year after ILIT, T regulatory cell frequencies and grass-induced IFN-γ levels increased only in the actively treated group.

Conclusion: In this randomized controlled trial, ILIT with birch and grass pollen extract was safe and accompanied by immunological changes. Further studies are required to confirm or refute the efficacy of the treatment.

Keywords: allergy; hypersensitivity; intralymphatic immunotherapy; rhinoconjunctivitis.

- 37 references

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Clin Exp Allergy

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-
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. 2023 Apr 3.
doi: 10.1111/cea.14310. Online ahead of print.

Thermo-SPT: A new skin prick test evaluation framework based on low-cost, portable smartphone thermography

Polat Goktas[1,2,3], Ozge Can Bostan[4], Duygu Gulseren[5], Mehmet Erdem Cakmak[4], Saltuk Bugra Kaya[4], Ebru Damadoglu[4], Gul Karakaya[4], Ali Fuat Kalyoncu[4]

Affiliations expand

- PMID: 37013254

- DOI: 10.1111/cea.14310

Abstract

Background: Although the skin prick test (SPT) is a reliable procedure to confirm IgE-dependent allergic sensitization in patients, the interpretation of the test is still performed manually, resulting in an error-prone procedure for the diagnosis of allergic diseases.

Objective: To design and implement an innovative SPT evaluation framework using a low-cost, portable smartphone thermography, named Thermo-SPT, to significantly improve the accuracy and reliability of SPT outcomes.

Methods: Thermographical images were captured every 60 s for a duration of 0 to 15 min using the FLIR One app, and then analysed with the FLIR Tool® . The definition of 'Skin Sensitization Region' area was introduced to analyse the time-lapse thermal changes in skin reactions over several time periods during the SPT. The Allergic Sensitization Index (ASI) and Min-Max Scaler Index (MMS) formulae were also developed to optimize the identification of the peak allergic response time point through the thermal assessment (TA) of allergic rhinitis patients.

Results: In these experimental trials, a statistically significant increase in temperature was detected from the fifth minute of TA for all tested aeroallergens (all p$\hat{\square}$ values <.001<.001). An increase was observed in the number of false-positive cases, where patients with clinical symptoms not consistent with SPT were evaluated as positive on TA assessment, specifically for patients diagnosed with Phleum pratense and Dermatophagoides pteronyssinus. Our proposed technique, the MMS, has demonstrated improved accuracy in identifying P. pratense and D. pteronyssinus compared with other SPT evaluation metrics, specifically starting from the fifth minute. For patients diagnosed with Cat epithelium, although not statistically significant initially, an increasing trend was determined in the results at the 15 min (ΔT (T_{15} - T_0), p=.07$\hat{\square}$=.07 ; ASI_{T15} , p<.001$\hat{\square}$<.001).

Conclusions: This proposed SPT evaluation framework utilizing a low-cost, smartphone-based thermographical imaging technique can enhance the interpretability of allergic responses during the SPT, potentially reducing the need for extensive manual interpretation experience as standard SPTs.

Keywords: allergic rhinitis; infrared thermography; skin prick test; smartphone; thermal camera; thermal imaging.

- 19 references

BMC Pediatr

. 2023 Apr 3;23(1):153.
doi: 10.1186/s12887-023-03963-w.

Exercise Induced Bronchospasm and associated factors in primary school children: a cross-sectional study

Ogochukwu C Ofiaeli[1,2], Chizalu I Ndukwu[3,4], Nwanneka O Ugwu[4], Kenechi O Nnamani[4], Joy C Ebenebe[3,4], Ifeoma Egbuonu[5]
Affiliations expand

- PMID: 37009907
- PMCID: PMC10069093
- DOI: 10.1186/s12887-023-03963-w

Free PMC article

Abstract

Background: Exercise Induced Bronchospasm(EIB) is not equivalent to asthma. As many as 20%of school aged children are estimated to have EIB. In Nigeria, there is still a dearth of information on EIB as a clinical entity. This study determined the presence of EIB(using pre and post-exercise percentage difference in peak expiratory flow rate(PEFR) and associated factors such as age, gender, social class and nutritional status in primary school children in Nnewi, Anambra state, South-East Nigeria. The study also grouped those with EIB into those with asthma(EIB_A) and those without asthma(EIB_{WA}).

Methods: This was a community based cross-sectional study involving 6-12 year olds. The PEFR was taken at rest and after a 6 min free running test on the school play-ground using a Peak Flow Meter. A diagnosis of EIB was made if there was a decline of ≥ 10%. Those who had EIB were grouped further based on the degree of decline in post-exercise PEFR (a decline ≥ 10% < 25% → Mild EIB, ≥ 25% < 50% → Moderate EIB and ≥ 50% → Severe EIB) and then categorized as those with EIB_{WA}/EIB_A.

Results: EIB in the various minutes post-exercise was as follows: 19.2%(1stmin), 20.9%(5thmin), 18.7%(10thmin), 10%(20thmin), 0.7%(30thmin). Mild EIB accounted for the greater proportion in all minutes post-exercise and none of the pupils had severe EIB. Using values obtained in the 5thmin post-exercise for further analysis, EIB_{WA}/EIB_A = 84.1%/15.9% respectively. Mean difference in the post-exercise PEFR of EIB/no EIB and EIB_{WA}/EIB_A was -48.45(t = -7.69, p = < 0.001) and 44.46(t = 3.77, p = 0.01) respectively. Age and gender had a significant association to the presence of EIB and 58% of the pupils with EIB were of high social class. The BMI for age and gender z-scores of all study subjects as well as those with EIB was -0.34 ± 1.21, -0.09 ± 1.09 respectively. Other features of allergy(history of allergic rhinitis: OR-5.832, p = 0.001; physical findings suggestive of allergic dermatitis: OR-2.740, p = 0.003)were present in pupils diagnosed with EIB.

Conclusion: EIB has a high prevalence in primary school children in Nnewi and the greater proportion of those with EIB had EIB_{WA}. EIB therefore needs to be recognized as a clinical entity and stratified properly based on the presence or absence of asthma. This will help the proper management and prognostication.

Keywords: Childhood; Exercise induced bronchoconstriction; Nigeria.

Conflict of interest statement

The authors declare no competing interests.

- 49 references

- 1 figure

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MeSH termsexpand

full text links

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Clin Exp Immunol

. 2023 Apr 7;212(1):14-28.
doi: 10.1093/cei/uxad031.

Clinical and experimental treatment of allergic asthma with an emphasis on allergen immunotherapy and its mechanisms

Scott Fiala[1], Howard B Fleit[1]

Affiliations expand

- PMID: 36879430
- PMCID: PMC10081111 (available on 2024-03-05)
- DOI: 10.1093/cei/uxad031

Abstract

Allergen immunotherapy (AIT) is currently the only form of treatment that modifies allergic asthma. Pharmacotherapy alone seeks to control the symptoms of allergic asthma, allergic rhinitis, and other atopic conditions. In contrast, AIT can induce long-term physiological modifications through the immune system. AIT enables individuals to live improved lives many years after treatment ends, where they are desensitized to the allergen(s) used or no longer have significant allergic reactions upon allergen provocation. The leading forms of treatment with AIT involve injections of allergen extracts with increasing doses via the subcutaneous route or drops/tablets via the sublingual route for several years. Since the initial attempts at this treatment as early as 1911 by Leonard Noon, the mechanisms by which AIT operates remain unclear. This literature-based review provides the primary care practitioner with a current understanding of the mechanisms of AIT, including its treatment safety, protocols, and long-term efficacy. The primary mechanisms

underlying AIT include changes in immunoglobulin classes (IgA, IgE, and IgG), immunosuppressive regulatory T-cell induction, helper T cell type 2 to helper T cell type 1 cell/cytokine profile shifts, decreased early-phase reaction activity and mediators, and increased production of IL-10, IL-35, TGF-β, and IFN-γ. Using the databases PubMed and Embase, a selective literature search was conducted searching for English, full-text, reviews published between 2015 and 2022 using the keywords (with wildcards) "allerg*," "immunotherap*," "mechanis*," and "asthma." Among the cited references, additional references were identified using a manual search.

Keywords: allergen immunotherapy (AIT); allergic asthma; regulatory T (Treg) cell; subcutaneous allergen immunotherapy (SCIT); sublingual allergen immunotherapy (SLIT).

Conflict of interest statement

The authors declare no conflicts of interest to report.

full text links

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

1

Ann Allergy Asthma Immunol

. 2023 Apr 6;S1081-1206(23)00248-X.

doi: 10.1016/j.anai.2023.03.032. Online ahead of print.

Tiotropium for refractory cough in asthma via cough reflex sensitivity: a randomized, parallel, open-label, trial

Kensuke Fukumitsu[1], Yoshihiro Kanemitsu[2], Ryota Kurokawa[1], Norihisa Takeda[1], Tomoko Tajiri[1], Hirono Nishiyama[1], Keima Ito[1], Yoshitsugu Inoue[1], Sayaka Yamamoto[1], Yuta Mori[1], Satoshi Fukuda[1], Takehiro Uemura[1], Hirotsugu Ohkubo[1], Ken Maeno[1], Yutaka Ito[1], Tetsuya Oguri[1], Masaya Takemura[1], Akio Niimi[1]

Affiliations expand

- PMID: 37030486

- DOI: 10.1016/j.anai.2023.03.032

Abstract

Background: We previously reported in an uncontrolled study that tiotropium alleviated chronic cough in asthma refractory to inhaled corticosteroids and long-acting β2 agonists (ICS/LABA) by modulating capsaicin cough reflex sensitivity (C-CRS).

Objective: We sought to demonstrate the antitussive effects of tiotropium for refractory cough in asthma in a randomized, parallel, open-label, trial.

Methods: Fifty-eight asthmatics with chronic cough refractory to ICS/LABA were randomized in a 2:1 ratio to add tiotropium 5 μg (39 patients) or theophylline 400 mg (19 patients) for 4 weeks. Patients underwent workup, including capsaicin cough challenge test and subjective measures such as cough severity visual analog scales (VAS). We adopted C5, the lowest capsaicin concentration to induce at least 5 coughs, as an index of C-CRS. We also performed a post hoc analysis to identify factors predicting tiotropium responders, who showed an improvement of ≥15 mm in cough severity VAS.

Results: Fifty-two patients (tiotropium; 38, theophylline; 14) completed the study. Both tiotropium and theophylline significantly improved cough severity VAS and cough-specific quality of life. Tiotropium, but not theophylline, significantly increased C5 values, whereas pulmonary function did not change in either group. Additionally, changes in cough severity VAS correlated with changes in C5 values in the tiotropium group. A post hoc analysis revealed that heightened C-CRS (C5 ≤1.22 μM) before the addition of tiotropium was an independent predictor for tiotropium responders.

Conclusion: Tiotropium may alleviate chronic cough in asthma refractory to ICS/LABA by modulating C-CRS. Heightened C-CRS may predict responsiveness to tiotropium for refractory cough in asthma.

Keywords: Asthma control; Capsaicin cough reflex sensitivity; Cough severity; Cough-specific quality of life; Neuronal dysfunction; Refractory cough; Tiotropium.

2

IEEE J Biomed Health Inform

. 2023 Apr 5;PP.

doi: 10.1109/JBHI.2023.3264783. Online ahead of print.

Robust Cough Detection with Out-of-Distribution Detection

Yuhan Chen, Pankaj Attri, Jeffrey Barahona, Michelle L Hernandez, Delesha Carpenter, Alper Bozkurt, Edgar Lobaton

- PMID: 37018102

- DOI: 10.1109/JBHI.2023.3264783

Abstract

Cough is an important defense mechanism of the respiratory system and is also a symptom of lung diseases, such as asthma. Acoustic cough detection collected by portable recording devices is a convenient way to track potential condition worsening for patients who have asthma. However, the data used in building current cough detection models are often clean, containing a limited set of sound categories, and thus perform poorly when they are exposed to a variety of real-world sounds which could be picked up by portable recording devices. The sounds that are not learned by the model are referred to as Out-of-Distribution (OOD) data. In this work, we propose two robust cough detection methods combined with an OOD detection module, that removes OOD data without sacrificing the cough detection performance of the original system. These methods include adding a learning confidence parameter and maximizing entropy loss. Our experiments show that 1) the OOD system can produce dependable In-Distribution (ID) and OOD results at a sampling rate above 750 Hz; 2) the OOD sample detection tends to perform better for larger audio window sizes; 3) the model's overall accuracy and precision get better as the proportion of OOD samples increase in the acoustic signals; 4) a higher percentage of OOD data is needed to realize performance gains at lower sampling rates. The incorporation of OOD detection techniques improves cough detection performance by a significant margin and provides a valuable solution to real-world acoustic cough detection problems.

. 2023 Apr 5.
doi: 10.1080/13543784.2023.2199920. Online ahead of print.

Navafenterol for chronic obstructive pulmonary disease therapy

Sabina Antonela Antoniu[1], Claudia Mariana Handra[2], Agripina Rascu[2], Bogdan Alexandru Barbu[2], Ioan Chirap Mitulschi[1]
Affiliations expand

- PMID: 37017626

- DOI: 10.1080/13543784.2023.2199920

Abstract

Introduction: Chronic obstructive pulmonary disease (COPD) is a prevalent disease of the airways in which inhaled bronchodilators can be given as monotherapy or fixed dose combination, in order to better control disease symptoms and to reduce its morbidity. A novel bronchodilator approach is represented by bifunctional molecules such as navafenterol which exert dual synergic bronchodilator effects as a monotherapy. Navafenterol is currently investigated for COPD.

Areas covered: this review summarizes the preclinical data regarding navafenterol synthesis and in vitro and in vivo testing. Clinical data coming from phase I and II studies are also discussed. Navafenterol was found to improve lung function, dyspnea and cough severity and was well tolerated, and its effect was comparable with that of fixed dose combinations in patients with moderate to severe COPD.

Expert opinion: despite clinical evidence of efficacy for navafenterol is still limited the existing data prompts further clinical evaluation and also consideration of other inhalation approaches such as pressure metered dose inhalers (pMDIs) or nebulization. Other interesting approach would be combination with another bifunctional molecule such as ensifentrine.

Keywords: aclidinium; formoterol- bronchodilators-chronic obstructive pulmonary disease-glycopyrrolate; formoterol-indacaterol; glycopyrrolate-muscarinic antagonist beta 2 agonist (MABA)-navafenterol- tiotropium; olodaterol.

Review

Cochrane Database Syst Rev

. 2023 Apr 4;4(4):CD006458.
doi: 10.1002/14651858.CD006458.pub5.

Nebulised hypertonic saline solution for acute bronchiolitis in infants

Linjie Zhang[1], Raúl Andrés Mendoza-Sassi[1], Claire E Wainwright[2], Alex Aregbesola[3], Terry P Klassen[3]
Affiliations expand

- PMID: 37014057
- PMCID: PMC10072872 (available on 2024-04-04)
- DOI: 10.1002/14651858.CD006458.pub5

Abstract

Background: Airway oedema (swelling) and mucus plugging are the principal pathological features in infants with acute viral bronchiolitis. Nebulised hypertonic saline solution (≥ 3%) may reduce these pathological changes and decrease airway obstruction. This is an update of a review first published in 2008, and updated in 2010, 2013, and 2017.

Objectives: To assess the effects of nebulised hypertonic (≥ 3%) saline solution in infants with acute bronchiolitis.

Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE Daily, Embase, CINAHL, LILACS, and Web of Science on 13 January 2022. We also searched the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) and ClinicalTrials.gov on 13 January 2022.

Selection criteria: We included randomised controlled trials (RCTs) and quasi-RCTs using nebulised hypertonic saline alone or in conjunction with bronchodilators as an active intervention and nebulised 0.9% saline or standard treatment as a comparator in children under 24 months with acute bronchiolitis. The primary outcome for inpatient trials was

length of hospital stay, and the primary outcome for outpatients or emergency department (ED) trials was rate of hospitalisation.

Data collection and analysis: Two review authors independently performed study selection, data extraction, and assessment of risk of bias in included studies. We conducted random-effects model meta-analyses using Review Manager 5. We used mean difference (MD), risk ratio (RR), and their 95% confidence intervals (CI) as effect size metrics.

Main results: We included six new trials (N = 1010) in this update, bringing the total number of included trials to 34, involving 5205 infants with acute bronchiolitis, of whom 2727 infants received hypertonic saline. Eleven trials await classification due to insufficient data for eligibility assessment. All included trials were randomised, parallel-group, controlled trials, of which 30 were double-blinded. Twelve trials were conducted in Asia, five in North America, one in South America, seven in Europe, and nine in Mediterranean and Middle East regions. The concentration of hypertonic saline was defined as 3% in all but six trials, in which 5% to 7% saline was used. Nine trials had no funding, and five trials were funded by sources from government or academic agencies. The remaining 20 trials did not provide funding sources. Hospitalised infants treated with nebulised hypertonic saline may have a shorter mean length of hospital stay compared to those treated with nebulised normal (0.9%) saline or standard care (mean difference (MD) -0.40 days, 95% confidence interval (CI) -0.69 to -0.11; 21 trials, 2479 infants; low-certainty evidence). Infants who received hypertonic saline may also have lower postinhalation clinical scores than infants who received normal saline in the first three days of treatment (day 1: MD -0.64, 95% CI -1.08 to -0.21; 10 trials (1 outpatient, 1 ED, 8 inpatient trials), 893 infants; day 2: MD -1.07, 95% CI -1.60 to -0.53; 10 trials (1 outpatient, 1 ED, 8 inpatient trials), 907 infants; day 3: MD -0.89, 95% CI -1.44 to -0.34; 10 trials (1 outpatient, 9 inpatient trials), 785 infants; low-certainty evidence). Nebulised hypertonic saline may reduce the risk of hospitalisation by 13% compared with nebulised normal saline amongst infants who were outpatients and those treated in the ED (risk ratio (RR) 0.87, 95% CI 0.78 to 0.97; 8 trials, 1760 infants; low-certainty evidence). However, hypertonic saline may not reduce the risk of readmission to hospital up to 28 days after discharge (RR 0.83, 95% CI 0.55 to 1.25; 6 trials, 1084 infants; low-certainty evidence). We are uncertain whether infants who received hypertonic saline have a lower number of days to resolution of wheezing compared to those who received normal saline (MD -1.16 days, 95% CI -1.43 to -0.89; 2 trials, 205 infants; very low-certainty evidence), cough (MD -0.87 days, 95% CI -1.31 to -0.44; 3 trials, 363 infants; very low-certainty evidence), and pulmonary moist crackles (MD -1.30 days, 95% CI -2.28 to -0.32; 2 trials, 205 infants; very low-certainty evidence). Twenty-seven trials presented safety data: 14 trials (1624 infants; 767 treated with hypertonic saline, of which 735 (96%) co-administered with bronchodilators) did not report any adverse events, and 13 trials (2792 infants; 1479 treated with hypertonic saline, of which 416 (28%) co-administered with bronchodilators and 1063 (72%) hypertonic saline alone) reported at least one adverse event such as worsening cough, agitation, bronchospasm, bradycardia, desaturation, vomiting and diarrhoea, most of which were mild and resolved spontaneously (low-certainty evidence).

Authors' conclusions: Nebulised hypertonic saline may modestly reduce length of stay amongst infants hospitalised with acute bronchiolitis and may slightly improve clinical severity score. Treatment with nebulised hypertonic saline may also reduce the risk of hospitalisation amongst outpatients and ED patients. Nebulised hypertonic saline seems to be a safe treatment in infants with bronchiolitis with only minor and spontaneously resolved adverse events, especially when administered in conjunction with a bronchodilator. The certainty of the evidence was low to very low for all outcomes, mainly due to inconsistency and risk of bias.

Trial registration: ClinicalTrials.gov NCT01238848.

Conflict of interest statement

Linjie Zhang: declared that he has no conflict of interest. Raúl A Mendoza-Sassi: declared that he has no conflict of interest. Claire Wainwright: declared that her institution has received funding to support participation in multiple clinical trials sponsored by Vertex Pharmaceuticals since 2009, but she has received no direct funding for this. Alex Aregbesola: declared that he has no conflict of interest. Terry P Klassen: declared that he was contracted by Alberta Research Centre for Child Health Evidence between 14 February 2004 and 3 March 2005 to conduct a clinical trial that was included in the 2022 update review (Grewal 2009).

Update of

- Nebulised hypertonic saline solution for acute bronchiolitis in infants.
  Zhang L, Mendoza-Sassi RA, Wainwright C, Klassen TP.Cochrane Database Syst Rev. 2017 Dec 21;12(12):CD006458. doi: 10.1002/14651858.CD006458.pub4.PMID: 29265171 **Free PMC article. Updated.** Review.

supplementary info

Publication types, MeSH terms, Substances, Associated dataexpand

full text links

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

Pulmonology

-
-

. 2023 Apr 6;S2531-0437(23)00056-9.
doi: 10.1016/j.pulmoe.2023.03.004. Online ahead of print.

Endotypes in bronchiectasis: moving towards precision medicine. A narrative review

M Martins[1], H R Keir[2], J D Chalmers[2]
Affiliations expand

- PMID: 37030997

- DOI: 10.1016/j.pulmoe.2023.03.004

Abstract

Bronchiectasis is a highly complex entity that can be very challenging to investigate and manage. Patients are diverse in their aetiology, symptoms, risk of complications and outcomes. "Endotypes"- subtypes of disease with distinct biological mechanisms, has been proposed as a means of better managing bronchiectasis. This review discusses the emerging field of endotyping in bronchiectasis. We searched PubMed and Google Scholar for randomized controlled trials (RCT), observational studies, systematic reviews and meta-analysis published from inception until October 2022, using the terms: "bronchiectasis", "endotypes", "biomarkers", "microbiome" and "inflammation". Exclusion criteria included commentaries and non-English language articles as well as case reports. Duplicate articles between databases were initially identified and appropriately excluded. Studies identified suggest that it is possible to classify bronchiectasis patients into multiple endotypes deriving from their co-morbidities or underlying causes to complex infective or inflammatory endotypes. Specific biomarkers closely related to a particular endotype might be used to determine response to treatment and prognosis. The most clearly defined examples of endotypes in bronchiectasis are the underlying causes such as immunodeficiency or allergic bronchopulmonary aspergillosis where the underlying causes are clearly related to a specific treatment. The heterogeneity of bronchiectasis extends, however, far beyond aetiology and it is now possible to identify subtypes of disease based on inflammatory mechanisms such airway neutrophil extracellular traps and eosinophilia. In future biomarkers of host response and infection, including the microbiome may be useful to guide treatments and to increase the success of randomized trials. Advances in the understanding the inflammatory pathways, microbiome, and genetics in bronchiectasis are key to move towards a personalized medicine in bronchiectasis.

Keywords: Bronchiectasis; biomarkers; endotypes; inflammation; microbiome.

Publication types

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

1
Medicine (Baltimore)

. 2023 Apr 7;102(14):e33362.
doi: 10.1097/MD.0000000000033362.

Cardiometabolic multimorbidity may identify a more severe subset of rheumatoid arthritis, results from a "real-life" study

Piero Ruscitti[1], Claudia Di Muzio[1], Alessandro Conforti[1], Ilenia Di Cola[1], Viktoriya Pavlych[1], Luca Navarini[2], Damiano Currado[2], Alice Biaggi[2], Stefano Di Donato[2], Annalisa Marino[2], Sebastiano Lorusso[2], Francesco Ursini[3,4], Roberto Giacomelli[2], Paola Cipriani[1]
Affiliations expand

- PMID: 37026953
- PMCID: PMC10082232
- DOI: 10.1097/MD.0000000000033362

Abstract

This "real-life" cross-sectional study has been designed to describe disease features of rheumatoid arthritis (RA) participants affected by cardiometabolic multimorbidity than those without. Our purpose was also the identification of possible associations between these cardiometabolic diseases and RA clinical characteristics. Consecutive RA participants with and without cardiometabolic multimorbidity were assessed and their clinical characteristics were recorded. Participants were grouped and compared by the presence or not of cardiometabolic multimorbidity (defined as ≥ 2 out of 3 cardiovascular risk factors including hypertension, dyslipidemia, and type 2 diabetes). The possible influence of cardiometabolic multimorbidity on RA features of poor prognosis was assessed. The positivity of anti-citrullinated protein antibodies, presence of extra-articular manifestations,

lack of clinical remission, and biologic Disease-Modifying anti-Rheumatic Drugs (bDMARDs) failure were considered as RA features of poor prognosis. In the present evaluation, 757 consecutive RA participants were evaluated. Among them, 13.5% showed cardiometabolic multimorbidity. These were older (P < .001) and characterized by a longer disease duration (P = .023). They were more often affected by extra-articular manifestations (P = .029) and frequently displayed smoking habit (P = .003). A lower percentage of these patients was in clinical remission (P = .048), and they showed a more frequent history of bDMARD failure (P < .001). Regression models showed that cardiometabolic multimorbidity was significantly correlated with RA features of disease severity. They were predictors of anti-citrullinated protein antibodies positivity, of extra-articular manifestations, and of lack of clinical remission, in both univariate and multivariate analyses. Cardiometabolic multimorbidity was significantly associated with a history of bDMARD failure. We described disease features of RA participants with cardiometabolic multimorbidity, identifying a possible more difficult to treat subset, which may need a new management approach to achieve the treatment goal.

Conflict of interest statement

The authors have no funding and conflicts of interest to disclose.

Review

BMC Womens Health

. 2023 Apr 6;23(1):162.
doi: 10.1186/s12905-023-02319-x.

Chronic conditions in women: the development of a National Institutes of health framework

Sarah M Temkin[1], Elizabeth Barr[2], Holly Moore[3], Juliane P Caviston[2], Judith G Regensteiner[4], Janine A Clayton[2]
Affiliations expand

- PMID: 37024841
- PMCID: PMC10077654
- DOI: 10.1186/s12905-023-02319-x

Abstract

Rising rates of chronic conditions were cited as one of the key public health concerns in the Fiscal Year (FY) 2021 U.S. Senate and House of Representatives appropriations bills, where a review of current National Institutes of Health (NIH) portfolios relevant to research on women's health was requested. Chronic conditions were last defined by the US Department of Health and Human Services (HHS) in 2010. However, existing definitions of chronic conditions do not incorporate sex or gender considerations. Sex and gender influence health, yet significant knowledge gaps exist in the evidence-base for prevention, diagnosis, and treatment of chronic diseases amongst women. The presentation, prevalence, and long-term effects of chronic conditions and multimorbidity differs in women from men. A clinical framework was developed to adequately assess the NIH investment in research related to chronic conditions in women. The public health needs and NIH investment related to conditions included in the framework were measured. By available measures, research within the NIH has not mapped to the burden of chronic conditions among women. Clinical research questions and endpoints centered around women can be developed and implemented; clinical trials networks with expanded or extended eligibility criteria can be created; and data science could be used to extrapolate the effects of overlapping or multiple morbidities on the health of women. Aligning NIH research priorities to address the specific needs of women with chronic diseases is critical to addressing women's health needs from a life course perspective.

Keywords: Chronic disease; Gender; Multimorbity; Sex differences; Women’s health.

Conflict of interest statement

The authors declare that they have no competing interests.

- 68 references
- 3 figures

supplementary info

Publication typesexpand

3
BMC Med Res Methodol
.
. 2023 Apr 5;23(1):83.
doi: 10.1186/s12874-023-01901-z.

A new data driven method for summarising multiple cause of death data

Annette Dobson[1], Paul McElwee[2], Mohammad Reza Baneshi[2], James Eynstone-Hinkins[3], Lauren Moran[3], Michael Waller[2]
Affiliations expand

- PMID: 37020203
- PMCID: PMC10074369
- DOI: 10.1186/s12874-023-01901-z

Free PMC article

Abstract

Background: National mortality statistics are based on a single underlying cause of death. This practice does not adequately represent the impact of the range of conditions experienced in an ageing population in which multimorbidity is common.

Methods: We propose a new method for weighting the percentages of deaths attributed to different causes that takes account of the patterns of associations among underlying and contributing causes of death. It is driven by the data and unlike previously proposed methods does not rely on arbitrary choices of weights which can over-emphasise the contribution of some causes of death. The method is illustrated using Australian mortality data for people aged 60 years or more.

Results: Compared to the usual method based only on the underlying cause of death the new method attributes higher percentages of deaths to conditions like diabetes and dementia that are frequently mentioned as contributing causes of death, rather than

underlying causes, and lower percentages to conditions to which they are closely related such as ischaemic heart disease and cerebrovascular disease. For some causes, notably cancers, which are usually recorded as underlying causes with few if any contributing causes the new method produces similar percentages to the usual method. These different patterns among groups of related conditions are not apparent if arbitrary weights are used.

Conclusion: The new method could be used by national statistical agencies to produce additional mortality tables to complement the current tables based only on underlying causes of death.

Keywords: Data-driven method; Death rates; Multimorbidity; Multiple causes of death.

Conflict of interest statement

The authors have no relevant financial or non-financial interests to disclose.

- 28 references
- 1 figure

supplementary info

Publication types, MeSH termsexpand
full text links

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Fam Pract

. 2023 Apr 4;cmad039.
doi: 10.1093/fampra/cmad039. Online ahead of print.

Recruiting general practitioners and older patients with multimorbidity to randomized trials

Caroline McCarthy[1], Ivana Pericin[2], Susan M Smith[1 3], Frank Moriarty[1 4], Barbara Clyne[1]
Affiliations expand

- PMID: 37014975

- DOI: 10.1093/fampra/cmad039

Abstract

Background: Older patients with multimorbidity are under-represented in experimental research.

Objective: To explore the barriers and facilitators to general practitioner (GP) and older patient recruitment and retention in a cluster randomized controlled trial (RCT).

Method: This descriptive study uses qualitative and quantitative data from a cluster RCT, designed to evaluate the effectiveness of a medicines optimization intervention. The SPPiRE cluster RCT enrolled 51 general practices and 404 patients aged ≥65 years and prescribed ≥15 medicines. Quantitative data were collected from all recruited practices and 32 additional practices who were enrolled, but unable to recruit sufficient participants. Qualitative data were collected from purposive samples of intervention GPs (18/26), patients (27/208), and researcher logs and analysed thematically using inductive coding.

Results: Enrolment rates for practices and patients were 37% and 25%, respectively. Barriers to GP recruitment were lack of resources and to patient recruitment were difficulty understanding trial material and concern about medicines being taken away. GPs' primary motivation was perceived importance of the research question, whereas patients' primary motivation was trust in their GP. All general practices were retained. Thirty-five patients (8.6%) were lost to follow-up for primary outcomes, mainly because they had died and 45% did not return patient-reported outcome measures (PROMs).

Conclusion: Patient retention for the primary outcome was high, as it was collected directly from patient records. Patient completion of PROM data was poor, reflecting difficulty in understanding trial material. Recruiting older patients with multimorbidity to clinical trials is possible but requires significant resource and planning.

Trial registration: ISRCTN Registry ISRCTN12752680.

Keywords: multimorbidity; polypharmacy; process evaluation; randomized controlled trial; research design.

Plain language summary

Randomized controlled trials (RCTs) often exclude older people with multiple medical conditions. The aim of this study was to explore how and why participants took part in a primary care based RCT that included 51 general practitioners (GPs) and 404 older patients prescribed ≥15 medicines. The RCT was designed to assess the usefulness of a supported medication review. The study team assessed information that was already collected as part of the RCT, to describe the process of inviting and enrolling GPs and older people. This included information on the numbers invited and enrolled and interviews from a smaller

sample of GPs (18) and older people (27). The study successfully enrolled the required number of participants but it took 26 months more than planned. 37% of invited GPs and 25% of invited patients took part. GPs felt the research was important but they identified lack of time and resources as barriers to participation. Older people predominantly took part because they trusted their GP but some were wary of having medicines taken away and were put off by trial documentation. It is important that RCTs including older people with multiple medical conditions carefully plan recruitment and pay careful attention to trial documentation.

Editorial

PLoS Med

. 2023 Apr 4;20(4):e1004229.
doi: 10.1371/journal.pmed.1004229. eCollection 2023 Apr.

Multimorbidity: Addressing the next global pandemic

PLOS Medicine Editors

- PMID: 37014909
- PMCID: PMC10072481
- DOI: 10.1371/journal.pmed.1004229

Free PMC article

No abstract available

Conflict of interest statement

The authors' individual competing interests are at http://journals.plos.org/plosmedicine/s/staff-editors. PLOS is funded partly through manuscript publication charges, but the PLOS Medicine Editors are paid a fixed salary (their salaries are not linked to the number of papers published in the journal). Till Bärnighausen is the Academic Editor-in-chief of PLOS Medicine.

- 15 references

supplementary info

Publication types, MeSH terms, Grant supportexpand

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Observational Study

PLoS Med

. 2023 Apr 4;20(4):e1004205.

doi: 10.1371/journal.pmed.1004205. eCollection 2023 Apr.

Estimating health spending associated with chronic multimorbidity in 2018: An observational study among adults in the United States

Angela Y Chang[1 2 3], Dana Bryazka[4], Joseph L Dieleman[4]

Affiliations expand

- PMID: 37014826
- PMCID: PMC10072449
- DOI: 10.1371/journal.pmed.1004205

Free PMC article

Abstract

Background: The rise in health spending in the United States and the prevalence of multimorbidity-having more than one chronic condition-are interlinked but not well understood. Multimorbidity is believed to have an impact on an individual's health spending, but how having one specific additional condition impacts spending is not well established. Moreover, most studies estimating spending for single diseases rarely adjust for multimorbidity. Having more accurate estimates of spending associated with each disease and different combinations could aid policymakers in designing prevention policies to more effectively reduce national health spending. This study explores the relationship between multimorbidity and spending from two distinct perspectives: (1) quantifying spending on different disease combinations; and (2) assessing how spending on a single diseases changes when we consider the contribution of multimorbidity (i.e., additional/reduced spending that could be attributed in the presence of other chronic conditions).

Methods and findings: We used data on private claims from Truven Health MarketScan Research Database, with 16,288,894 unique enrollees ages 18 to 64 from the US, and their annual inpatient and outpatient diagnoses and spending from 2018. We selected conditions that have an average duration of greater than one year among all Global Burden of Disease causes. We used penalized linear regression with stochastic gradient descent approach to assess relationship between spending and multimorbidity, including all possible disease combinations with two or three different conditions (dyads and triads) and for each condition after multimorbidity adjustment. We decomposed the change in multimorbidity-adjusted spending by the type of combination (single, dyads, and triads) and multimorbidity disease category. We defined 63 chronic conditions and observed that 56.2% of the study population had at least two chronic conditions. Approximately 60.1% of disease combinations had super-additive spending (e.g., spending for the combination was significantly greater than the sum of the individual diseases), 15.7% had additive spending, and 23.6% had sub-additive spending (e.g., spending for the combination was significantly less than the sum of the individual diseases). Relatively frequent disease combinations (higher observed prevalence) with high estimated spending were combinations that included endocrine, metabolic, blood, and immune disorders (EMBI disorders), chronic kidney disease, anemias, and blood cancers. When looking at multimorbidity-adjusted spending for single diseases, the following had the highest spending per treated patient and were among those with high observed prevalence: chronic kidney disease ($14,376 [12,291,16,670]), cirrhosis ($6,465 [6,090,6,930]), ischemic heart disease (IHD)-related heart conditions ($6,029 [5,529,6,529]), and inflammatory bowel disease ($4,697 [4,594,4,813]). Relative to unadjusted single-disease spending estimates, 50 conditions had higher spending after adjusting for multimorbidity, 7 had less than 5% difference, and 6 had lower spending after adjustment.

Conclusions: We consistently found chronic kidney disease and IHD to be associated with high spending per treated case, high observed prevalence, and contributing the most to spending when in combination with other chronic conditions. In the midst of a surging health spending globally, and especially in the US, pinpointing high-prevalence, high-spending conditions and disease combinations, as especially conditions that are associated

with larger super-additive spending, could help policymakers, insurers, and providers prioritize and design interventions to improve treatment effectiveness and reduce spending.

Conflict of interest statement

The authors have declared that no competing interests exist.

- 47 references
- 3 figures

supplementary info

Publication types, MeSH terms, Grant supportexpand

full text links

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Eur Geriatr Med

-
-
-

. 2023 Apr 3.

doi: 10.1007/s41999-023-00770-5. Online ahead of print.

Higher levels of multimorbidity are associated with increased risk of readmission for older people during post-acute transitional care

Ornagh Griffin[1], Tracy Li[2,3], Alexander Beveridge[1,4], Danielle Ní Chróinín[5,6]

Affiliations expand

- PMID: 37010792

- DOI: 10.1007/s41999-023-00770-5

Abstract

Purpose: Older patients are at high risk for poor outcomes after an acute hospital admission. The Transitional Aged Care Programme (TACP) was established by the Australian government to provide a short-term care service aiming to optimise functional independence following hospital discharge. We aim to investigate the association between multimorbidity and readmission amongst patients on TACP.

Methods: Retrospective cohort study of all TACP patients over 12 months. Multimorbidity was defined using the Charlson Comorbidity Index (CCI), and prolonged TACP (pTACP) as TACP ≥ 8 weeks.

Results: Amongst 227 TACP patients, the mean age was 83.3 ± 8.0 years, and 142 (62.6%) were females. The median length-of-stay on TACP was 8 weeks (IQR 5-9.67), and median CCI 7 (IQR 6-8). 21.6% were readmitted to hospital. Amongst the remainder, 26.9% remained at home independently, 49.3% remained home with supports; < 1% were transferred to a residential facility (0.9%) or died (0.9%). Hospital readmission rates increased with multimorbidity (OR 1.37 per unit increase in CCI, 95% CI 1.18-1.60, $p < 0.001$). On multivariable logistic regression analysis, including polypharmacy, CCI, and living alone, CCI remained independently associated with 30-day readmission (aOR 1.43, 95% CI 1.22-1.68, $p < 0.001$).

Conclusions: CCI is independently associated with a 30-day hospital readmission in TACP cohort. Identifying vulnerability to readmission, such as multimorbidity, may allow future exploration of targeted interventions.

Keywords: Aged care; Multimorbidity; Readmission; Transitional care.

- 40 references

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