LIBRA JOURNAL CLUB
13-18 AUG 2024

Our legal office confirmed that articles NOT OPEN ACCESS cannot be distributed to the members of the list. Thus, we will transmit only the titles of articles.
ABSTRACTS of almost all these articles are available from PubMed, and full papers can be obtained through your institutions' library.
OPEN ACCESS articles are available by accessing the articles from PubMed using just the PMID for the search (eg PMID: 35514131 without . at the end)

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

1

BMC Pulm Med

-
-
-

. 2024 Aug 17;24(1):395.

doi: 10.1186/s12890-024-03194-4.

Treatment patterns in patients with newly diagnosed COPD in the USA

Antonio Anzueto [1], Sheri Rogers [2], Bonnie Donato [2], Beverly Jones [2], Kushal Modi [3], Abisola Olopoenia [3], Robert Wise [4]

Affiliations Expand

- **PMID: 39153976**

- **DOI: 10.1186/s12890-024-03194-4**

Abstract

Background: Prompt and effective management with maintenance therapy (single or dual bronchodilator therapy) is recommended after the initial diagnosis of chronic obstructive pulmonary disease (COPD) to maintain lung function and prevent exacerbations. Contrary to guideline-based recommendations, most patients are not prescribed maintenance treatment at initial diagnosis. The current study assessed

the pharmacologic treatment patterns and outcomes of newly diagnosed patients with COPD in the USA.

Methods: This retrospective, noninterventional study used de-identified data from the Inovalon Insights' database (Commercial, Medicaid Managed Care, and Medicare Advantage-insured individuals) between January 1, 2015, and December 31, 2021. The "patient journey" from initial diagnosis was followed over a 4-year period. The primary outcome measure was the number of moderate or severe exacerbations. Secondary outcome measures included the cumulative incidence of exacerbations, mean cumulative count of moderate and severe exacerbations, rates of moderate and severe exacerbations in patients who remained untreated after diagnosis in 12-month time periods for 4 years, sociodemographic and clinical characteristics, and pharmacologic treatment patterns.

Results: The cohort consisted of 238,158 newly diagnosed patients with COPD (female [52.9%]; mean age 63.8 years). The majority of patients with COPD had Medicaid as their primary insurance (46.2%). Overall, during the 4-year follow-up period, 32.9% of the patients had at least one moderate or severe exacerbation, and 25.8% and 13.8% experienced moderate and severe exacerbations, respectively. At diagnosis, 86.2% of the patients were untreated and most remained untreated by the end of the follow-up (63.8%). Most patients (62.0%) received long-acting beta-agonist (LABA)/inhaled corticosteroids (ICS) as their initial treatment at diagnosis, and LABA/ICS continued to be the most common initial treatment during the 4-year period (64.0% at year 1; 58.0% at year 4).

Conclusions: Most patients with COPD were not treated at initial diagnosis and remained untreated during follow-up. Our data highlight a lack of adherence to recommendations for clinical practice.

Keywords: COPD; Exacerbations; Maintenance therapy; Newly diagnosed; Treatment patterns.

- 20 references

Supplementary info

MeSH terms, SubstancesExpand

Full text links

UNIMORE

Proceed to details

Cite

Share

2

Am J Infect Control

-
-
-

. 2024 Aug 15:S0196-6553(24)00657-6.

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

National trends and disparities in herpes zoster vaccination among U.S. older adults with chronic obstructive pulmonary disease, 2008-2022

Chun-Tse Hung [1], Li-Min Wang [2], Chi-Won Suk [3]

Affiliations Expand

- PMID: 39153516

- DOI: 10.1016/j.ajic.2024.08.010

Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a risk factor for herpes zoster. Vaccination can prevent or attenuate herpes zoster and its related complications. However, evidence regarding vaccine uptake among patients with COPD is limited. Therefore, this cross-sectional study aimed to evaluate trends in herpes zoster vaccination and characteristics associated with vaccination among U.S. older adults with COPD.

Methods: Data from the 2008-2022 National Health Interview Survey were used. Participants aged ≥50 years were included. Joinpoint regression analysis was performed to analyze trends in herpes zoster vaccination. A multivariable logistic regression model was used to identify factors associated with herpes zoster vaccination.

Results: This study included 22,853 participants with COPD, representing approximately 9.8 million U.S. older adults with COPD. From 2008 to 2022, an increasing trend in herpes zoster vaccination was observed (average annual percent change=15.10, P<0.01) This increasing trend was also observed when stratified by age groups. Disparities in vaccination were found across several factors, including age, sex, race/ethnicity, region, educational level, health insurance, income, smoking status, perceived health status, and flu and pneumococcal vaccination.

Conclusions: While there has been an upward trend in herpes zoster vaccination over the past 15 years among older adults with COPD, disparities across several characteristics were identified. These findings underscore the necessity for targeted policies and interventions to promote equity in vaccination.

Keywords: National Health Interview Survey; chronic obstructive pulmonary disease; herpes zoster; immunization; vaccination; vaccine.

3

Meta-Analysis

Biomol Biomed

-
-
-

. 2024 Aug 16.

doi: 10.17305/bb.2024.10875. Online ahead of print.

Serum pentraxin-3 in patients with chronic obstructive pulmonary disease: A meta-analysis

Yan Zhu [1], Chongyang Wang [1]

Affiliations Expand

- PMID: 39151096

- DOI: 10.17305/bb.2024.10875

Free article

Abstract

The association between serum pentraxin-3 (PTX-3) levels and chronic obstructive pulmonary disease (COPD) has been explored in several studies. However, the results remain inconsistent. This meta-analysis aims to evaluate the differences in serum PTX-3 levels between COPD patients and healthy controls, as well as between patients with acute exacerbations of COPD (AECOPD) and stable COPD. Databases including PubMed, Embase, Web of Science, Wanfang, and China National Knowledge Infrastructure (CNKI) were systematically searched. A random-effects model was used to pool the results, accounting for the potential impact of

heterogeneity. Subgroup and meta-regression analyses were performed to evaluate the influence of study characteristics on the outcome. The initial search identified 274 articles, with 17 studies meeting the inclusion criteria. These studies included a total of 996 AECOPD patients, 1414 stable COPD patients, and 1016 healthy controls. The meta-analysis showed significantly higher serum PTX-3 levels in COPD patients compared to healthy controls (standardized mean difference [SMD]: 0.51, 95% confidence interval [CI]: 0.30 to 0.73, $P < 0.001$; $I^2 = 85\%$). Subgroup and meta-regression analyses suggested that the results were not significantly affected by the age, sex, or smoking status of the patients. Additionally, serum PTX-3 levels were higher in AECOPD patients compared to stable COPD patients (SMD: 0.58, 95% CI: 0.41 to 0.74, $P < 0.001$; $I^2 = 59\%$). In conclusion, serum PTX-3 levels are elevated in COPD patients, particularly during acute exacerbations, compared to stable COPD patients and healthy controls. PTX-3 may serve as a potential biomarker for COPD severity and exacerbation status.

Supplementary info

Publication typesExpand

Full text links

4

Eur Respir J

. 2024 Aug 15:2302071.

doi: 10.1183/13993003.02071-2023. Online ahead of print.

Airway derived emphysema-specific alveolar type II cells exhibit impaired regenerative potential in COPD

Yan Hu [1], Qianjiang Hu [2], Meshal Ansari [3], Kent Riemondy [4], Ricardo Pineda [2], John Sembrat [2], Adriana S Leme [2], Kenny Ngo [1], Olivia Morgenthaler [1], Kellie Ha [1], Bifeng Gao [1], William J Janssen [5], Maria C Basil [6 7 8], Corrine R Kliment [2], Edward Morrisey [6 7 9], Mareike Lehmann [3 10], Christopher M Evans [1 11], Herbert B Schiller [12 11], Melanie Königshoff [13 14 11]

Affiliations Expand

- PMID: 39147413

- DOI: 10.1183/13993003.02071-2023

Abstract

Emphysema, the progressive destruction of gas exchange surfaces in the lungs, is a hallmark of chronic obstructive pulmonary disease (COPD) that is presently incurable. This therapeutic gap is largely due to a poor understanding of potential drivers of impaired tissue regeneration, such as abnormal lung epithelial progenitor cells, including alveolar type II (ATII) and airway club cells. We discovered an emphysema-specific sub-population of ATII cells located in enlarged distal alveolar sacs, termed asATII cells. Single cell RNA-seq and *in situ* localisation revealed that asATII cells co-express the alveolar marker surfactant protein C (SPC) and the club cell marker secretaglobin-3A2 (SCGB3A2). A similar ATII sub-population derived from club cells was also identified in mouse COPD models using lineage labeling. Human and mouse ATII sub-populations formed 80-90% fewer alveolar organoids than healthy controls, indicating reduced progenitor function. Targeting asATII cells or their progenitor club cells could reveal novel COPD treatment strategies.

5

Eur Respir J

-
-
-

. 2024 Aug 15:2302240.

doi: 10.1183/13993003.02240-2023. Online ahead of print.

Exacerbation history and blood eosinophil count prior to diagnosis of COPD and risk of subsequent exacerbations

David M G Halpin [1 2], Heath Healey [3], Derek Skinner [3], Victoria Carter [3], Rachel Pullen [2], David Price [2 3 4]

Affiliations Expand

- PMID: 39147410

- DOI: 10.1183/13993003.02240-2023

Abstract

Background: Prior exacerbation history is used to guide initial maintenance therapy in chronic obstructive pulmonary disease (COPD); however, the recommendations were derived from patients already diagnosed and treated.

Method: We assessed the rates of moderate (*i.e.* treated with antibiotics and/or systemic corticosteroids) and severe (*i.e.* hospitalised) exacerbations in the year following diagnosis in patients newly diagnosed with COPD according to their prior history of exacerbations, blood eosinophil counts (BEC) and whether maintenance therapy was started. Data were extracted from the Optimum Patient Care Research Database.

Results: 73 189 patients were included. 61.9% had no exacerbations prior to diagnosis, 21.5% had 1 moderate, 16.5% had ≥2 moderate, and 0.3% had ≥1 severe. 50% were started on maintenance therapy. In patients not started on maintenance therapy the rates (95% confidence intervals) of moderate exacerbations in the year after diagnosis in patients with 0, 1 moderate, ≥2 moderate, ≥1 severe prior exacerbations were 0.34 (0.33-0.35), 0.59 (0.56-0.61), 1.18 (1.14-1.23) and 1.21 (0.73-1.69) respectively. Similar results were seen in patients started on maintenance therapy. BEC did not add significantly to the prediction of future exacerbation risk.

Conclusion: A single moderate exacerbation in the year prior to diagnosis increases the risk of subsequent exacerbations and more frequent or severe exacerbations prior to diagnosis are associated with a higher risk.

-

. 2024 Aug 15:2400347.

doi: 10.1183/13993003.00347-2024. Online ahead of print.

Association of airway inflammation and smoking status with IL-33 level in sputum of patients with asthma or COPD

Mustafa Abdo [1 2], Frauke Pedersen [3 4 2], Anne-Marie Kirsten [4], Frederik Trinkmann [5 6], Espen E Groth [3], Thomas Bahmer [7], Henrik Watz [4], Klaus F Rabe [3 7]

Affiliations Expand

- PMID: 39147409

- DOI: 10.1183/13993003.00347-2024

Free article

No abstract available

Supplementary info

Publication typesExpand

Full text links

7

Case Reports

J Bronchology Interv Pulmonol

-

-

-

. 2024 Aug 15;31(4):e0977.

doi: 10.1097/LBR.0000000000000977. eCollection 2024 Oct 1.

Using Sub-lobar Bronchoscopic Lung Volume Reduction to Optimize Safety and Efficacy in a Case of High-risk Emphysema

Aleezay Asghar [1], Victoria Forth [2], Majid Shafiq [2]

Affiliations Expand

- PMID: 39143697

- DOI: 10.1097/LBR.0000000000000977

No abstract available

Conflict of interest statement

Disclosure: M.S. reports being a member of the scientific advisory board for Ambu A/S. The remaining authors report no conflicts of interest.

- 9 references

Supplementary info

Publication types, MeSH termsExpand

Full text links

Proceed to details

Cite

Share

8

Observational Study

Respir Res

-
-
-

. 2024 Aug 14;25(1):308.

doi: 10.1186/s12931-024-02931-x.

The clinical impacts of lung microbiome in bronchiectasis with fixed airflow obstruction: a prospective cohort study

Yen-Fu Chen [1 2 3], Hsin-Han Hou [4], Ning Chien [5], Kai-Zen Lu [6], Chieh-Hua Lin [7 8], Yu-Chieh Liao [8], Kuo-Lung Lor [9], Jung-Yien Chien [2 6], Chung-Ming Chen [9], Chung-Yu Chen [1 2 3], Shih-Lung Cheng [10 11], Hao-Chien Wang [6 12], Po-Ren Hsueh [13 14 15 16], Chong-Jen Yu [17 18 19]

Affiliations Expand

- PMID: 39143556
- PMCID: PMC11325704
- DOI: 10.1186/s12931-024-02931-x

Abstract

Background: Airflow obstruction is a hallmark of disease severity and prognosis in bronchiectasis. The relationship between lung microbiota, airway inflammation, and outcomes in bronchiectasis with fixed airflow obstruction (FAO) remains unclear. This study explores these interactions in bronchiectasis patients, with and without FAO, and compares them to those diagnosed with chronic obstructive pulmonary disease (COPD).

Methods: This prospective observational study in Taiwan enrolled patients with either bronchiectasis or COPD. To analyze the lung microbiome and assess inflammatory markers, bronchoalveolar lavage (BAL) samples were collected for 16S rRNA gene sequencing. The study cohort comprised 181 patients: 86 with COPD, 46 with bronchiectasis, and 49 with bronchiectasis and FAO, as confirmed by spirometry.

Results: Patients with bronchiectasis, with or without FAO, had similar microbiome profiles characterized by reduced alpha diversity and a predominance of Proteobacteria, distinctly different from COPD patients who exhibited more Firmicutes, greater diversity, and more commensal taxa. Furthermore, compared to COPD and bronchiectasis without FAO, bronchiectasis with FAO showed more severe disease and a higher risk of exacerbations. A significant correlation was found between the presence of Pseudomonas aeruginosa and increased airway neutrophilic inflammation such as Interleukin [IL]-1β, IL-8, and tumor necrosis factor-alpha [TNF]-α, as well as with higher bronchiectasis severity, which might contribute to an increased risk of exacerbations. Moreover, in bronchiectasis patients with FAO, the ROSE (Radiology, Obstruction, Symptoms, and Exposure) criteria were employed to classify individuals as either ROSE (+) or ROSE (-), based on smoking history. This classification highlighted differences in clinical features, inflammatory profiles, and slight microbiome variations between ROSE (-) and ROSE (+) patients, suggesting diverse endotypes within the bronchiectasis with FAO group.

Conclusion: Bronchiectasis patients with FAO may exhibit two distinct endotypes, as defined by ROSE criteria, characterized by greater disease severity and a lung microbiome more similar to bronchiectasis without FAO than to COPD. The significant correlation between Pseudomonas aeruginosa colonization and

increased airway neutrophilic inflammation, as well as disease severity, underscores the clinical relevance of microbial patterns. This finding reinforces the potential role of these patterns in the progression and exacerbations of bronchiectasis with FAO.

Keywords: Bronchiectasis; Bronchoalveolar lavage; COPD; Fixed airflow obstruction; Lung microbiota; Neutrophilic inflammation; ROSE criteria.

Conflict of interest statement

The authors declare no competing interests.

- **62 references**
- **8 figures**

Supplementary info

Publication types, MeSH terms, Grants and fundingExpand

Full text links

Proceed to details

Cite

Share

9

Meta-Analysis

BMC Pulm Med

-
-
-

. 2024 Aug 14;24(1):393.

doi: 10.1186/s12890-024-03180-w.

The impact of chronic obstructive pulmonary disease on the risk of immune-related pneumonitis in lung cancer patients undergoing immunotherapy: a systematic review and meta-analysis

Fangyuan Li [1], Lei Zheng [1], Xiaoxia Xu [1], Jianjiang Jin [1], Xingxing Li [1], Li Zhou [2]

Affiliations Expand

- PMID: 39143553

- PMCID: PMC11323643

- DOI: 10.1186/s12890-024-03180-w

Abstract

Background: Lung cancer, a leading cause of cancer mortality, poses significant treatment challenges. The use of immune checkpoint inhibitors (ICIs) has revolutionized therapy, but it is associated with immune-related pneumonitis (IRP). This study systematically reviews and analyzes the impact of Chronic Obstructive Pulmonary Disease (COPD) on the risk of IRP in lung cancer patients undergoing immunotherapy.

Methods: Adhering to PRISMA guidelines and using the PICO framework, a comprehensive search across PubMed, Embase, Web of Science, and the Cochrane Library was conducted. Inclusion criteria encompassed peer-reviewed studies involving lung cancer patients treated with ICIs, comparing those with and without COPD. The primary outcome was the incidence and risk of IRP. The Newcastle-Ottawa Scale evaluated study quality. The effect size was calculated using random or fixed-effects models based on the observed heterogeneity. We assessed the heterogeneity between studies and conducted a sensitivity analysis.

Results: The search identified 1026 articles, with six meeting the criteria for inclusion. Studies varied in design and geography, predominantly retrospective cohort studies. Patients with COPD had an increased risk of IRP (OR = 1.54, 95% CI [1.24, 1.92, P < 0.01). Subgroup analysis based on radiation therapy exposure (< 40% and ≥ 40%) also indicated a heightened IRP risk in COPD patients. Sensitivity analysis affirmed the robustness of the results, and publication bias was not significant.

Conclusions: Lung cancer patients with COPD undergoing immunotherapy have a significantly increased risk of developing IRP. This highlights the necessity for vigilant monitoring and individualized treatment strategies to improve the safety and effectiveness of immunotherapy in this group.

Keywords: Chronic obstructive pulmonary disease; Immune-related pneumonitis; Immunotherapy; Lung cancer; Meta-analysis.

Conflict of interest statement

The authors declare no competing interests.

- 29 references
- 5 figures

Supplementary info

Publication types, MeSH terms, SubstancesExpand

Full text links

Proceed to details

Cite

Share

10

BMJ Open Respir Res

-
-
-

. 2024 Aug 13;11(1):e002430.

doi: 10.1136/bmjresp-2024-002430.

Development and validation of a novel questionnaire to describe and assess sensations and triggers associated with refractory and unexplained chronic cough

Shannon Galgani [# 1], Chelsea Sawyer [# 2], Jenny King [3], Rachel Dockry [3], James Wingfield-Digby [3], Kimberly Holt [3], Joanne Mitchell [1], Shilpi Sen [1], Danielle Birchall [4], Francesca Solari [5], Jacky Smith [3], Janelle Yorke [6]

Affiliations Expand

- PMID: 39142695

- DOI: 10.1136/bmjresp-2024-002430

Free article

Abstract

Introduction: Refractory or unexplained chronic cough (RUCC) is a common clinical problem with no effective diagnostic tools. The Sensations and Triggers Provoking Cough questionnaire (TOPIC) was developed to characterise cough in RUCC versus cough in other conditions.

Methods: Content analysis of participant interviews discussing the sensations and triggers of chronic cough informed TOPIC development. Participants with chronic cough completed the draft-TOPIC (a subset repeating 5-7 days later), St George's

Respiratory Questionnaire (SGRQ), Cough Severity Diary (CSD) and Global Rating of Change Scale. The draft-TOPIC item list was reduced in hierarchical and Rasch analysis to refine the questionnaire to the TOPIC.

Results: 49 items describing the triggers and sensations of cough were generated from participant interviews (RUCC n=14, chronic obstructive pulmonary disease (COPD) n=11, interstitial lung disease (ILD) n=10, asthma n=11, bronchiectasis n=3, cystic fibrosis n=7). 140 participants (median age 60.0 (19.0-88.0), female 56.4%; RUCC n=39, ILD n=38, asthma n=45, COPD n=6, bronchiectasis n=12) completed draft-TOPIC, where items with poor 'fit' for RUCC were removed to create TOPIC (8 trigger items, 7 sensation items). Median TOPIC score was significantly higher in RUCC (37.0) vs ILD (24.5, p=0.009) and asthma (7.0, p<0.001), but not bronchiectasis (20.0, p=0.318) or COPD (18.5, p=0.238), likely due to small sample sizes. The Rasch model demonstrated excellent fit in RUCC (χ^2=22.04, p=0.85; PSI=0.88); as expected. When all participant groups were included, fit was no longer demonstrated (χ^2=66.43, p=0.0001, PSI=0.89) due to the increased heterogeneity (CI=0.077). TOPIC correlated positively with SGRQ (r=0.47, p<0.001) and CSD (r=0.63, p<0.001). The test-retest reliability of TOPIC (intraclass correlation coefficient) was excellent (r=0.90, p<0.001).

Conclusions: High TOPIC scores in the RUCC patients suggest their cough is characterised by specific sensations and triggers. Validation of TOPIC in cough clinics may demonstrate value as an aid to identify features of RUCC versus cough in other conditions.

Keywords: Cough/Mechanisms/Pharmacology; Surveys and Questionnaires.

Conflict of interest statement

Competing interests: JAS is an inventor on a cough monitoring system that is licensed to Vitalograph who pays royalties to the hospital in which she works. She does not receive any royalties personally. She also advises pharmaceutical companies on the design and delivery of studies assessing new treatments for chronic cough. None of the other authors have competing interests.

Cochrane Database Syst Rev

. 2024 Aug 14;8(8):CD015800.

doi: 10.1002/14651858.CD015800.

Care pathways versus usual care for chronic obstructive pulmonary disease (COPD)

Mahtab Pajand Birjandi [1], Omar Ammous [2], Regina Kampo [2], Sarah Stanzel [3], Maximilian Wollsching-Strobel [3], Tim Mathes [2]

Affiliations Expand

- PMID: 39140370
- PMCID: PMC11323265
- DOI: 10.1002/14651858.CD015800

Abstract

This is a protocol for a Cochrane Review (intervention). The objectives are as follows: To assess the effects of care pathways (CPs) compared to usual care/no CPs for people with chronic obstructive pulmonary disease (COPD).

Conflict of interest statement

Pajand Birjandi M: none known.

Ammous O: none known.

Kampo R: none known.

Stanzel S: received a personal travel grant from CSL Behring (from 25 May 2022 to 27 May 2022), an institutional grant (Cologne Research Group) from Löwenstein Medical, a grant from Chiesi USA, and now holds the position of chairman section of respiratory and intensive care medicine at the German Society of Pneumology.

Wollsching Strobel M: received two personal travel grants from CSL Behring (from 24 May 2022 to 28 May 2022) and Löwenstein Medical (9 June 2022 to 12 June 2022), payment for a lecture on 18 November 2022 from Novartis Pharma, and works as a doctor at Kliniken der Stadt Köln gGmbH.

Mathes T: none known.

- 84 references

Supplementary info

MeSH termsExpand

Full text links

Proceed to details

Cite

Share

12

COPD

-
-
-

. 2024 Dec;21(1):2379811.

doi: 10.1080/15412555.2024.2379811. Epub 2024 Aug 13.

Identification and Validation of Aging Related Genes Signature in Chronic Obstructive Pulmonary Disease

Tian-Tian Li [1], Hong-Yan Bai [1], Jing-Hong Zhang [1], Xiu-He Kang [1], Yi-Qing Qu [1]

Affiliations Expand

- PMID: 39138958

- DOI: 10.1080/15412555.2024.2379811

Abstract

Purpose: Chronic Obstructive Pulmonary Disease (COPD) is regarded as an accelerated aging disease. Aging-related genes in COPD are still poorly understood.

Method: Data set GSE76925 was obtained from the Gene Expression Omnibus (GEO) database. The "limma" package identified the differentially expressed genes. The weighted gene co-expression network analysis (WGCNA) constructes co-expression modules and detect COPD-related modules. The least absolute shrinkage and selection operator (LASSO) and the support vector machine recursive feature elimination (SVM-RFE) algorithms were chosen to identify the hub genes and the diagnostic ability. Three external datasets were used to identify

differences in the expression of hub genes. Real-time reverse transcription polymerase chain reaction (RT-qPCR) was used to verify the expression of hub genes.

Result: We identified 15 differentially expressed genes associated with aging (ARDEGs). The SVM-RFE and LASSO algorithms pinpointed four potential diagnostic biomarkers. Analysis of external datasets confirmed significant differences in PIK3R1 expression. RT-qPCR results indicated decreased expression of hub genes. The ROC curve demonstrated that PIK3R1 exhibited strong diagnostic capability for COPD.

Conclusion: We identified 15 differentially expressed genes associated with aging. Among them, PIK3R1 showed differences in external data sets and RT-qPCR results. Therefore, PIK3R1 may play an essential role in regulating aging involved in COPD.

Keywords: COPD; PIK3R1; aging; bioinformatics.

13

Review

Expert Rev Respir Med

. 2024 Aug 13:1-14.

doi: 10.1080/17476348.2024.2384024. Online ahead of print.

Clinical evidence and technical aspects of innovative technology and monitoring of chronic NIV in COPD: a narrative review

F Soleimani [1], D W Donker [1 2], E Oppersma [1], M L Duiverman [3 4]

Affiliations Expand

- PMID: 39138642

- DOI: 10.1080/17476348.2024.2384024

Abstract

Introduction: Chronic nocturnal noninvasive ventilation (NIV) improves outcomes in COPD patients with chronic hypercapnic respiratory failure. The aim of chronic NIV in COPD is to control chronic hypercapnic respiratory insufficiency and reduce symptoms of nocturnal hypoventilation, thereby improving quality of life. Chronic NIV care is more and more offered exclusively at home, enabling promising outcomes in terms of patient and caregiver satisfaction, hospital care consumption and cost reduction. Yet, to achieve and maintain optimal ventilation, during adaptation and follow-up, effective feasible (home) monitoring poses a significant challenge.

Areas covered: Comprehensive monitoring of COPD patients receiving chronic NIV requires integrating data from ventilators and assessment of the patient's status including gas exchange, sleep quality, and patient-reported outcomes. The present article describes the physiological background of monitoring during NIV and aims to provide an overview of existing methods for monitoring, assessing their reliability and clinical relevance.

Expert opinion: Patients on chronic NIV are 'ideal' candidates for home monitoring; the advantages of transforming hospital to home care are huge for patients and caregivers and for healthcare systems facing increasing patient numbers. Despite the multitude of available monitoring methods, identifying and characterizing the most relevant parameters associated with optimal patient well-being remains unclear.

Keywords: COPD; gas exchange; monitoring; noninvasive mechanical ventilation; patient-ventilator asynchrony; quality of life; sleep quality; telemonitoring.

. 2024 Aug 14;16(1):180.

doi: 10.1186/s13195-024-01511-x.

Herpes zoster and long-term risk of subjective cognitive decline

Tian-Shin Yeh [1 2 3 4 5 6], Gary C Curhan [7 8 9], Barbara P Yawn [10], Walter C Willett [11], Sharon G Curhan [7 8]

Affiliations Expand

- PMID: 39138535
- PMCID: PMC11323373
- DOI: 10.1186/s13195-024-01511-x

Abstract

Background: Herpes zoster (HZ), commonly known as "shingles," may contribute to cognitive decline through mechanisms such as neuroinflammation or direct neuronal injury. However, evidence on the longitudinal association between HZ and cognitive decline is conflicting and whether the risk differs by APOE ε4-carrier status has not been studied; prospective cohort studies on the association between HZ vaccination and cognitive decline are also lacking.

Methods: We included 149,327 participants from three large cohorts-the Nurses' Health Study (NHS), NHSII, and Health Professionals Follow-Up Study (HPFS)-to prospectively examine the association between HZ and subsequent subjective cognitive decline (SCD). Poisson regression was used to estimate the multivariable-adjusted relative risk (MVRR) of a 3-unit increment in SCD score according to years since HZ compared with participants with no history of HZ.

Results: Compared with individuals with no history of HZ, the MVRR (95% CI) of a 3-unit increment in SCD score was significantly and independently higher among individuals with a history of HZ, but the duration of time since HZ when the elevated risk of SCD was statistically significant differed among the cohorts. In NHS, HZ was associated with higher long-term risk of SCD; compared with individuals with no history of HZ, the MVRR (95% CI) of a 3-unit increment in SCD score was 1.14 (1.01, 1.32) for ≥ 13 years since HZ. In NHS II, HZ was associated with higher risk of SCD in both the short-term [MVRR 1.34 (1.18, 1.53) for 1-4 years] and long-term [MVRR 1.20 (1.08, 1.34) for ≥ 13 years since HZ]. In HPFS, an elevated risk of SCD was suggested across all time points. Among the subset of participants with information on APOE ε4, there was a suggestion that the association differed by APOE ε4 carrier status, but the results were not consistent between women and men. Among the subset of women with information on HZ vaccination, there was a suggestion that the long-

term risk of SCD may be greater among women who were not vaccinated against HZ.

Conclusions: Data from three large independent cohorts of women and men showed that HZ was associated with higher long-term risk of SCD, and the risk may differ by APOE ε4-carrier status.

Keywords: APOE ε4; Herpes zoster; Immunocompromise; Prospective cohort study; Shingles; Subjective cognitive decline; Vaccination.

Conflict of interest statement

SGC received an investigator-initiated grant from GlaxoSmithKline Biologicals SA to examine the long-term outcomes potentially associated with herpes zoster. GCC is an employee of OM1, receives support from an investigator-initiated grant from GlaxoSmithKline Biologicals SA to examine the long-term outcomes potentially associated with herpes zoster, and receives royalties from UpToDate for being an author and Section Editor. BY reports consulting with GlaxoSmithKline related to herpes zoster epidemiology and receipt of an investigator-initiated grant related to herpes zoster and chronic obstructive pulmonary disease. GSK was provided with the opportunity to review a preliminary version of this manuscript for factual accuracy, but the authors are solely responsible for the final content and interpretation. TSY and WCW have no disclosures to report.

- 66 references
- 1 figure

Supplementary info

MeSH terms, SubstancesExpand

Full text links

15

Am J Physiol Lung Cell Mol Physiol

-
-
-

. 2024 Aug 13.

doi: 10.1152/ajplung.00185.2024. Online ahead of print.

Citrullination, a novel post-translational modification of elastin, is involved in COPD Pathogenesis

Mark P Murphy [1], Marina Zieger [2], Michael Henry [3], Paula Meleady [4], Christian Mueller [5], Noel G McElvaney [1], Emer P Reeves [1]

Affiliations Expand

- PMID: 39137524

- DOI: 10.1152/ajplung.00185.2024

Abstract

Elastin is an extracellular matrix protein (ECM) that supports elasticity of the lung, and in patients with chronic obstructive pulmonary disease (COPD) and emphysema, the structural changes that reduce the amount of elastic recoil, lead to loss of pulmonary function. We recently demonstrated that elastin is a target of peptidyl arginine deiminase (PAD) enzyme-induced citrullination, thereby leading to enhanced susceptibility of this ECM protein to proteolysis. The current study aimed to investigate the impact of PAD activity *in vivo* and furthermore assessed whether pharmacological inhibition of PAD activity protects against pulmonary emphysema. Using a *Serpina1a-e* knockout mouse model, previously shown to develop inflammation-mediated emphysema, we validated the involvement of PADs in airway disease. In line with emphysema development, intratracheal administration of lipopolysaccharide in combination with PADs provoked significant airspace enlargement ($P < 0.001$) and diminished lung function, including loss of lung tissue elastance ($P = 0.0217$) and increases in lung volumes ($P = 0.0463$). Intraperitoneal treatment of mice with the PAD inhibitor, BB-Cl-amidine, prevented PAD/LPS-mediated lung function decline and emphysema and reduced levels of citrullinated airway elastin ($P = 0.0199$). These results provide evidence for the impact of PADs on lung function decline, indicating promising potential for the future development of PAD-based therapeutics for preserving lung function in patients with COPD.

Keywords: Peptidyl arginine deiminase enzymes; chronic obstructive pulmonary disease; citrullination; elastin.

Supplementary info

Grants and fundingExpand

Full text links

Proceed to details

Cite

Share

16

Ann Am Thorac Soc

-
-
-

. 2024 Aug 13.

doi: 10.1513/AnnalsATS.202402-196OC. Online ahead of print.

Use of Pulmonary Rehabilitation After COPD Hospitalization: An Analysis of Statewide Patient and Hospital Data

Whitney W Fu [1], Kristin P Hassett [1], Wassim W Labaki [2], Thomas S Valley [3], Michael P Thompson [4]

Affiliations Expand

- PMID: 39137381

- DOI: 10.1513/AnnalsATS.202402-196OC

Abstract

Rationale: Pulmonary rehabilitation (PR) is a clinically and cost-effective outpatient treatment for COPD that remains highly underutilized. Existing analyses of PR utilization patterns have been largely focused on patient characteristics, however hospital level analysis is lacking, and is needed to inform interventions aimed at improving utilization after COPD hospitalization.

Objective: To evaluate PR utilization across hospitals after COPD hospitalization in the state of Michigan, with the goal of characterizing hospital level variation and identifying the characteristics of high-performing hospitals.

Methods: This is a retrospective study of patients with a COPD hospitalization between 1/1/18 and 12/31/21 using claims data from the Michigan Value Collaborative (MVC) and hospital data from the American Hospital Association annual survey. Our primary outcome was initiation of PR within 30 days of discharge. Chi-square tests and ANOVA were used to test for differences in patient and hospital covariates. Multilevel logistic regression was used to analyze associations between patient covariates and the primary outcome, and to characterize hospital level variation.

Results: A total of 36,389 patients and 99 hospitals were included in the analysis. The majority of patients were older than 65 years of age, female, White, and Medicare fee-for-service insured. The rate of PR initiation within 30 days after

hospitalization was 0.8%. Adjusted rates of PR initiation by hospital ranged from 0.4-2.0%. Compared to the set reference groups, being female, in the 5th Distressed Community Index quintile, and being older than 85 years of age independently decreased the odds of initiating PR. Some variation in initiation rate was attributed to the hospital level (7% ICC 0.07, 95% CI 0.03-0.15). The median odds ratio was 1.6 for PR initiation by hospital.

Conclusions: Rates of PR initiation after COPD hospitalization are universally low across all hospitals, though there is some variation. Interventions targeted at patients alone are not sufficient to improve utilization. Hospital-based strategies to improve PR utilization after discharge, adapted from those being successfully used with cardiac rehabilitation, should be further explored.

17

Am J Respir Cell Mol Biol

. 2024 Aug 13.

doi: 10.1165/rcmb.2024-0344ED. Online ahead of print.

Sex Matters: A Deep Dive into Sex Differences in COPD

Yun Michael Shim [1], Jamie L MacLeod [2]

Affiliations Expand

- PMID: 39137333

- DOI: 10.1165/rcmb.2024-0344ED

No abstract available

Proceed to details

Cite

Share

18

PLoS Med

-
-
-

. 2024 Aug 13;21(8):e1004444.

doi: 10.1371/journal.pmed.1004444. Online ahead of print.

Identification of factors directly linked to incident chronic obstructive pulmonary disease: A causal graph modeling study

Robert W Gregg [1 2], Chad M Karoleski [3], Edwin K Silverman [4], Frank C Sciurba [3], Dawn L DeMeo [4], Panayiotis V Benos [1]

Affiliations Expand

- PMID: 39137208

- DOI: 10.1371/journal.pmed.1004444

Free article

Abstract

Background: Beyond exposure to cigarette smoking and aging, the factors that influence lung function decline to incident chronic obstructive pulmonary disease (COPD) remain unclear. Advancements have been made in categorizing COPD into emphysema and airway predominant disease subtypes; however, predicting which healthy individuals will progress to COPD is difficult because they can exhibit profoundly different disease trajectories despite similar initial risk factors. This study aimed to identify clinical, genetic, and radiological features that are directly linked-and subsequently predict-abnormal lung function.

Methods and findings: We employed graph modeling on 2,643 COPDGene participants (aged 45 to 80 years, 51.25% female, 35.1% African Americans; enrollment 11/2007-4/2011) with smoking history but normal spirometry at study enrollment to identify variables that are directly linked to future lung function abnormalities. We developed logistic regression and random forest predictive models for distinguishing individuals who maintain lung function from those who decline. Of the 131 variables analyzed, 6 were identified as informative to future lung function abnormalities, namely forced expiratory flow in the middle range (FEF25-

75%), average lung wall thickness in a 10 mm radius (Pi10), severe emphysema, age, sex, and height. We investigated whether these features predict individuals leaving GOLD 0 status (normal spirometry according to Global Initiative for Obstructive Lung Disease (GOLD) criteria). Linear models, trained with these features, were quite predictive (area under receiver operator characteristic curve or AUROC = 0.75). Random forest predictors performed similarly to logistic regression (AUROC = 0.7), indicating that no significant nonlinear effects were present. The results were externally validated on 150 participants from Specialized Center for Clinically Oriented Research (SCCOR) cohort (aged 45 to 80 years, 52.7% female, 4.7% African Americans; enrollment: 7/2007-12/2012) (AUROC = 0.89). The main limitation of longitudinal studies with 5- and 10-year follow-up is the introduction of mortality bias that disproportionately affects the more severe cases. However, our study focused on spirometrically normal individuals, who have a lower mortality rate. Another limitation is the use of strict criteria to define spirometrically normal individuals, which was unavoidable when studying factors associated with changes in normalized forced expiratory volume in 1 s (FEV1%predicted) or the ratio of FEV1/FVC (forced vital capacity).

Conclusions: This study took an agnostic approach to identify which baseline measurements differentiate and predict the early stages of lung function decline in individuals with previous smoking history. Our analysis suggests that emphysema affects obstruction onset, while airway predominant pathology may play a more important role in future FEV1 (%predicted) decline without obstruction, and FEF25-75% may affect both.

Conflict of interest statement

I have read the journal's policy and the authors of this manuscript have the following competing interests: RWG, CMK, and PVB have no competing interests. FCS has received grant support and consulting fees from Sanofi/Regeneron, AstraZeneca, Verona Pharma, Nuvaira, Gala Therapeutics, GlaxoSmithKline, Boehringer Ingelheim. EKS has received grant support from Bayer and Northpond Laboratories. DLD has received grant support from Bayer and the Alpha-1 Foundation.

Full text links

Proceed to details

Cite

Share

19

Clin Sci (Lond)

. 2024 Aug 13:CS20240721.

doi: 10.1042/CS20240721. Online ahead of print.

TGFβ1, SMAD and β-Catenin in pulmonary arteries of smokers, patients with small airway disease and COPD: potential drivers of EndMT

Prem Bhattarai [1], Wenying Lu [1], Ashutosh Hardikar [2], Archana Vijay Gaikwad [1], Surajit Dey [1], Affan Mahmood Shahzad [1], Stephen Myers [3], Andrew Williams [1], Darren Sutherland [4], Gurpreet Kaur Singhera [4], Tillie Hackett [5], Mathew S Eapen [6], Sukhwinder Singh Sohal [1]

Affiliations Expand

- PMID: 39136529

- DOI: 10.1042/CS20240721

Abstract

We previously reported pulmonary arterial remodelling and active endothelial to mesenchymal transition (EndMT) in smokers and patients with early COPD. In this study, we aimed to evaluate the role of different drivers of EndMT. Immunohistochemical staining for EndMT drivers, TGF-β1, pSMAD-2/3, SMAD-7, and β-catenin, was performed on lung resections from 46 subjects. Twelve were non-smoker-controls (NC), six normal lung function smokers (NLFS), nine patients with small-airway diseases (SAD), nine mild-moderate COPD-current smokers (COPD-CS) and ten COPD-ex-smokers (COPD-ES). Histopathological measurements were done using Image ProPlus softwarev7.0. We observed lower levels of total TGF-β1 ($p<0.05$) in all smoking groups than in the non-smoking control (NC). Across arterial sizes, smoking groups exhibited significantly higher ($p <0.05$) total and individual layer pSMAD-2/3 and SMAD-7 than in the NC group. The ratio of SAMD-7 to pSMAD-2/3 was higher in COPD patients compared to NC. Total β-catenin expression was significantly higher in smoking groups across arterial sizes ($p <0.05$), except for COPD-ES and NLFS groups in small and medium arteries, respectively. Increased total β-catenin was positively correlated with total S100A4 in small and medium arteries ($r= 0.35, 0.50$; $p=0.02, 0.01$, respectively), with vimentin in medium arteries ($r=0.42$, $p=0.07$), and with arterial thickness of medium and large arteries ($r= 0.34, 0.41$, $p=0.02, 0.01$, respectively). This is the first study uncovering active endothelial SMAD pathway independent of TGF-β1 in smokers, SAD, and COPD patients. Increased expression of β-catenin indicates its potential interaction with SMAD pathway, warranting further research to identify the deviation of this classical pathway.

Keywords: Endothelial to mesenchymal transition; Small airway disease; Smoking; TGF-β1/SMAD pathway; Vascular remodelling; chronic obstructive pulmonary disease.

Full text links

Proceed to details

Cite

Share

20

Review

Expert Opin Drug Deliv

-
-
-

. 2024 Aug 13.

doi: 10.1080/17425247.2024.2392790. Online ahead of print.

The effects of airway disease on the deposition of inhaled drugs

Chantal Darquenne [1], Timothy E Corcoran [2], Federico Lavorini [3], Alessandra Sorano [3], Omar S Usmani [4]

Affiliations Expand

- **PMID: 39136493**

- **DOI: 10.1080/17425247.2024.2392790**

Abstract

Introduction: The deposition of inhaled medications is the first step in the pulmonary pharmacokinetic process to produce a therapeutic response. Not only lung dose, but more importantly the distribution of deposited drug in the different regions of the lung determines local bioavailability, efficacy, and clinical safety. Assessing aerosol deposition patterns has been the focus of intense research that combines the fields of physics, radiology, physiology, and biology.

Areas covered: The review covers the physics of aerosol transport in the lung, experimental and in-silico modeling approaches to determine lung dose and aerosol deposition patterns, the effect of asthma, chronic obstructive pulmonary disease and cystic fibrosis on aerosol deposition, and the clinical translation potential of determining aerosol deposited dose.

Expert opinion: Recent advances in in-silico modeling and lung imaging have enabled the development of realistic subject-specific aerosol deposition models, albeit mainly in health. Accurate modeling of lung disease still requires additional refinements in existing imaging and modeling approaches to better characterize disease heterogeneity in peripheral airways. Nevertheless, recent patient-centric innovation in inhaler device engineering and the incorporation of digital technology have led to more consistent lung deposition and improved targeting of the distal airways, which better serve the clinical needs of patients.

Keywords: Aerosol dosimetry; COPD; asthma; gamma scintigraphy; in-silico modeling.

21

Biomark Med

-
-
-

. 2024 Aug 13:1-9.

doi: 10.1080/17520363.2024.2347199. Online ahead of print.

Blood *MALT1* reflects acute exacerbation risk and inflammation in elderly chronic obstructive pulmonary disease patients

Cui Liu [1], Jinsong Zhu [1], Lei Zhao [1], Guanying Li [1], Jiawei Sun [1], Shengli Zhang [1], Xijun Liang [1]

Affiliations Expand

- PMID: 39136445

- DOI: 10.1080/17520363.2024.2347199

Abstract

Aim: This study intended to investigate the ability of blood *MALT1* to estimate acute exacerbation risk in elderly chronic obstructive pulmonary disease (COPD) patients. Methods: Blood *MALT1* was detected in 176 elderly COPD patients (aged more than 60 years). Results: *MALT1* was elevated in patients with COPD acute exacerbation versus patients with stable COPD ($p < 0.001$). In patients with COPD acute exacerbation, *MALT1* was negatively related to forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) ($p = 0.024$) and FEV_1% predicted ($p = 0.002$), but positively linked with global initiative for chronic obstructive lung disease stage ($p = 0.005$). Conclusion: Blood *MALT1* reflects increased acute exacerbation risk and inflammation in elderly COPD patients.

Keywords: MALT1; acute exacerbation; chronic obstructive pulmonary disease; disease severity; inflammation.

Plain language summary

[Box: see text].

Full text links

View full text UNIMORE

Proceed to details

Cite

Share

22

Randomized Controlled Trial

JAMA

-
-
-

. 2024 Aug 13;332(6):462-470.

doi: 10.1001/jama.2024.8771.

Bisoprolol in Patients With Chronic Obstructive Pulmonary Disease at High Risk of Exacerbation: The BICS Randomized Clinical Trial

Graham Devereux [1 2 3], Seonaidh Cotton [2], Mintu Nath [4], Nicola McMeekin [5], Karen Campbell [2], Rekha Chaudhuri [6], Gourab Choudhury [7], Anthony De Soyza [8], Shona Fielding [4], Simon Gompertz [9], John Haughney [10], Amanda J Lee [4], Graeme MacLennan [2], Alyn Morice [11], John Norrie [12], David Price [10], Philip Short [13], Jorgen Vestbo [14], Paul Walker [3], Jadwiga Wedzicha [15], Andrew Wilson [16], Olivia Wu [5], Brian J Lipworth [17]

Affiliations Expand

- PMID: 38762800

- PMCID: PMC11322848 (available on 2024-11-19)

- DOI: 10.1001/jama.2024.8771

Abstract

Importance: Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide. Observational studies report that β-blocker use may be associated with reduced risk of COPD exacerbations. However, a recent trial reported that metoprolol did not reduce COPD exacerbations and increased COPD exacerbations requiring hospital admission.

Objective: To test whether bisoprolol decreased COPD exacerbations in people with COPD at high risk of exacerbations.

Design, setting, and participants: The Bisoprolol in COPD Study (BICS) was a double-blind placebo-controlled randomized clinical trial conducted in 76 UK sites (45 primary care clinics and 31 secondary clinics). Patients with COPD who had at least moderate airflow obstruction on spirometry (ratio of forced expiratory volume in the first second of expiration [FEV1] to forced vital capacity <0.7; FEV1 <80% predicted) and at least 2 COPD exacerbations treated with oral corticosteroids, antibiotics, or both in the prior 12 months were enrolled from October 17, 2018, to May 31, 2022. Follow-up concluded on April 18, 2023.

Interventions: Patients were randomly assigned to bisoprolol (n = 261) or placebo (n = 258). Bisoprolol was started at 1.25 mg orally daily and was titrated as tolerated during 4 sessions to a maximum dose of 5 mg/d, using a standardized protocol.

Main outcomes and measures: The primary clinical outcome was the number of patient-reported COPD exacerbations treated with oral corticosteroids, antibiotics, or both during the 1-year treatment period. Safety outcomes included serious adverse events and adverse reactions.

Results: Although the trial planned to enroll 1574 patients, recruitment was suspended from March 16, 2020, to July 31, 2021, due to the COVID-19 pandemic. Two patients in each group were excluded postrandomization. Among the 515 patients (mean [SD] age, 68 [7.9] years; 274 men [53%]; mean FEV1, 50.1%), primary

outcome data were available for 514 patients (99.8%) and 371 (72.0%) continued taking the study drug. The primary outcome of patient-reported COPD exacerbations treated with oral corticosteroids, antibiotics, or both was 526 in the bisoprolol group, with a mean exacerbation rate of 2.03/y, vs 513 exacerbations in the placebo group, with a mean exacerbation rate of 2.01/y. The adjusted incidence rate ratio was 0.97 (95% CI, 0.84-1.13; P = .72). Serious adverse events occurred in 37 of 255 patients in the bisoprolol group (14.5%) vs 36 of 251 in the placebo group (14.3%; relative risk, 1.01; 95% CI, 0.62-1.66; P = .96).

Conclusions and relevance: Among people with COPD at high risk of exacerbation, treatment with bisoprolol did not reduce the number of self-reported COPD exacerbations requiring treatment with oral corticosteroids, antibiotics, or both.

Trial registration: isrctn.org Identifier: ISRCTN10497306.

Conflict of interest statement

Conflict of Interest Disclosures: Dr Cotton reported receiving grants from the National Institute for Health and Care Research (NIHR) Health Technology Assessment (HTA) Programme (to her institution) during the conduct of the study. Dr Nath reported receiving grants from the University of Aberdeen during the conduct of the study. Dr Campbell reported receiving grants from the NIHR HTA Programme during the conduct of the study. Dr Chaudhuri reported receiving grants from AstraZeneca for an asthma study; meeting and lecture fees from AstraZeneca and GSK; lecture fees from Sanofi, Chiesi, and Teva Pharmaceuticals; advisory board meeting fees from Celltrion; and conference attendance support from Sanofi, Chiesi, and GSK outside the submitted work. Dr Choudhury reported receiving grants from GSK and AstraZeneca; receiving fees for lectures from AstraZeneca, GSK, and Chiesi during the conduct of the study; chairing the Lothian Respiratory Managed Clinical Network for respiratory medicine; being the Scottish Government lead for COPD Respiratory Care Action Plan planning; and chairing the Act on COPD group for AstraZeneca in Scotland. Dr De Soyza reported receiving grants from AstraZeneca, Bayer, GSK, Teva Pharmaceuticals, and Pfizer; and speaker fees and travel support fees from AstraZeneca, Bayer, GSK, Teva Pharmaceuticals, and Pfizer to attend congress outside the submitted work. Dr Fielding reported receiving grants from NIHR during the conduct of the study. Dr Gompertz reported receiving grants from NIHR and per-patient payments for recruited patients from the UK funding body, NIHR, during the conduct of the study. Dr Haughney reported receiving consulting fees from AstraZeneca and speaker fees from Chiesi outside the submitted work. Dr MacLennan reported receiving grants from NIHR to deliver the project to his institution during the conduct of the study. Dr Morice reported receiving grants from NIHR HTA during the conduct of the study; consulting fees from Merck; and grants from GSK, Trevi, and Nocion outside the submitted work. Dr Norrie reported receiving grants from the University of Aberdeen NIHR during the conduct of the study; receiving grants from GSK to the University of Edinburgh; receiving grants from RESPIRE to the University of Edinburgh; and chairing the MRC/NIHR Efficacy and Mechanism Evaluation Board, 2019 to present, outside the submitted work. Dr Price reported having advisory board membership and consultancy agreements with AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Novartis, Viatris, and Teva Pharmaceuticals; receiving grants and unrestricted funding for investigator-initiated studies (conducted through the Observational and Pragmatic Research Institute) from AstraZeneca, Chiesi, Viatris, Novartis,

Regeneron Pharmaceuticals, Sanofi Genzyme, and the UK National Health Service; receiving payment for lectures and speaking engagements from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, GSK, Viatris, Novartis, Regeneron Pharmaceuticals, Sanofi Genzyme, and Teva Pharmaceuticals; receiving payment for travel, accommodation, and meeting expenses from AstraZeneca, Boehringer Ingelheim, Novartis, and Teva Pharmaceuticals; having stock and stock options from AKL Research and Development Ltd, which produces phytopharmaceuticals; owning 74% of the social enterprise Optimum Patient Care Ltd (Australia and United Kingdom) and 92.61% of Observational and Pragmatic Research Institute (Singapore); having 5% shareholding in Timestamp, which develops adherence monitoring technology; being a peer reviewer for grant committees of the UK Efficacy and Mechanism Evaluation program and for HTA; and having been an expert witness for GSK. Dr Vestbo reported receiving advising fees from ALK-Abelló; advising and presentation fees from AstraZeneca and Chiesi; presentation fees from Boehringer Ingelheim; and advising fees from Teva Pharmaceuticals outside the submitted work. Dr Walker reported chairing the British Thoracic Society. Dr Wedzicha reported receiving grants from GSK, AstraZeneca, Boehringer Ingelheim, Novartis, Chiesi, and 37 Clinical; and consulting fees for serving on advisory boards for GSK, AstraZeneca, Boehringer Ingelheim, Novartis, Chiesi, Roche, Sanofi, Gilead, Empirico, Recipharm, EpiEndo, Bristol Myers Squibb, Pulmatrix, and Pieris outside the submitted work. Dr Wilson reported receiving institutional research funding from Aseptika, Brainomix, Celgene Corporation, GSK, and Insmed; speaker fees from Boehringer Ingelheim and Trevi Therapeutics; and support to attend conferences from Chiesi. Dr Wu reported receiving grants from NIHR during the conduct of the study. Dr Lipworth reported receiving grants from AstraZeneca, Sanofi, and Chiesi; and consulting fees from Glenmark and Lupin outside the submitted work. No other disclosures were reported.

Comment on

- β-Blockers in Chronic Obstructive Pulmonary Disease-Walking the Tightrope.

Han MK, Dransfield MT.JAMA. 2024 Aug 13;332(6):458-459. doi: 10.1001/jama.2024.8743.PMID: 38762796 No abstract available.

- 35 references

Supplementary info

Publication types, MeSH terms, SubstancesExpand

Full text links

Proceed to details

Cite

Share

23

Editorial

JAMA

-
-
-

. 2024 Aug 13;332(6):458-459.

doi: 10.1001/jama.2024.8743.

β-Blockers in Chronic Obstructive Pulmonary Disease-Walking the Tightrope

MeiLan K Han [1], Mark T Dransfield [2]

Affiliations Expand

- PMID: 38762796

- DOI: 10.1001/jama.2024.8743

No abstract available

Comment in

- Bisoprolol in Patients With Chronic Obstructive Pulmonary Disease at High Risk of Exacerbation: The BICS Randomized Clinical Trial.

Devereux G, Cotton S, Nath M, McMeekin N, Campbell K, Chaudhuri R, Choudhury G, De Soyza A, Fielding S, Gompertz S, Haughney J, Lee AJ, MacLennan G, Morice A, Norrie J, Price D, Short P, Vestbo J, Walker P, Wedzicha J, Wilson A, Wu O, Lipworth BJ.JAMA. 2024 Aug 13;332(6):462-470. doi: 10.1001/jama.2024.8771.PMID: 38762800 Clinical Trial.

Supplementary info

Publication types, MeSH terms, SubstancesExpand

Full text links

Review

Respir Care

.

.

.

. 2024 Aug 13:respcare.11805.

doi: 10.4187/respcare.11805. Online ahead of print.

Home Respiratory Strategies in Patients With COPD With Chronic Hypercapnic Respiratory Failure

Tyler Pitre [1], Saad Abbasi [2], George V Kachkovski [2], Levi Burns [2], Peter Huan [2], Jasmine Mah [3], Claudia Crimi [4], Andrea Cortegiani [5], Bram Rochwerg [6], Dena Zeraatkar [7]

Affiliations Expand

- PMID: 38569922

- DOI: 10.4187/respcare.11805

Abstract

Background: Home noninvasive ventilation (NIV) may improve chronic hypercarbia in COPD and patient-important outcomes. The efficacy of home high-flow nasal cannula (HFNC) as an alternative is unclear.

Methods: We searched MEDLINE, Embase, Cochrane CENTRAL, Scopus, and ClinicalTrials.gov for randomized trials of subjects from inception to March 31, 2023, and updated the search on July 14, 2023. We performed a frequentist network meta-analysis and assessed the certainty of the evidence using the Grading of Recommendations Assessment, Development, and Evaluation approach. We analyzed randomized controlled trials (RCTs) comparing NIV, HFNC, or standard care in adult subjects with COPD with chronic hypercapnic respiratory failure. Outcomes included mortality, COPD exacerbations, hospitalizations, and quality of life (St George Respiratory Questionnaire [SGRQ]).

Results: We analyzed 24 RCTs (1,850 subjects). We found that NIV may reduce the risk of death compared to standard care (relative risk 0.82 [95% CI 0.66-1.00]) and probably reduces exacerbations (relative risk 0.71 [95% CI 0.58-0.87]). HFNC probably reduces exacerbations compared to standard care (relative risk 0.77 [0.68-0.88]), but its effect on mortality is uncertain (relative risk 1.20 [95% CI 0.63-2.28]). HFNC probably improves SGRQ scores (mean difference -7.01 [95% CI -12.27 to -1.77]) and may reduce hospitalizations (relative risk 0.87 [0.69-1.09]) compared to standard care. No significant difference was observed between HFNC and NIV in reducing exacerbations.

Conclusions: Both NIV and HFNC reduce exacerbation risks in subjects with COPD compared to standard care. HFNC may offer advantages in improving quality of life.

Keywords: COPD; HFNC; NIV; network meta-analysis.

Supplementary info

Publication typesExpand

Full text links

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

1

Review

BMC Med

-
-
-

. 2024 Aug 15;22(1):331.

doi: 10.1186/s12916-024-03555-0.

Chronic kidney disease: detect, diagnose, disclose-a UK primary care perspective of barriers and enablers to effective kidney care

Stuart Stewart [1 2 3], Philip A Kalra [4], Tom Blakeman [5], Evangelos Kontopantelis [5], Howard Cranmer-Gordon [4], Smeeta Sinha [4 6]

Affiliations Expand

- **PMID: 39148079**
- **PMCID: PMC11328380**
- **DOI: 10.1186/s12916-024-03555-0**

Abstract

Chronic kidney disease (CKD) is a global public health problem with major human and economic consequences. Despite advances in clinical guidelines, classification systems and evidence-based treatments, CKD remains underdiagnosed and undertreated and is predicted to be the fifth leading cause of death globally by 2040. This review aims to identify barriers and enablers to the effective detection, diagnosis, disclosure and management of CKD since the introduction of the Kidney Disease Outcomes Quality Initiative (KDOQI) classification in 2002, advocating for a renewed approach in response to updated Kidney Disease: Improving Global Outcomes (KDIGO) 2024 clinical guidelines. The last two decades of improvements in CKD care in the UK are underpinned by international adoption of the KDIGO classification system, mixed adoption of evidence-based treatments and research informed clinical guidelines and policy. Interpretation of evidence within clinical and academic communities has stimulated significant debate of how best to implement such evidence which has frequently fuelled and frustratingly forestalled progress in CKD care. Key enablers of effective CKD care include clinical classification systems (KDIGO), evidence-based treatments, electronic health record tools, financially incentivised care, medical education and policy changes. Barriers to effective CKD care are extensive; key barriers include clinician concerns regarding overdiagnosis, a lack of financially incentivised care in primary care, complex clinical guidelines, managing CKD in the context of multimorbidity, bureaucratic burden in primary care, underutilisation of sodium-glucose co-transporter-2 inhibitor (SGLT2i) medications, insufficient medical education in CKD, and most recently - a sustained disruption to routine CKD care during and after the COVID-19 pandemic. Future CKD care in UK primary care must be informed by lessons of the last two decades. Making step change, over incremental improvements in CKD care at scale requires a renewed approach that addresses key barriers to detection, diagnosis, disclosure and management across traditional boundaries of healthcare, social care, and public health. Improved coding accuracy in primary care, increased use of SGLT2i medications, and risk-based care offer promising, cost-effective avenues to improve patient and population-level kidney health. Financial incentives generally improve achievement of care quality indicators - a review of financial and non-financial incentives in CKD care is urgently needed.

Keywords: COVID-19; Chronic kidney disease; Detection; Incentivised care; Integrated care systems; Population health; Primary care; Primary care networks; Screening.

Conflict of interest statement

SSt receives funding from Kidney Research UK; award number AHPF_001_20220705. SSi received honoraria from AZ, Boehringer, Menarini, Novartis, GSK, CSL Vifor and Bayer. PK received grant funding from CSL Vifor and Astellas, consulting fees from Astra Zeneca, Vifor, Unicyte and UCB, honoraria from Astra Zeneca, Pfizer, Pharmacosmos, Medice, GSK, Bayer and CSL Vifor. EK – None to declare. TB – No financial conflicts of interest; NHS England Think Kidneys Programme Board Member (2014–17); Royal College of General Practitioners' AKI Clinical Champion (2017–20); NHSE Renal Services Transformation Programme Post-AKI care Lead (2021–23); Specialist Committee Member for NICE AKI Quality

Standard (QS76) (2022–23); Kidney Disease Improving Global Outcomes (KDIGO) AKI Guideline Work Group (2023-To date). HCG none to declare.

- 94 references
- 1 figure

Supplementary info

Publication types, MeSH terms, Grants and fundingExpand

Full text links

Proceed to details

Cite

Share

2

Fam Pract

-
-
-

. 2024 Aug 14;41(4):419-425.

doi: 10.1093/fampra/cmac114.

Prescription of benzodiazepines and Z-drugs among older patients in primary care: a French, national, cohort study

Jonathan Yana [1 2], Laura Moscova [1], Julien Le Breton [1 3 4 5], Emmanuelle Boutin [3 6], Tiphaine Siess [1], Pascal Clerc [4 7], Sylvie Bastuji-Garin [3 8], Emilie Ferrat [1 2 3]

Affiliations Expand

- PMID: 36308516

- DOI: 10.1093/fampra/cmac114

Free article

Abstract

Background: In France, general practitioners (GPs) prescribe benzodiazepines and Z-drugs (BZD/ZDs) widely, and especially to older adults. Several characteristics of

patients and/or GPs linked to BZD/ZD overprescription have been described in the general population but not among older patients in primary care.

Objectives: To estimate the proportion of GP consultations by patients aged 65 and over that resulted in a BZD/ZD prescription, and determine whether any GP-related factors predicted BZD/ZD overprescription in this setting.

Methods: We analyzed sociodemographic and practice-related GP characteristics, and aggregated data on consultations recorded prospectively by 117 GPs in a database between 2000 and 2010. Next, we used logistic regression models to look for factors potentially associated with BZD/ZD overprescription (defined as an above-median prescription rate).

Results: The GPs' mean age at inclusion was 47.4 (7.1), and 87.9% were male. During the study period, the median (95% confidence interval) proportion of consultations with patients aged 65 and over resulting in a BZD/ZD prescription was 21.8% (18.1-26.1) (range per GP: 5-34.1%). In a multivariable analysis, a greater number of chronic disease (OR [95% CI] = 2.10 [1.22-3.64]), a greater number of drugs prescribed per consultation (5.29 [2.72-10.28]), and shorter study participation were independently associated with BZD/ZD overprescription.

Conclusions: BZD/ZD overprescription was associated with a greater chronic disease burden and the number of drugs prescribed per consultation but not with any sociodemographic or practice-related GP characteristics. Targeted actions are needed to help GPs limit their prescription of BZD/ZDs to older patients with multiple comorbidities and polypharmacy.

Keywords: aged; benzodiazepines; cohort studies; general practice; hypnotics and sedatives; inappropriate prescriptions.

Plain language summary

In France, general practitioners (GPs) prescribe benzodiazepines and Z-drugs (BZD/ZDs) widely, and especially to older adults. Even though BZD/ZDs may not have a favorable risk–benefit ratio in older patients, we lack data on GP-related factors that might influence BZD/ZD overprescription in our population. The objectives of the present study were to (i) estimate the proportion of GP consultations by patients aged 65 and over that resulted in a BZD/ZD prescription and (ii) identify GP-related factors that were predictive of overprescription. To achieve this goal, we analyzed consultation notes registered by 117 GPs in a database curated by the French Society of General Practice between 2000 and 2010. About 22% of consultations by patients aged 65 and over resulted in a BZD/ZD prescription. With regard to the GPs, we did not find any sociodemographic or practice-related characteristics associated with overprescription. A greater chronic disease burden and the number of drug prescriptions (other than BZD/ZDs) per consultation was independently associated with overprescription. Targeted actions are therefore needed to help GPs limit their prescription of BZD/ZDs in older patients with multimorbidity and polypharmacy.

service via the Permissions link on the article page on our site—for further information please contact journals.permissions@oup.com.

Supplementary info

MeSH terms, Substances, Grants and fundingExpand

Full text links

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

1

Allergy

-
-
-

. 2024 Aug 16.

doi: 10.1111/all.16283. Online ahead of print.

Indirect case-matched comparison of anti-IL4Rα versus anti-IL5Rα on airway hyperresponsiveness

Rory Chan [1], Kirsten Stewart [1], Chris RuiWen Kuo [1], Brian Lipworth [1]

Affiliations Expand

- PMID: 39152564

- DOI: 10.1111/all.16283

No abstract available

Keywords: airway hyperresponsiveness; asthma; benralizumab; dupilumab; mannitol.

- 6 references

Supplementary info

Publication types, Grants and fundingExpand

Full text links

Proceed to details

Cite

Share

2

Medicine (Baltimore)

-
-
-

. 2024 Aug 16;103(33):e39290.

doi: 10.1097/MD.0000000000039290.

The visceral adiposity index is associated with asthma, especially current asthma: A cross-sectional study of NHANES, 2003 to 2018

Jiao Xu [1], Xiaowu Liu [2], Jianlei Tang [3]

Affiliations Expand

- PMID: 39151544

- DOI: 10.1097/MD.0000000000039290

Free article

Abstract

To investigate the association between the visceral adiposity index (VAI) and asthma using data from National Health and Nutrition Examination Survey 2003 to 2018 by a cross-sectional study. We explored the potential relationship between the VAI and asthma incidence via a cross-sectional study of the National Health and Nutrition Examination Survey from 2003 to 2018. Multiple logistic regression analysis, restricted cubic spline analysis and subgroup analysis were performed. Among the 80,312 participants, 1984 had been told by a doctor or other health professional, and 1142 still had asthma. With all confounders controlled, the VAI was positively associated with asthma incidence (odds ratios 1.04, 95% confidence interval: 1.01, 1.08). When comparing the second, third, and fourth VAI quartiles to the lowest quartile, the adjusted odds ratios (95% confidence intervals) for asthma risk were 1.02 (0.86, 1.21), 1.14 (0.96, 1.36), and 1.18 (1, 1.39), respectively (P for trend = .02). Subgroup analysis revealed no significant interaction effect among the subgroups (P > .05). The positive association was stronger in current asthma patients (odds ratios 1.13, 95% confidence interval: 1.03, 1.24). When comparing the second, third, and fourth VAI quartiles to the lowest quartile, the adjusted odds ratios for current asthma risk were 1.15 (0.81, 1.64), 1.29 (0.91, 1.84), and 1.51 (1.01,

2.24), respectively (P for trend .04). The restricted cubic spline regression analysis did not reveal a nonlinear correlation between the VAI and asthma or current asthma. Subgroup analysis revealed a significant interaction effect between age (P for interaction = .03) and diabetes status (P for interaction = .02). Except in the age ≥60 years, Less than high school, normal body mass index subgroup, VAI, and current asthma were positively correlated. A positive relationship between the VAI and asthma incidence was observed. In particular, there was a strong positive correlation between the VAI score and current asthma. According to the subgroup analysis, more attention should be given to individuals aged 40 to 59 years who have diabetes.

Conflict of interest statement

The authors have no conflicts of interest to disclose.

- 33 references

Supplementary info

MeSH termsExpand

Full text links

Proceed to details

Cite

Share

3

Eur Respir J

-
-
-

. 2024 Aug 15:2400347.

doi: 10.1183/13993003.00347-2024. Online ahead of print.

Association of airway inflammation and smoking status with IL-33 level in sputum of patients with asthma or COPD

Mustafa Abdo [1 2], Frauke Pedersen [3 4 2], Anne-Marie Kirsten [4], Frederik Trinkmann [5 6], Espen E Groth [3], Thomas Bahmer [7], Henrik Watz [4], Klaus F Rabe [3 7]

Affiliations Expand

- **PMID: 39147409**

- **DOI: 10.1183/13993003.00347-2024**

Free article

No abstract available

Supplementary info

Publication typesExpand

Full text links

Proceed to details

Cite

Share

4

Meta-Analysis

BMJ Open Respir Res

-
-
-

. 2024 Aug 15;11(1):e001630.

doi: 10.1136/bmjresp-2023-001630.

Physical activity, sedentary behaviour, and childhood asthma: a European collaborative analysis

Marianne Eijkemans [1 2], Monique Mommers [3], Margreet W Harskamp-van Ginkel [4], Tanja G M Vrijkotte [4], Johnny Ludvigsson [5], Åshild Faresjö [6], Anna Bergström [7 8], Sandra Ekström [7 8], Veit Grote [9], Berthold Koletzko [9], Klaus Bønnelykke [10], Anders Ulrik Eliasen [10 11], Peter Bager [12], Mads Melbye [13 14 15 16], Isabella Annesi-Maesano [17], Nour Baïz [17], Henrique Barros [18 19 20], Ana Cristina Santos [18 19], Liesbeth Duijts [21 22 23], Sara M Mensink-Bout [21 22], Claudia Flexeder [24 25 26], Sibylle Koletzko [9 27], Tamara Schikowski [28], Merete Åse Eggesbø [29], Virissa Lenters [29 30], Guillermo Fernández-Tardón [31], Mikel Subiza-Perez [32 33], Judith Garcia-Aymerich [34], Mónica López-Vicente [35 36], Jordi Sunyer [33 35 37], Maties Torrent [38], Ferran Ballester [33 39 40], Cecily Kelleher [41], John

Mehegan [41], Andrea von Berg [42], Gunda Herberth [43], Marie Standl [24 44], Claudia E Kuehni [45 46], Eva S L Pedersen [45], Maria Jansen [47 48], Ulrike Gehring [49], Jolanda M A Boer [50], Graham Devereux [51], Steve Turner [52 53], Ville Peltola [54], Hanna Lagström [55 56], Hazel M Inskip [57 58], Katharine C Pike [59], Geertje W Dalmeijer [30], Cornelis K van der Ent [60], Carel Thijs [3]

Affiliations Expand

- PMID: 39147399

- DOI: 10.1136/bmjresp-2023-001630

Free article

Abstract

Objectives: To investigate the associations of physical activity (PA) and sedentary behaviour in early childhood with asthma and reduced lung function in later childhood within a large collaborative study.

Design: Pooling of longitudinal data from collaborating birth cohorts using meta-analysis of separate cohort-specific estimates and analysis of individual participant data of all cohorts combined.

Setting: Children aged 0-18 years from 26 European birth cohorts.

Participants: 136 071 individual children from 26 cohorts, with information on PA and/or sedentary behaviour in early childhood and asthma assessment in later childhood.

Main outcome measure: Questionnaire-based current asthma and lung function measured by spirometry (forced expiratory volume in 1 s (FEV_1), FEV_1/forced vital capacity) at age 6-18 years.

Results: Questionnaire-based and accelerometry-based PA and sedentary behaviour at age 3-5 years was not associated with asthma at age 6-18 years (PA in hours/day adjusted OR 1.01, 95% CI 0.98 to 1.04; sedentary behaviour in hours/day adjusted OR 1.03, 95% CI 0.99 to 1.07). PA was not associated with lung function at any age. Analyses of sedentary behaviour and lung function showed inconsistent results.

Conclusions: Reduced PA and increased sedentary behaviour before 6 years of age were not associated with the presence of asthma later in childhood.

Keywords: Asthma; Exercise; Paediatric asthma.

Conflict of interest statement

Competing interests: None declared.

Supplementary info

Publication types, MeSH termsExpand

Full text links

Proceed to details

Cite

Share

5

BMC Pulm Med

-
-
-

. 2024 Aug 14;24(1):394.

doi: 10.1186/s12890-024-03210-7.

The analysis of lung sounds in infants and children with a history of wheezing/asthma using an automatic procedure

Hiroyuki Mochizuki [1 2], Kota Hirai [3 4], Hiroyuki Furuya [5], Fumio Niimura [3 4], Kenta Suzuki [6], Tsuyoshi Okino [6], Miki Ikeda [6], Hironori Noto [6]

Affiliations Expand

- **PMID: 39143523**

- **PMCID: PMC11323603**

- **DOI: 10.1186/s12890-024-03210-7**

Abstract

Background: Lung sound analysis parameters have been reported to be useful biomarkers for evaluating airway condition. We developed an automatic lung sound analysis software program for infants and children based on lung sound spectral curves of frequency and power by leveraging machine learning (ML) technology.

Methods: To put this software program into clinical practice, in Study 1, the reliability and reproducibility of the software program using data from younger children were examined. In Study 2, the relationship between lung sound parameters and respiratory flow (L/s) was evaluated using data from older children.

In Study 3, we conducted a survey using the ATS-DLD questionnaire to evaluate the clinical usefulness. The survey focused on the history of wheezing and allergies, among healthy 3-year-old infants, and then measured lung sounds. The clinical usefulness was evaluated by comparing the questionnaire results with the results of the new lung sound parameters.

Results: In Studies 1 and 2, the parameters of the new software program demonstrated excellent reproducibility and reliability, and were not affected by airflow (L/s). In Study 3, infants with a history of wheezing showed lower FAP_0 and RPF_{75p} ($p < 0.001$ and $p = 0.025$, respectively) and higher PAP_0 ($p = 0.001$) than healthy infants. Furthermore, infants with asthma/asthma-like bronchitis showed lower FAP_0 ($p = 0.002$) and higher PAP_0 ($p = 0.001$) than healthy infants.

Conclusions: Lung sound parameters obtained using the ML algorithm were able to accurately assess the respiratory condition of infants. These parameters are useful for the early detection and intervention of childhood asthma.

Keywords: Asthma; Infants; Lung sound analysis; Machine learning; Software.

Conflict of interest statement

The authors declare no competing interests.

- **38 references**
- **3 figures**

Supplementary info

MeSH termsExpand

Full text links

6

BMJ Open Respir Res

-
-
-

. 2024 Aug 13;11(1):e002430.

doi: 10.1136/bmjresp-2024-002430.

Development and validation of a novel questionnaire to describe and assess sensations and triggers associated with refractory and unexplained chronic cough

Shannon Galgani [# 1], Chelsea Sawyer [# 2], Jenny King [3], Rachel Dockry [3], James Wingfield-Digby [3], Kimberly Holt [3], Joanne Mitchell [1], Shilpi Sen [1], Danielle Birchall [4], Francesca Solari [5], Jacky Smith [3], Janelle Yorke [6]

Affiliations Expand

- PMID: 39142695

- DOI: 10.1136/bmjresp-2024-002430

Free article

Abstract

Introduction: Refractory or unexplained chronic cough (RUCC) is a common clinical problem with no effective diagnostic tools. The Sensations and Triggers Provoking Cough questionnaire (TOPIC) was developed to characterise cough in RUCC versus cough in other conditions.

Methods: Content analysis of participant interviews discussing the sensations and triggers of chronic cough informed TOPIC development. Participants with chronic cough completed the draft-TOPIC (a subset repeating 5-7 days later), St George's Respiratory Questionnaire (SGRQ), Cough Severity Diary (CSD) and Global Rating of Change Scale. The draft-TOPIC item list was reduced in hierarchical and Rasch analysis to refine the questionnaire to the TOPIC.

Results: 49 items describing the triggers and sensations of cough were generated from participant interviews (RUCC n=14, chronic obstructive pulmonary disease (COPD) n=11, interstitial lung disease (ILD) n=10, asthma n=11, bronchiectasis n=3, cystic fibrosis n=7). 140 participants (median age 60.0 (19.0-88.0), female 56.4%; RUCC n=39, ILD n=38, asthma n=45, COPD n=6, bronchiectasis n=12) completed draft-TOPIC, where items with poor 'fit' for RUCC were removed to create TOPIC (8 trigger items, 7 sensation items). Median TOPIC score was significantly higher in RUCC (37.0) vs ILD (24.5, p=0.009) and asthma (7.0, p<0.001), but not bronchiectasis (20.0, p=0.318) or COPD (18.5, p=0.238), likely due to small sample sizes. The Rasch model demonstrated excellent fit in RUCC (χ^2=22.04, p=0.85; PSI=0.88); as expected. When all participant groups were included, fit was no longer demonstrated (χ^2=66.43, p=0.0001, PSI=0.89) due to the increased heterogeneity (CI=0.077). TOPIC correlated positively with SGRQ (r=0.47, p<0.001) and CSD (r=0.63, p<0.001). The test-retest reliability of TOPIC (intraclass correlation coefficient) was excellent (r=0.90, p<0.001).

Conclusions: High TOPIC scores in the RUCC patients suggest their cough is characterised by specific sensations and triggers. Validation of TOPIC in cough clinics may demonstrate value as an aid to identify features of RUCC versus cough in other conditions.

Keywords: Cough/Mechanisms/Pharmacology; Surveys and Questionnaires.

Conflict of interest statement

Competing interests: JAS is an inventor on a cough monitoring system that is licensed to Vitalograph who pays royalties to the hospital in which she works. She does not receive any royalties personally. She also advises pharmaceutical companies on the design and delivery of studies assessing new treatments for chronic cough. None of the other authors have competing interests.

Supplementary info

Publication types, MeSH termsExpand

Full text links

Proceed to details

Cite

Share

7

Clin Exp Allergy

-
-
-

. 2024 Aug 13.

doi: 10.1111/cea.14550. Online ahead of print.

Onset and Offset of Early Dupilumab Response Using Domiciliary Monitoring in Type 2 High Unified Airway Disease

Kirsten Stewart [1], Chris RuiWen Kuo [1], Rory Chan [1], Brian Lipworth [1]

Affiliations Expand

- **PMID: 39138649**

- **DOI: 10.1111/cea.14550**

No abstract available

Keywords: application; asthma; chronic rhinosinusitis; digital diary; dupilumab; nasal polyps; visual analogue scale.

Review

Expert Opin Drug Deliv

-
-
-

. 2024 Aug 13.

doi: 10.1080/17425247.2024.2392790. Online ahead of print.

The effects of airway disease on the deposition of inhaled drugs

Chantal Darquenne [1], Timothy E Corcoran [2], Federico Lavorini [3], Alessandra Sorano [3], Omar S Usmani [4]

Affiliations Expand

- PMID: 39136493

- DOI: 10.1080/17425247.2024.2392790

Abstract

Introduction: The deposition of inhaled medications is the first step in the pulmonary pharmacokinetic process to produce a therapeutic response. Not only lung dose, but more importantly the distribution of deposited drug in the different regions of the lung determines local bioavailability, efficacy, and clinical safety. Assessing aerosol deposition patterns has been the focus of intense research that combines the fields of physics, radiology, physiology, and biology.

Areas covered: The review covers the physics of aerosol transport in the lung, experimental and in-silico modeling approaches to determine lung dose and aerosol deposition patterns, the effect of asthma, chronic obstructive pulmonary disease and cystic fibrosis on aerosol deposition, and the clinical translation potential of determining aerosol deposited dose.

Expert opinion: Recent advances in in-silico modeling and lung imaging have enabled the development of realistic subject-specific aerosol deposition models, albeit mainly in health. Accurate modeling of lung disease still requires additional refinements in existing imaging and modeling approaches to better characterize disease heterogeneity in peripheral airways. Nevertheless, recent patient-centric innovation in inhaler device engineering and the incorporation of digital technology have led to more consistent lung deposition and improved targeting of the distal airways, which better serve the clinical needs of patients.

Keywords: Aerosol dosimetry; COPD; asthma; gamma scintigraphy; in-silico modeling.

Supplementary info

Publication types, Grants and fundingExpand

Full text links

9

J Asthma

-
-
-

. 2024 Aug 15:1-9.

doi: 10.1080/02770903.2024.2388774. Online ahead of print.

Association between cardiometabolic index and asthma in adults: evidence from NHANES 2005-2018

Chengjia Li [1], Tianwei Meng [1], Boyu Wang [1], Changxing Liu [1], Nan Jiang [2], Jiarui Li [1], Huijun Chen [3]

Affiliations Expand

- **PMID: 39105683**

- **DOI: 10.1080/02770903.2024.2388774**

Abstract

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

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

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

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

Keywords: Cardiometabolic index; NHANES; asthma; cross-sectional study.

10

Arch Dis Child

-
-
-

. 2024 Aug 16;109(9):724-729.

doi: 10.1136/archdischild-2023-326306.

Direct and indirect costs of paediatric asthma in the UK: a cost analysis

Charlotte T Kennedy [1], Graham S Scotland [2], Seonaidh Cotton [3], Stephen W Turner [4]

Affiliations Expand

- PMID: 38802171

- DOI: 10.1136/archdischild-2023-326306

Free article

Abstract

Objective: To estimate the cost of paediatric asthma from a UK National Health Service (NHS) and societal perspective and explore determinants of these costs.

Design: Cost analysis based on data from a large clinical trial between 2017 and 2019. Case report forms recorded healthcare resource use and productivity losses attributable to asthma over a 12-month period. These were combined with national unit cost data to generate estimates of health service and indirect costs.

Setting: Asthma clinics in primary and secondary care in England and Scotland.

Main outcome measures: Cost per asthma attack stratified by highest level of care received. Total annual health service and indirect costs. Modelled effect of sex, age, severity, number of attacks and adherence on total annual costs.

Results: Of 506 children included in the analysis, 252 experienced at least one attack. The mean (SD) cost per attack was £297 (806) (median £46, IQR 40-138) and the mean total annual cost to the NHS was £1086 (2504) (median £462, IQR 296-731). On average, children missed 6 days of school and their carers missed 13 hours of paid work, contributing to a mean annual indirect cost of £412 (879) (median £30, IQR 0-477). Health service costs increased significantly with number of attacks and participant age (>11 years). Indirect costs increased with asthma severity and number of attacks but were found to be lower in older children.

Conclusions: Paediatric asthma imparts a significant economic burden on the health service, families and society. Efforts to improve asthma control may generate significant cost savings.

Trial registration number: ISRCTN 67875351.

Keywords: Child Health; Health Care Economics and Organizations; Paediatrics; Respiratory Medicine.

Conflict of interest statement

Competing interests: None declared.

Supplementary info

MeSH termsExpand

Review

Eur Respir J

-
-
-

. 2024 Aug 15;64(2):2300826.

doi: 10.1183/13993003.00826-2023. Print 2024 Aug.

Advances in non-type 2 severe asthma: from molecular insights to novel treatment strategies

Tao Liu [1 2 3], Prescott G Woodruff [4], Xiaobo Zhou [5]

Affiliations Expand

- PMID: 38697650
- PMCID: PMC11325267
- DOI: 10.1183/13993003.00826-2023

Abstract

Asthma is a prevalent pulmonary disease that affects more than 300 million people worldwide and imposes a substantial economic burden. While medication can effectively control symptoms in some patients, severe asthma attacks, driven by airway inflammation induced by environmental and infectious exposures, continue to be a major cause of asthma-related mortality. Heterogeneous phenotypes of asthma include type 2 (T2) and non-T2 asthma. Non-T2 asthma is often observed in patients with severe and/or steroid-resistant asthma. This review covers the molecular mechanisms, clinical phenotypes, causes and promising treatments of

non-T2 severe asthma. Specifically, we discuss the signalling pathways for non-T2 asthma including the activation of inflammasomes, interferon responses and interleukin-17 pathways, and their contributions to the subtypes, progression and severity of non-T2 asthma. Understanding the molecular mechanisms and genetic determinants underlying non-T2 asthma could form the basis for precision medicine in severe asthma treatment.

Conflict of interest statement

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

. 2024 Aug 15:919:148502.

doi: 10.1016/j.gene.2024.148502. Epub 2024 Apr 24.

Cellular senescence-Related genes define the immune microenvironment and molecular characteristics in severe asthma patients

Qibin Lin [1], Zhishui Zheng [1], Haiyang Ni [1], Yaqing Xu [2], Hanxiang Nie [3]

Affiliations Expand

- PMID: 38670389

- DOI: 10.1016/j.gene.2024.148502

Abstract

Recent studies have shown that cellular senescence is involved in the pathogenesis of severe asthma (SA). The objective of this study was to investigate the role of cellular senescence-related genes (CSGs) in the pathogenesis of SA. Here, 54 differentially expressed CSGs were identified in SA patients compared to healthy control individuals. Among the 54 differentially expressed CSGs, 3 CSGs (ETS2, ETS1 and AURKA) were screened using the LASSO regression analysis and logistic regression analysis to establish the CSG-based prediction model to predict severe asthma. Moreover, we found that the protein expression levels of ETS2, ETS1 and AURKA were increased in the severe asthma mouse model. Then, two distinct senescence subtypes of SA with distinct immune microenvironments and molecular biological characteristics were identified. Cluster 1 was characterized by increased infiltration of immature dendritic cells, regulatory T cells, and other cells. Cluster 2 was characterized by increased infiltration levels of eosinophils, neutrophils, and other cells. The molecular biological characteristics of Cluster 1 included aerobic respiration and oxidative phosphorylation, whereas the molecular biological characteristics of Cluster 2 included activation of the immune response and immune receptor activity. Then, we established an Random Forest model to predict the senescence subtypes of SA to guide treatment. Finally, potential drugs were searched for each senescence subgroup of SA patients via the Connectivity Map database. A peroxisome proliferator-activated receptor agonist may be a potential therapeutic drug for patients in Cluster 1, whereas a tachykinin antagonist may be a potential therapeutic drug for patients in Cluster 2. In summary, CSGs are likely involved in the pathogenesis of SA, which may lead to new therapeutic options for SA patients.

Keywords: Cellular senescence; Immune microenvironment; Molecular biological characteristics; Senescence subtypes; Severe asthma; Treatment.

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.

Supplementary info

MeSH termsExpand

Full text links

Share

13

Case Reports

Intern Med

-
-
-

. 2024 Aug 15;63(16):2317-2320.

doi: 10.2169/internalmedicine.2918-23. Epub 2024 Jan 13.

Relief of Airflow Limitation and Airway Inflammation by Endoscopic Sinus Surgery in a Patient with Severe Asthma with Eosinophilic Chronic Rhinosinusitis

Kosuke Matsumori [1], Kazuki Hamada [2], Keiji Oishi [2], Masatoshi Okimura [2], Kosei Yonezawa [2], Michiya Watanabe [2], Yukari Hisamoto [2], Keita Murakawa [2], Ayumi Fukatsu-Chikumoto [2], Kazuki Matsuda [2], Syuichiro Ohata [2], Ryo Suetake [2], Toshiaki Utsunomiya [2], Yoriyuki Murata [2], Yoshikazu Yamaji [2], Maki Asami-Noyama [2], Nobutaka Edakuni [2], Tomoyuki Kakugawa [3], Tsunahiko Hirano [2], Kazuto Matsunaga [2]

Affiliations Expand

- PMID: 38220196

- DOI: 10.2169/internalmedicine.2918-23

Free article

Abstract

Although endoscopic sinus surgery (ESS) is beneficial in improving asthma symptoms, its impact on the lung function in patients with asthma and chronic rhinosinusitis remains unclear. We herein report a case of severe asthma with eosinophilic chronic rhinosinusitis, in which ESS substantially improved airflow limitation and concomitantly reduced fractional exhaled nitric oxide and blood eosinophil counts. ESS likely relieved airflow limitation by suppressing type 2 inflammatory pathways. This case highlights ESS as a promising strategy for achieving clinical remission in patients with severe asthma and chronic rhinosinusitis.

Keywords: airflow limitation; asthma remission; chronic rhinosinusitis; endoscopic sinus surgery; severe asthma.

Supplementary info

Publication types, MeSH termsExpand

Full text links

Proceed to details

Cite

Share

14

Meta-Analysis

Fam Pract

-
-
-

. 2024 Aug 14;41(4):460-469.

doi: 10.1093/fampra/cmad052.

The quality of paediatric asthma guidelines: evidence underpinning diagnostic test recommendations from a meta-epidemiological study

Elizabeth T Thomas [1], Sarah T Thomas [2], Rafael Perera [3], Peter J Gill [3 4 5], Susan Moloney [6 7 8], Carl J Heneghan [1]

Affiliations Expand

- PMID: 37196169

- PMCID: PMC11324322

- DOI: 10.1093/fampra/cmad052

Abstract

Background: Asthma is one of the most frequent reasons children visit a general practitioner (GP). The diagnosis of childhood asthma is challenging, and a variety of diagnostic tests for asthma exist. GPs may refer to clinical practice guidelines when

deciding which tests, if any, are appropriate, but the quality of these guidelines is unknown.

Objectives: To determine (i) the methodological quality and reporting of paediatric guidelines for the diagnosis of childhood asthma in primary care, and (ii) the strength of evidence supporting diagnostic test recommendations.

Design: Meta-epidemiological study of English-language guidelines from the United Kingdom and other high-income countries with comparable primary care systems including diagnostic testing recommendations for childhood asthma in primary care. The AGREE-II tool was used to assess the quality and reporting of the guidelines. The quality of the evidence was assessed using GRADE.

Results: Eleven guidelines met the eligibility criteria. The methodology and reporting quality varied across the AGREE II domains (median score 4.5 out of 7, range 2-6). The quality of evidence supporting diagnostic recommendations was generally of very low quality. All guidelines recommended the use of spirometry and reversibility testing for children aged ≥5 years, however, the recommended spirometry thresholds for diagnosis differed across guidelines. There were disagreements in testing recommendations for 3 of the 7 included tests.

Conclusions: The variable quality of guidelines, lack of good quality evidence, and inconsistent recommendations for diagnostic tests may contribute to poor clinician adherence to guidelines and variation in testing for diagnosing childhood asthma.

Keywords: asthma; child health; diagnostic tests; practice guideline; primary health care.

Conflict of interest statement

The authors declare no competing interests.

- **38 references**
- **2 figures**

Supplementary info

Publication types, MeSH terms, Grants and fundingExpand

Full text links

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

1

Am J Rhinol Allergy

-

. 2024 Aug 16:19458924241269786.

doi: 10.1177/19458924241269786. Online ahead of print.

The Evaluation Value of the Modified Lund-Kennedy Nasal Endoscopy Score on the Efficacy of Sublingual Immunotherapy for Allergic Rhinitis

Yinglong Zhang [1], Hong Jiang [1], Yu Long [1], Jie Li [1]

Affiliations Expand

- PMID: 39152637

- DOI: 10.1177/19458924241269786

Abstract

Objective: Allergic rhinitis (AR) is a growing public health problem worldwide. Respecting the significance of the modified Lund-Kennedy (MLK) score in rhinitis assessment, we delved into its evaluation value on the sublingual immunotherapy (SLIT) efficacy in AR patients.

Methods: Totally 100 AR patients were enrolled, with pre- and post-SLIT MLK score, total nasal symptoms score (TNSS), total medication score (TMS), visual analogue scale (VAS), inflammatory cytokines, and immune function-related parameters compared. The correlations of MLK score with TNSS/TMS/VAS, as well as with IL-4/INF-γ/eosinophil (EOS)/percentage/specific immunoglobulin (sIgE)/sIgG were assessed by Spearman correlation analysis. The value of MLK score on assessing SLIT efficacy in AR patients was analyzed.

Results: SLIT treatment reduced MLK/TNSS/TMS/VAS scores, abated IL-4 level/EOS percentage/sIgE, and elevated INF-γ/sIgG levels. MLK score was positively correlated with pre- and post-SLIT TNSS score ($r_{pre\text{-}treatment}$ = 0.592, $r_{post\text{-}treatment}$ = 0.756), TMS score ($r_{pre\text{-}treatment}$ = 0.385, $r_{post\text{-}treatment}$ = 0.718), VAS score ($r_{pre\text{-}treatment}$ = 0.369, $r_{post\text{-}treatment}$ = 0.704), IL-4 ($r_{pre\text{-}treatment}$ = 0.553, $r_{post\text{-}treatment}$ = 0.639), EOS percentage ($r_{pre\text{-}treatment}$ = 0.511, $r_{post\text{-}treatment}$ = 0.632), and sIgE ($r_{pre\text{-}treatment}$ = 0.472, $r_{post\text{-}treatment}$ = 0.524), and negatively with INF-γ ($r_{pre\text{-}treatment}$ = -0.418, $r_{post\text{-}treatment}$ = -0.578) and sIgG4 ($r_{pre\text{-}treatment}$ = -0.460, $r_{post\text{-}treatment}$ = -0.613). The MLK score had an area under curve of 0.846 (77.01% sensitivity, 76.92% specificity, 4 cut-off value) and 0.944 (91.67% sensitivity, 92.11% specificity, 2 cut-off value) for assessing SLIT treatment as effective and markedly effective for the patients, respectively.

Conclusion: The MLK score had good evaluation value on the efficacy of SLIT treatment in AR patients.

Keywords: SLIT; allergic rhinitis; curative effect; immune function; inflammatory cytokines; modified lund-Kennedy score; receiver operating characteristic curve; total medication score; total nasal symptoms score; visual analogue scale score.

Conflict of interest statement

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

Full text links

Proceed to details

Cite

Share

2

Int J Biometeorol

-
-
-

. 2024 Aug 14.

doi: 10.1007/s00484-024-02737-y. Online ahead of print.

Pollen effects in a changing climate: Ragweed pollen exposure and sleepiness in immunotherapy patients of a Southeastern Michigan allergy clinic

Peter S Larson [1 2], Allison L Steiner [3], Erica Bennion [4], Alan P Baptist [4 5], Marie S O'Neill [4 6], Carina J Gronlund [7 4]

Affiliations Expand

- **PMID: 39141134**

- **DOI: 10.1007/s00484-024-02737-y**

Abstract

Allergic rhino-conjunctivitis (AR) is a globally relevant health disorder characterized by sneezing, rhinorrhea and sleep disturbance. Ragweed (Ambrosia artemisiifolia) is a plant common to North America and an important allergen. Coarse methods of measuring airborne pollen counts are used to predict seasonal allergy symptoms. This research used a longitudinal study design with a novel, model-based raster of predicted pollen counts to test associations with self-reported symptoms of AR collected from patients receiving immunotherapy for pollen allergies at an allergy clinic. Researchers visited a clinic six times over three weeks. Immunotherapy patients were asked to fill out a brief intake survey on allergic and symptomatic profiles, daytime sleepiness, housing quality, and demographics. Participants responded to a daily, emailed survey on sleepiness and asthma symptoms for 21

days. Using the date and location of responses, ragweed pollen counts were extracted from a prognostic, model based raster (25km pixels). Lag associations of pollen counts with sleepiness were tested using a logistic regression model , adjusted for housing and demographic characteristics, in a distributed lag non-linear model (DLNM) framework. 49 people participated in the study. 26 (52%) were female. The mean age was 37.9 years. Asthma/allergy symptoms were not associated with ragweed pollen but sleepiness was highest two days after exposure (Estimate: 0.33 [0.04,0.62]). Subjects traveled widely during the study period. Intense exposures to ragweed pollen may be associated with daytime sleepiness within small exposure windows. Model-based predicted pollen counts could be used to study health impacts of pollen in people with disease severe enough to receive immunotherapy. Daytime sleepiness can affect productivity and injury risk, and pollen season length and allergenicity may be increasing with climate change. Thus our results may have important implications for population health.

Keywords: Allergic rhinitis; Allergy; Climate change; Pollen.

- 57 references

Supplementary info

Grants and fundingExpand

Full text links

Proceed to details

Cite

Share

3

Case Reports

Intern Med

-
-
-

. 2024 Aug 15;63(16):2317-2320.

doi: 10.2169/internalmedicine.2918-23. Epub 2024 Jan 13.

Relief of Airflow Limitation and Airway Inflammation by Endoscopic Sinus Surgery in a Patient with Severe Asthma with Eosinophilic Chronic Rhinosinusitis

Kosuke Matsumori [1], Kazuki Hamada [2], Keiji Oishi [2], Masatoshi Okimura [2], Kosei Yonezawa [2], Michiya Watanabe [2], Yukari Hisamoto [2], Keita Murakawa [2], Ayumi Fukatsu-Chikumoto [2], Kazuki Matsuda [2], Syuichiro Ohata [2], Ryo Suetake [2], Toshiaki Utsunomiya [2], Yoriyuki Murata [2], Yoshikazu Yamaji [2], Maki Asami-Noyama [2], Nobutaka Edakuni [2], Tomoyuki Kakugawa [3], Tsunahiko Hirano [2], Kazuto Matsunaga [2]

Affiliations Expand

- PMID: 38220196

- DOI: 10.2169/internalmedicine.2918-23

Free article

Abstract

Although endoscopic sinus surgery (ESS) is beneficial in improving asthma symptoms, its impact on the lung function in patients with asthma and chronic rhinosinusitis remains unclear. We herein report a case of severe asthma with eosinophilic chronic rhinosinusitis, in which ESS substantially improved airflow limitation and concomitantly reduced fractional exhaled nitric oxide and blood eosinophil counts. ESS likely relieved airflow limitation by suppressing type 2 inflammatory pathways. This case highlights ESS as a promising strategy for achieving clinical remission in patients with severe asthma and chronic rhinosinusitis.

Keywords: airflow limitation; asthma remission; chronic rhinosinusitis; endoscopic sinus surgery; severe asthma.

Supplementary info

Publication types, MeSH termsExpand

Full text links

chronic cough

1

BMJ Open Respir Res

-

-

. 2024 Aug 13;11(1):e002430.

doi: 10.1136/bmjresp-2024-002430.

Development and validation of a novel questionnaire to describe and assess sensations and triggers associated with refractory and unexplained chronic cough

Shannon Galgani [# 1], Chelsea Sawyer [# 2], Jenny King [3], Rachel Dockry [3], James Wingfield-Digby [3], Kimberly Holt [3], Joanne Mitchell [1], Shilpi Sen [1], Danielle Birchall [4], Francesca Solari [5], Jacky Smith [3], Janelle Yorke [6]

Affiliations Expand

- PMID: 39142695

- DOI: 10.1136/bmjresp-2024-002430

Free article

Abstract

Introduction: Refractory or unexplained chronic cough (RUCC) is a common clinical problem with no effective diagnostic tools. The Sensations and Triggers Provoking Cough questionnaire (TOPIC) was developed to characterise cough in RUCC versus cough in other conditions.

Methods: Content analysis of participant interviews discussing the sensations and triggers of chronic cough informed TOPIC development. Participants with chronic cough completed the draft-TOPIC (a subset repeating 5-7 days later), St George's Respiratory Questionnaire (SGRQ), Cough Severity Diary (CSD) and Global Rating of Change Scale. The draft-TOPIC item list was reduced in hierarchical and Rasch analysis to refine the questionnaire to the TOPIC.

Results: 49 items describing the triggers and sensations of cough were generated from participant interviews (RUCC n=14, chronic obstructive pulmonary disease (COPD) n=11, interstitial lung disease (ILD) n=10, asthma n=11, bronchiectasis n=3, cystic fibrosis n=7). 140 participants (median age 60.0 (19.0-88.0), female 56.4%; RUCC n=39, ILD n=38, asthma n=45, COPD n=6, bronchiectasis n=12) completed draft-TOPIC, where items with poor 'fit' for RUCC were removed to create TOPIC (8 trigger items, 7 sensation items). Median TOPIC score was significantly higher in RUCC (37.0) vs ILD (24.5, p=0.009) and asthma (7.0, p<0.001), but not bronchiectasis (20.0, p=0.318) or COPD (18.5, p=0.238), likely due to small sample sizes. The Rasch model demonstrated excellent fit in RUCC (χ^2=22.04, p=0.85; PSI=0.88); as expected. When all participant groups were included, fit was no longer demonstrated (χ^2=66.43, p=0.0001, PSI=0.89) due to the increased heterogeneity (CI=0.077). TOPIC correlated positively with SGRQ (r=0.47, p<0.001) and CSD (r=0.63, p<0.001). The test-retest reliability of TOPIC (intraclass correlation coefficient) was excellent (r=0.90, p<0.001).

Conclusions: High TOPIC scores in the RUCC patients suggest their cough is characterised by specific sensations and triggers. Validation of TOPIC in cough

clinics may demonstrate value as an aid to identify features of RUCC versus cough in other conditions.

Keywords: Cough/Mechanisms/Pharmacology; Surveys and Questionnaires.

Conflict of interest statement

Competing interests: JAS is an inventor on a cough monitoring system that is licensed to Vitalograph who pays royalties to the hospital in which she works. She does not receive any royalties personally. She also advises pharmaceutical companies on the design and delivery of studies assessing new treatments for chronic cough. None of the other authors have competing interests.

Supplementary info

Publication types, MeSH termsExpand

Full text links

2

Tuberc Respir Dis (Seoul)

-
-
-

. 2024 Aug 14.

doi: 10.4046/trd.2024.0015. Online ahead of print.

Secondary immunodeficiency and non-cystic fibrosis bronchiectasis

Sungmin Zo [1], Ji-Yong Moon [2], Kyung Hoon Min [3], Hyun Lee [2]

Affiliations Expand

- PMID: 39139079

- DOI: 10.4046/trd.2024.0015

Free article

Abstract

Bronchiectasis is a chronic respiratory disease characterized by the abnormal dilation of the bronchi that causes cough, sputum, and recurrent infections. Identifying the underlying cause is a critical aspect of managing bronchiectasis because it may be associated with various respiratory or systemic diseases. Immunodeficiency is a rare but important cause of bronchiectasis, and its treatability is a significant trait for bronchiectasis management. Primary immunodeficiencies in bronchiectasis are well recognized, but secondary immunodeficiencies remain under-reported and under-researched. Secondary immunodeficiencies may result from various diseases and conditions, such as hematologic malignancies, human immunodeficiency virus infection, renal transplantation, and the use of immunosuppressive drugs, and may contribute to the occurrence of bronchiectasis. Recurrent pulmonary and/or extra-pulmonary infections in bronchiectasis may indicate the presence of secondary immunodeficiency in patients with these underlying conditions. Regarding treatment, examining the underlying condition, managing bronchiectasis adequately, and prophylactic antibiotics (e.g., macrolide) and/or supplementing immunoglobulin G therapy may provide potential benefits. Considering the projected increase in the prevalence of secondary immunodeficiencies and bronchiectasis, future guidelines and research on the diagnosis and optimized treatment are needed.

3

Expert Opin Drug Discov

-
-
-

. 2024 Aug 13:1-14.

doi: 10.1080/17460441.2024.2391902. Online ahead of print.

The discovery and development of gefapixant as a novel antitussive therapy

Maria Gabriella Matera [1], Paola Rogliani [2], Clive P Page [3], Luigino Calzetta [4], Mario Cazzola [2]

Affiliations Expand

- **PMID: 39138872**

- **DOI: 10.1080/17460441.2024.2391902**

Abstract

Introduction: Gefapixant, a P2X 3 receptor antagonist, shows considerable potential in managing refractory or unexplained chronic cough. Clinical trials have consistently demonstrated its efficacy in significantly reducing cough frequency and alleviating associated symptoms. However, its adverse effect profile, particularly taste disturbances such as dysgeusia and hypogeusia, the incidence of which is dose-dependent, poses a significant challenge to patient compliance and overall treatment satisfaction.

Areas covered: The authors review the mechanism of action of gefapixant, the dose-dependent nature of its adverse effects and the findings from various clinical trials, including Phase 1, Phase 2, and Phase 3 studies. The authors also cover its regulatory status, post-marketing data, and its main competitors.

Expert opinion: Gefapixant represents a significant advancement in treating chronic cough. However, balancing efficacy and tolerability is crucial. Lower effective doses and potential combination therapies may mitigate taste disturbances. Patient education and close monitoring during treatment are also important for optimal outcomes. Further research is needed to refine dosing strategies to minimize side effects while maintaining therapeutic efficacy. This research and personalized treatment approaches are key to optimizing gefapixant therapy, ensuring improved management of chronic cough while reducing adverse effects. However, pharmaceutical trials and proposals must be adapted to align with each regulatory body's specific requirements and concerns.

Keywords: Adenosine triphosphate; P2X3 receptor antagonists; cough; dysgeusia; gefapixant; purinergic receptors.

. 2024 Aug 13.

doi: 10.7326/AITC202408200. Online ahead of print.

Gastroesophageal Reflux Disease

Kerry B Dunbar [1]

Affiliations Expand

- PMID: 39133924

- DOI: 10.7326/AITC202408200

Abstract

Gastroesophageal reflux disease (GERD) is a condition that occurs when reflux of gastric contents into the esophagus causes symptoms and/or complications. The prevalence of GERD in Western societies has been estimated at 30%, making it one of the most commonly encountered disorders in primary care. The spectrum of GERD includes typical symptoms of esophageal reflux (heartburn and/or regurgitation); esophageal injury (erosive esophagitis; stricture; Barrett esophagus; and, rarely, adenocarcinoma); and extraesophageal symptoms, such as hoarseness and chronic cough. Proper diagnosis and treatment of GERD includes symptom control, exclusion of other disorders, avoiding overuse of medications and invasive testing, and minimizing complications.

Conflict of interest statement

Disclosures: All relevant financial relationships have been mitigated. Disclosures can also be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M24-0087.

Supplementary info

Publication typesExpand

Full text links

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

1

Editorial

Eur Respir J

-
-
-

. 2024 Aug 15;64(2):2400997.

doi: 10.1183/13993003.00997-2024. Print 2024 Aug.

The importance of airway IL-1β in patients with bronchiectasis

Jeremy S Brown [1]

Affiliations Expand

- **PMID: 39147424**

- **DOI: 10.1183/13993003.00997-2024**

No abstract available

Conflict of interest statement

Conflict of interest: J.S. Brown has no relevant conflicts of interest to disclose.

Comment on

- **Airway IL-1β is related to disease severity and mucociliary function in bronchiectasis.**

Perea L, Bottier M, Cant E, Richardson H, Dicker AJ, Shuttleworth M, Giam YH, Abo-Leyah H, Finch S, Huang JT, Shteinberg M, Goeminne PC, Polverino E, Altenburg J, Blasi F, Welte T, Aliberti S, Sibila O, Chalmers JD, Shoemark A.Eur Respir J. 2024 Aug 15;64(2):2301966. doi: 10.1183/13993003.01966-2023. Print 2024 Aug.PMID: 38811046

Supplementary info

Publication types, MeSH terms, SubstancesExpand

Full text links

2

Observational Study

Respir Res

-
-
-

. 2024 Aug 14;25(1):308.

doi: 10.1186/s12931-024-02931-x.

The clinical impacts of lung microbiome in bronchiectasis with fixed airflow obstruction: a prospective cohort study

Yen-Fu Chen [1 2 3], Hsin-Han Hou [4], Ning Chien [5], Kai-Zen Lu [6], Chieh-Hua Lin [7 8], Yu-Chieh Liao [8], Kuo-Lung Lor [9], Jung-Yien Chien [2 6], Chung-Ming Chen [9], Chung-Yu Chen [1 2 3], Shih-Lung Cheng [10 11], Hao-Chien Wang [6 12], Po-Ren Hsueh [13 14 15 16], Chong-Jen Yu [17 18 19]

Affiliations Expand

- PMID: 39143556

- PMCID: PMC11325704

- DOI: 10.1186/s12931-024-02931-x

Abstract

Background: Airflow obstruction is a hallmark of disease severity and prognosis in bronchiectasis. The relationship between lung microbiota, airway inflammation, and outcomes in bronchiectasis with fixed airflow obstruction (FAO) remains unclear. This study explores these interactions in bronchiectasis patients, with and without FAO, and compares them to those diagnosed with chronic obstructive pulmonary disease (COPD).

Methods: This prospective observational study in Taiwan enrolled patients with either bronchiectasis or COPD. To analyze the lung microbiome and assess inflammatory markers, bronchoalveolar lavage (BAL) samples were collected for 16S rRNA gene sequencing. The study cohort comprised 181 patients: 86 with COPD, 46 with bronchiectasis, and 49 with bronchiectasis and FAO, as confirmed by spirometry.

Results: Patients with bronchiectasis, with or without FAO, had similar microbiome profiles characterized by reduced alpha diversity and a predominance of Proteobacteria, distinctly different from COPD patients who exhibited more

Firmicutes, greater diversity, and more commensal taxa. Furthermore, compared to COPD and bronchiectasis without FAO, bronchiectasis with FAO showed more severe disease and a higher risk of exacerbations. A significant correlation was found between the presence of Pseudomonas aeruginosa and increased airway neutrophilic inflammation such as Interleukin [IL]-1β, IL-8, and tumor necrosis factor-alpha [TNF]-α, as well as with higher bronchiectasis severity, which might contribute to an increased risk of exacerbations. Moreover, in bronchiectasis patients with FAO, the ROSE (Radiology, Obstruction, Symptoms, and Exposure) criteria were employed to classify individuals as either ROSE (+) or ROSE (-), based on smoking history. This classification highlighted differences in clinical features, inflammatory profiles, and slight microbiome variations between ROSE (-) and ROSE (+) patients, suggesting diverse endotypes within the bronchiectasis with FAO group.

Conclusion: Bronchiectasis patients with FAO may exhibit two distinct endotypes, as defined by ROSE criteria, characterized by greater disease severity and a lung microbiome more similar to bronchiectasis without FAO than to COPD. The significant correlation between Pseudomonas aeruginosa colonization and increased airway neutrophilic inflammation, as well as disease severity, underscores the clinical relevance of microbial patterns. This finding reinforces the potential role of these patterns in the progression and exacerbations of bronchiectasis with FAO.

Keywords: Bronchiectasis; Bronchoalveolar lavage; COPD; Fixed airflow obstruction; Lung microbiota; Neutrophilic inflammation; ROSE criteria.

Conflict of interest statement

The authors declare no competing interests.

- 62 references
- 8 figures

Supplementary info

Publication types, MeSH terms, Grants and fundingExpand

Full text links

3

BMJ Open Respir Res

. 2024 Aug 13;11(1):e002430.

doi: 10.1136/bmjresp-2024-002430.

Development and validation of a novel questionnaire to describe and assess sensations and triggers associated with refractory and unexplained chronic cough

Shannon Galgani [# 1], Chelsea Sawyer [# 2], Jenny King [3], Rachel Dockry [3], James Wingfield-Digby [3], Kimberly Holt [3], Joanne Mitchell [1], Shilpi Sen [1], Danielle Birchall [4], Francesca Solari [5], Jacky Smith [3], Janelle Yorke [6]

Affiliations Expand

- PMID: 39142695

- DOI: 10.1136/bmjresp-2024-002430

Free article

Abstract

Introduction: Refractory or unexplained chronic cough (RUCC) is a common clinical problem with no effective diagnostic tools. The Sensations and Triggers Provoking Cough questionnaire (TOPIC) was developed to characterise cough in RUCC versus cough in other conditions.

Methods: Content analysis of participant interviews discussing the sensations and triggers of chronic cough informed TOPIC development. Participants with chronic cough completed the draft-TOPIC (a subset repeating 5-7 days later), St George's Respiratory Questionnaire (SGRQ), Cough Severity Diary (CSD) and Global Rating of Change Scale. The draft-TOPIC item list was reduced in hierarchical and Rasch analysis to refine the questionnaire to the TOPIC.

Results: 49 items describing the triggers and sensations of cough were generated from participant interviews (RUCC n=14, chronic obstructive pulmonary disease (COPD) n=11, interstitial lung disease (ILD) n=10, asthma n=11, bronchiectasis n=3, cystic fibrosis n=7). 140 participants (median age 60.0 (19.0-88.0), female 56.4%; RUCC n=39, ILD n=38, asthma n=45, COPD n=6, bronchiectasis n=12) completed draft-TOPIC, where items with poor 'fit' for RUCC were removed to create TOPIC (8 trigger items, 7 sensation items). Median TOPIC score was significantly higher in RUCC (37.0) vs ILD (24.5, p=0.009) and asthma (7.0, p<0.001), but not bronchiectasis (20.0, p=0.318) or COPD (18.5, p=0.238), likely due to small sample sizes. The Rasch model demonstrated excellent fit in RUCC (χ^2=22.04, p=0.85; PSI=0.88); as expected. When all participant groups were included, fit was no longer demonstrated (χ^2=66.43, p=0.0001, PSI=0.89) due to the increased heterogeneity (CI=0.077). TOPIC correlated positively with SGRQ (r=0.47, p<0.001) and CSD (r=0.63, p<0.001). The

test-retest reliability of TOPIC (intraclass correlation coefficient) was excellent (r=0.90, p<0.001).

Conclusions: High TOPIC scores in the RUCC patients suggest their cough is characterised by specific sensations and triggers. Validation of TOPIC in cough clinics may demonstrate value as an aid to identify features of RUCC versus cough in other conditions.

Keywords: Cough/Mechanisms/Pharmacology; Surveys and Questionnaires.

Conflict of interest statement

Competing interests: JAS is an inventor on a cough monitoring system that is licensed to Vitalograph who pays royalties to the hospital in which she works. She does not receive any royalties personally. She also advises pharmaceutical companies on the design and delivery of studies assessing new treatments for chronic cough. None of the other authors have competing interests.

Supplementary info

Publication types, MeSH termsExpand

Full text links

4

Tuberc Respir Dis (Seoul)

-
-
-

. 2024 Aug 14.

doi: 10.4046/trd.2024.0015. Online ahead of print.

Secondary immunodeficiency and non-cystic fibrosis bronchiectasis

Sungmin Zo [1], Ji-Yong Moon [2], Kyung Hoon Min [3], Hyun Lee [2]

Affiliations Expand

- PMID: 39139079

- DOI: 10.4046/trd.2024.0015

Free article

Abstract

Bronchiectasis is a chronic respiratory disease characterized by the abnormal dilation of the bronchi that causes cough, sputum, and recurrent infections. Identifying the underlying cause is a critical aspect of managing bronchiectasis because it may be associated with various respiratory or systemic diseases. Immunodeficiency is a rare but important cause of bronchiectasis, and its treatability is a significant trait for bronchiectasis management. Primary immunodeficiencies in bronchiectasis are well recognized, but secondary immunodeficiencies remain under-reported and under-researched. Secondary immunodeficiencies may result from various diseases and conditions, such as hematologic malignancies, human immunodeficiency virus infection, renal transplantation, and the use of immunosuppressive drugs, and may contribute to the occurrence of bronchiectasis. Recurrent pulmonary and/or extra-pulmonary infections in bronchiectasis may indicate the presence of secondary immunodeficiency in patients with these underlying conditions. Regarding treatment, examining the underlying condition, managing bronchiectasis adequately, and prophylactic antibiotics (e.g., macrolide) and/or supplementing immunoglobulin G therapy may provide potential benefits. Considering the projected increase in the prevalence of secondary immunodeficiencies and bronchiectasis, future guidelines and research on the diagnosis and optimized treatment are needed.

5

Eur Respir J

-
-
-

. 2024 Aug 15;64(2):2301966.

doi: 10.1183/13993003.01966-2023. Print 2024 Aug.

Airway IL-1β is related to disease severity and mucociliary function in bronchiectasis

Lidia Perea [1 2], Mathieu Bottier [1 3], Erin Cant [1], Hollian Richardson [1], Alison J Dicker [1], Morven Shuttleworth [1], Yan Hui Giam [1], Hani Abo-Leyah [1], Simon Finch [1], Jeffrey T-J Huang [4], Michal Shteinberg [5], Pieter C Goeminne [6], Eva Polverino [7], Josje Altenburg [8], Francesco Blasi [9 10], Tobias Welte [11], Stefano Aliberti [12 13], Oriol Sibila [14], James D Chalmers [1 15], Amelia Shoemark [16 15]

Affiliations Expand

- PMID: 38811046

- DOI: 10.1183/13993003.01966-2023

Abstract

Rationale: The inflammasome is a key regulatory complex of the inflammatory response leading to interleukin-1β (IL-1β) release and activation. IL-1β amplifies inflammatory responses and induces mucus secretion and hyperconcentration in other diseases. The role of IL-1β in bronchiectasis has not been investigated.

Objectives: To characterise the role of airway IL-1β in bronchiectasis, including the association with mucus properties, ciliary function, airway inflammation, microbiome and disease severity.

Methods: Stable bronchiectasis patients were enrolled in an international cohort study (n=269). IL-1β was measured in sputum supernatant. A validation cohort also had sputum rheology and hydration measured (n=53). For analysis, patients were stratified according to the median value of IL-1β in the population (high *versus* low) to compare disease severity, airway infection, microbiome (16S rRNA sequencing), inflammation and caspase-1 activity. Primary human nasal epithelial cells grown in air-liquid interface culture were used to study the effect of IL-1β on cilia function.

Results: Patients with high sputum IL-1β had more severe disease, increased caspase-1 activity and an increased T-helper type 1, T-helper type 2 and neutrophil inflammatory response compared with patients with low IL-1β. The active-dominant form of IL-1β was associated with increased disease severity. High IL-1β was related to higher relative abundance of Proteobacteria in the microbiome and increased mucus solid content and viscoelastic properties. Chronic IL-1β treatment reduced the functionality of cilia and tight junctions of epithelial cells *in vitro*.

Conclusions: A subset of stable bronchiectasis patients show increased airway IL-1β, suggesting pulmonary inflammasome activation is linked with more severe disease, airway infection, mucus dehydration and epithelial dysfunction.

Conflict of interest statement

Conflict of interest: M. Shteinberg reports consulting fees from GSK, Boehringer Ingelheim, Kamada and Zambon; payment or honoraria for lectures, presentations,

manuscript writing or educational events from Insmed, Boehringer Ingelheim, GSK, AstraZeneca, Teva, Novartis, Kamada and Sanofi; support for attending meetings and/or travel from Novartis, Actelion, Boehringer Ingelheim, GSK and Rafa; participation on a data safety monitoring board or advisory board for Bonus Therapeutics, Israel; leadership roles for EMBARC Management, Israel Pulmonology Society Board, Israel Society for TB and Mycobacterial Diseases; receipt of equipment, materials, drugs, medical writing, gifts or other services from Trudell Medical Int; and is an associate editor of the American Journal of Respiratory and Critical Care Medicine. P.C. Goeminne reports payment or honoraria for lectures, presentations, manuscript writing or educational events from Insmed, GSK and Chiesi; support for attending meetings and/or travel from Chiesi; and participation on a data safety monitoring board or advisory board for Boehringer, GSK and Pfizer. E. Polverino reports grants or contracts from Grifols; consulting fees from Insmed, Bayer, Chiesi and Zambon; payment or honoraria for lectures, presentations, manuscript writing or educational events from Bayer, Chiesi, Grifols, GSK, Insmed, Menarini and Zambon; and support for attending meetings and/or travel from Insmed, Pfizer and Moderna. F. Blasi reports grants or contracts from AstraZeneca, Chiesi and Insmed; consulting fees from Menarini; and payment or honoraria for lectures, presentations, manuscript writing or educational events from AstraZeneca, Chiesi, GSK, Guidotti, Grifols, Insmed, Menarini, Novartis, OM Pharma, Pfizer, Sanofi, Viatris, Vertex and Zambon. S. Aliberti reports grants or contracts from Insmed Incorporated, Chiesi, Fisher and Paykel and GSK; royalties or licences from McGraw Hill; consulting fees from Insmed Incorporated, Insmed Italy, Insmed Ireland Ltd, Zambon Spa, AstraZeneca UK Ltd, AstraZeneca Pharmaceutical LP, CSL Behring GmbH, Grifols, Fondazione Internazionale Menarini, Moderna, Chiesi, MCD Italis SrL, Brahms, Physioassist SAS and GSK SpA; payment or honoraria for lectures, presentations, manuscript writing or educational events from GSK SpA, Thermofisher Scientific, Insmed Italy, Insmed Ireland, Zambon and Fondazione Internazionale Menarini; and participation on a data safety monitoring board or advisory board for Insmed Incorporated, Insmed Italy, AstraZeneca UK Ltd and MSD Italia SrL. J.D. Chalmers reports grants or contracts from AstraZeneca, Boehringer Ingelheim, Genentech, Gilead Sciences, GSK, Grifols, Insmed, LifeArc and Novartis; and consulting fees from AstraZeneca, Chiesi, GSK, Insmed, Grifols, Novartis, Boehringer Ingelheim, Pfizer, Janssen, Antabio and Zambon. A. Shoemark reports consulting fees from Spirovant and Translate Bio; payment or honoraria for lectures, presentations, manuscript writing or educational events from Translate Bio, Ethris and Insmed; and a leadership role in European Respiratory Society Clinical Research Collaborations (EMBARC, BEATPCD, AMR). The remaining authors have no potential conflicts of interest to disclose.

Comment in

- **The importance of airway IL-1β in patients with bronchiectasis.**

Brown JS.Eur Respir J. 2024 Aug 15;64(2):2400997. doi: 10.1183/13993003.00997-2024. Print 2024 Aug.PMID: 39147424 No abstract available.

Supplementary info

MeSH terms, SubstancesExpand

Full text links