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

1
Hum Vaccin Immunother

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. 2024 Dec 31;20(1):2343544.

doi: 10.1080/21645515.2024.2343544. Epub 2024 Apr 24.

Lung mucosal immunity to NTHi vaccine antigens: Antibodies in sputum of chronic obstructive pulmonary disease patients

Federica Baffetta[1], Cecilia Buonsanti[1], Luca Moraschini[1], Susanna Aprea[1], Martina Canè[2], Stefano Lombardi[1], Mario Contorni[1], Simona Rondini[3], Ashwani Kumar Arora[3], Monia Bardelli[1], Oretta Finco[1], Davide Serruto[1], Silvia Rossi Paccani[1]

Affiliations expand

- PMID: 38655676

- DOI: 10.1080/21645515.2024.2343544

Abstract

Chronic obstructive pulmonary disease (COPD) is a common chronic respiratory illness in older adults. A major cause of COPD-related morbidity and mortality is acute exacerbation of COPD (AECOPD). Bacteria in the lungs play a role in exacerbation development, and the most common pathogen is non-typeable *Haemophilus influenzae* (NTHi). A vaccine to prevent AECOPD containing NTHi surface antigens was tested in a clinical trial. This study measured IgG and IgA against NTHi vaccine antigens in sputum. Sputum samples from 40 COPD patients vaccinated with the NTHi vaccine were collected at baseline and 30 days after the second dose. IgG and IgA antibodies against the target antigens and albumin were analyzed in the sputum. We compared antibody signals before and after vaccination, analyzed correlation with disease severity and between sputum and serum samples, and assessed transudation. Antigen-specific IgG were absent before vaccination and present with high titers after vaccination. Antigen-specific IgA before and after vaccination were low but significantly different for two antigens. IgG correlated between sputum and serum, and between sputum and disease severity. Sputum albumin was higher in patients with severe COPD than in those with moderate COPD, suggesting changes in transudation played a role. We demonstrated that immunization with the NTHi vaccine induces antigen-specific antibodies in sputum. The correlation between IgG from sputum and serum and the presence of albumin in the sputum of severe COPD patients suggested transudation of antibodies from the serum to the lungs, although local IgG production could not be excluded.**Clinical Trial Registration**: NCT02075541.

Keywords: COPD exacerbations; COPD pathology; bacterial infection; infection control; respiratory infection.

Plain language summary

What is the context? Chronic obstructive pulmonary disease (COPD) is the most common chronic respiratory illness in older adults and the third leading cause of death worldwide.One bacterium in the lungs, non-typeable *Haemophilus influenzae* (NTHi), is responsible for acute exacerbation of the disease, characterized by an increase in airway wall inflammation and symptoms, leading to high morbidity and mortality.A vaccine targeting NTHi was previously developed but did not show efficacy in reducing exacerbations in COPD patients, probably because the vaccine did not elicit an immune response in the lung mucosae, where the bacteria are located.**What is the impact?** Parenteral immunization with new vaccines targeting NTHi is able to elicit immune defense at the level of lung mucosae.Now that antibodies can be measured in sputum, new vaccines against COPD exacerbations or other lung infections can be tested for efficacy in the actual target tissue.Also, lung immunity against specific pathogens can now be tested.**What is new?** We determined that antigen-specific antibodies were present in the lungs after vaccination; these were assessed in sputum after vaccination with NTHi surface antigens.NTHi-specific IgG were present in the lungs and appeared to have arrived

there primarily by transudation, a type of leakage from the serum to the lung mucosae.Transudation appeared to be stronger in severe than in moderate COPD patients.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated dataexpand

FULL TEXT LINKS

2

COPD

. 2024 Dec;21(1):2321379.

doi: 10.1080/15412555.2024.2321379. Epub 2024 Apr 24.

Diagnosis and Severity Assessment of COPD Using a Novel Fast-Response Capnometer and Interpretable Machine Learning

Leeran Talker[1], Cihan Dogan[1], Daniel Neville[2], Rui Hen Lim[1], Henry Broomfield[1], Gabriel Lambert[3], Ahmed Selim[1], Thomas Brown[2], Laura Wiffen[2], Julian Carter[4], Helen F Ashdown[5], Gail Hayward[5], Elango Vijaykumar[6], Scott T Weiss[7], Anoop Chauhan[2], Ameera X Patel[8]

Affiliations expand

- PMID: 38655897

- DOI: 10.1080/15412555.2024.2321379

Abstract

Introduction: Spirometry is the gold standard for COPD diagnosis and severity determination, but is technique-dependent, nonspecific, and requires administration by a trained healthcare professional. There is a need for a fast, reliable, and precise alternative diagnostic test. This study's aim was to use interpretable machine learning to diagnose COPD and assess severity using 75-second carbon dioxide (CO_2) breath records captured with TidalSense's N-Tidal™ capnometer.

Method: For COPD diagnosis, machine learning algorithms were trained and evaluated on 294 COPD (including GOLD stages 1-4) and 705 non-COPD participants. A logistic regression model was also trained to distinguish GOLD 1 from GOLD 4 COPD with the output probability used as an index of severity.

Results: The best diagnostic model achieved an AUROC of 0.890, sensitivity of 0.771, specificity of 0.850 and positive predictive value (PPV) of 0.834. Evaluating performance on all test capnograms that were confidently ruled in or out yielded PPV of 0.930 and NPV of 0.890. The severity determination model yielded an AUROC of 0.980, sensitivity of 0.958, specificity of 0.961 and PPV of 0.958 in distinguishing GOLD 1 from GOLD 4. Output probabilities from the severity determination model produced a correlation of 0.71 with percentage predicted FEV_1.

Conclusion: The N-Tidal™ device could be used alongside interpretable machine learning as an accurate, point-of-care diagnostic test for COPD, particularly in primary care as a rapid rule-in or rule-out test. N-Tidal™ also could be effective in monitoring disease progression, providing a possible alternative to spirometry for disease monitoring.

Keywords: Pulmonary Disease; capnometry; chronic obstructive; diagnosis; machine learning; severity assessment.

Br J Gen Pract

. 2024 Apr 25;74(742):e283-e289.

doi: 10.3399/BJGP.2023.0195. Print 2024 May.

Does shortage of GPs matter? A cross-sectional study of practice population life expectancy

Richard Baker[1], Louis S Levene[1], Christopher Newby[2], George K Freeman[3]

Affiliations expand

- PMID: 38621806

- PMCID: PMC11044019

- DOI: 10.3399/BJGP.2023.0195

Abstract

Background: There are not enough GPs in England. Access to general practice and continuity of care are declining.

Aim: To investigate whether practice characteristics are associated with life expectancy of practice populations.

Design and setting: A cross-sectional ecological study of patient life expectancy from 2015-2019.

Method: Selection of independent variables was based on conceptual frameworks describing general practice's influence on outcomes. Sixteen non-correlated variables were entered into multivariable weighted regression models: population characteristics (Index of Multiple Deprivation, region, % White ethnicity, and % on diabetes register); practice organisation (total NHS payments to practices expressed as payment per registered patient, full-time equivalent fully qualified GPs, GP registrars, advanced nurse practitioners, other nurses, and receptionists per 1000 patients); access (% seen on the same day); clinical

performance (% aged ≥45 years with blood pressure checked, % with chronic obstructive pulmonary disease vaccinated against flu, % with diabetes in glycaemic control, and % with coronary heart disease on antiplatelet therapy); and the therapeutic relationship (% continuity).

Results: Deprivation was strongly negatively associated with life expectancy. Regions outside London and White ethnicity were associated with lower life expectancy. Higher payment per patient, full-time equivalent fully qualified GPs per 1000 patients, continuity, % with chronic obstructive pulmonary disease having the flu vaccination, and % with diabetes with glycaemic control were associated with higher life expectancy; the % being seen on the same day was associated with higher life expectancy in males only. The variable aged ≥45 years with blood pressure checked was a negative predictor in females.

Conclusion: The number of GPs, continuity of care, and access in England are declining, and it is worrying that these features of general practice were positively associated with life expectancy.

Keywords: continuity of patient care; cross-sectional studies; health inequities; health workforce; life expectancy; primary health care.

Conflict of interest statement

The authors have declared no competing interests.

- 38 references

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

Br J Gen Pract

. 2024 Apr 25;74(742):e347-e354.

doi: 10.3399/BJGP.2023.0211. Print 2024 May.

Continuity and breaches in GP care and their associations with mortality for patients with chronic disease: an observational study using Norwegian registry data

Sahar Pahlavanyali[1], Øystein Hetlevik[1], Valborg Baste[2], Jesper Blinkenberg[2], Steinar Hunskaar[3]

Affiliations expand

- PMID: 38621803

- PMCID: PMC11044022

- DOI: 10.3399/BJGP.2023.0211

Abstract

Background: Despite many benefits of continuity of care with a named regular GP (RGP), continuity is deteriorating in many countries.

Aim: To investigate the association between RGP continuity and mortality, in a personal list system, in addition to examining how breaches in continuity affect this association for patients with chronic diseases.

Design and setting: A registry-based observational study using Norwegian primary care consultation data for patients with asthma, chronic obstructive pulmonary disease (COPD), diabetes mellitus, or heart failure.

Method: The Usual Provider of Care (UPC, value 0-1) Index was used to measure both disease-related ($UPC^{disease}$) and overall (UPC^{all}) continuity with the RGP at the time of consultation. In most analyses, patients who changed RGP during the study period were excluded. In the combined group of all four chronic conditions, the proportion of consultations with other GPs and out-of-hours services was calculated. Cox regression models calculated the associations between continuity during 2013-2016 and mortality in 2017-2018.

Results: Patients with COPD with $UPC^{disease}$ <0.25 had 47% increased risk of dying within 2 years (hazard ratio 1.47, 95% confidence interval = 1.22 to 1.64) compared with those with $UPC^{disease}$ ≥0.75. Mortality also increased with decreasing $UPC^{disease}$ for patients with heart failure and decreasing UPC^{all} for those with diabetes. In the combined group of chronic conditions, mortality increased with decreasing UPC^{all}. This latter association was also found for patients who had changed RGP.

Conclusion: Higher disease-related and overall RGP UPC are both associated with lower mortality. However, changing RGP did not significantly affect mortality, indicating a compensatory benefit of informational and management continuity in a patient list system.

Keywords: chronic disease; continuity of care; general practice; mortality; observational study; primary health care.

Conflict of interest statement

The authors have declared no competing interests.

- 35 references
- 3 figures

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Review

Eur Respir Rev

. 2024 Apr 24;33(172):230253.

doi: 10.1183/16000617.0253-2023. Print 2024 Apr 30.

Gait differences between COPD and healthy controls: systematic review and meta-analysis

Joren Buekers[1 2 3], Laura Delgado-Ortiz[4 2 3], Dimitrios Megaritis[5], Ashley Polhemus[6], Sofie Breuls[7 8], Sara C Buttery[9], Nikolaos Chynkiamis[5 10], Heleen Demeyer[7 11], Elena Gimeno-Santos[4 2 3 12], Emily Hume[5], Sarah Koch[4 2 3], Parris Williams[9 13], Marieke Wuyts[7], Nicholas S Hopkinson[9], Ioannis Vogiatzis[5 10], Thierry Troosters[7 8], Anja Frei[6], Judith Garcia-Aymerich[4 2 3]

Affiliations expand

- PMID: 38657998

- PMCID: PMC11040389

- DOI: 10.1183/16000617.0253-2023

Abstract

Background: Despite the importance of gait as a determinant of falls, disability and mortality in older people, understanding of gait impairment in COPD is limited. This study aimed to identify differences in gait characteristics during supervised walking tests between people with COPD and healthy controls.

Methods: We searched 11 electronic databases, supplemented by Google Scholar searches and manual collation of references, in November 2019 and updated the search in July 2021. Record screening and information extraction were performed independently by

one reviewer and checked for accuracy by a second. Meta-analyses were performed in studies not considered at a high risk of bias.

Results: Searches yielded 21 085 unique records, of which 25 were included in the systematic review (including 1015 people with COPD and 2229 healthy controls). Gait speed was assessed in 17 studies (usual speed: 12; fast speed: three; both speeds: two), step length in nine, step duration in seven, cadence in six, and step width in five. Five studies were considered at a high risk of bias. Low-quality evidence indicated that people with COPD walk more slowly than healthy controls at their usual speed (mean difference (MD) -19 $cm{\cdot}s^{-1}$, 95% CI -28 to -11 $cm{\cdot}s^{-1}$) and at a fast speed (MD -30 $cm{\cdot}s^{-1}$, 95% CI -47 to -13 $cm{\cdot}s^{-1}$). Alterations in other gait characteristics were not statistically significant.

Conclusion: Low-quality evidence shows that people with COPD walk more slowly than healthy controls, which could contribute to an increased falls risk. The evidence for alterations in spatial and temporal components of gait was inconclusive. Gait impairment appears to be an important but understudied area in COPD.

Conflict of interest statement

Conflict of interest: A. Polhemus is a paid employee of Merck & Co, Inc. and IQVIA AG. S.C. Buttery reports educational speaker fees for Pulmonx. J. Garcia-Aymerich reports speaker honoraria from Chiesi and a grant from AstraZeneca paid to her institution for a COVID-19-related project and is also a paid advisory board member for AstraZeneca. All other authors report no conflicts of interest.

- 80 references
- 3 figures

Observational Study

BMC Cardiovasc Disord

. 2024 Apr 26;24(1):227.

doi: 10.1186/s12872-024-03871-6.

Factors affecting hospitalization and mortality in a retrospective study of elderly patients with heart failure

Johan Björklund[1], Louise Pettersson[2 3], Björn Agvall[4 5]

Affiliations expand

- PMID: 38671397

- DOI: 10.1186/s12872-024-03871-6

Abstract

Background: Heart failure (HF) has a high prevalence in an elderly population and leads to a substantial hospitalization and mortality. The objective of this study was to investigate factors that affect hospitalization and mortality in an elderly population.

Methods: A retrospective observational study was conducted of HF patients aged 76-95 years residing in Region Halland, Sweden. Between 2013 and 2019, a total of 3134 patients received a novel diagnosis of HF and were subsequently monitored for one year using data from a healthcare database. The patients were categorized into HF-phenotypes according to ejection fraction (EF) and those with HF diagnose solely based on clinical criteria with no defined EF. Cox regression analysis for hospital admissions and mortality was evaluated adjusted for pharmacotherapies, healthcare utilization and clinical characteristics.

Results: Echocardiogram was performed in 56% of the patients and 51% were treated with recommended HF pharmacotherapy with betablockers combined with renin-angiotensin-aldosterone-system inhibition. The average number of inpatient days was 10.7 while the

average number of visits to primary care physician was 5.4 and 8.7 to primary care nurse respectively. A Cox regression analysis for hospital admissions and mortality revealed that an eGFR < 30 ml/min was associated with a hazard ratio (HR) of 1.88 (confidence interval [CI] 1.56-2.28), elevated NT-proBNP with an HR of 2.09 (CI 1.59-2.76), diabetes with an HR of 1.31 (CI 1.13-1.52), and chronic obstructive pulmonary disease with an HR of 1.51 (CI 1.29-1.77). Having a primary care physician visit was associated to an HR of 0.16 (CI 0.14-0.19), and the use of recommended heart failure pharmacotherapy was associated with an HR of 0.52 (CI 0.44-0.61).

Conclusions: In a Swedish elderly population with HF, factors such as advancing age, kidney dysfunction, elevated NT-proBNP levels, diabetes, and COPD were associated with an increased risk of both mortality and hospitalization. Conversely, patients who received recommended heart failure treatment and made regular visits to their primary care physician were associated with a decreased risk. This indicates that elderly patients with HF benefit from recommended HF treatment and highlights that follow-ups in primary care could be advantageous.

Keywords: Elderly; Heart failure; Hospitalization and mortality; Risk factors.

- 33 references

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

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Review

Adv Ther

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. 2024 Apr 25.

doi: 10.1007/s12325-024-02855-4. Online ahead of print.

Implications of Cardiopulmonary Risk for the Management of COPD: A Narrative Review

Dave Singh[1], MeiLan K Han[2], Nathaniel M Hawkins[3], John R Hurst[4], Janwillem W H Kocks[5,6,7,8], Neil Skolnik[9], Daiana Stolz[10], Jad El Khoury[11], Chris P Gale[12,13,14]

Affiliations expand

- PMID: 38664329

- DOI: 10.1007/s12325-024-02855-4

Abstract

Chronic obstructive pulmonary disease (COPD) constitutes a major global health burden and is the third leading cause of death worldwide. A high proportion of patients with COPD have cardiovascular disease, but there is also evidence that COPD is a risk factor for adverse outcomes in cardiovascular disease. Patients with COPD frequently die of respiratory and cardiovascular causes, yet the identification and management of cardiopulmonary risk remain suboptimal owing to limited awareness and clinical intervention. Acute exacerbations punctuate the progression of COPD in many patients, reducing lung function and increasing the risk of subsequent exacerbations and cardiovascular events that may lead to early death. This narrative review defines and summarises the principles of COPD-associated cardiopulmonary risk, and examines respiratory interventions currently available to modify this risk, as well as providing expert opinion on future approaches to addressing cardiopulmonary risk.

Keywords: Cardiopulmonary risk; Cardiovascular disease; Chronic obstructive pulmonary disease; Exacerbation; Inhaled therapy; Mortality.

- 95 references

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

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8

Review

Int J Clin Pharm

. 2024 Apr 25.

doi: 10.1007/s11096-024-01736-8. Online ahead of print.

Intraclass comparison of inhaled corticosteroids for the risk of pneumonia in chronic obstructive pulmonary airway disorder: a network meta-analysis and meta-regression

Kannan Sridharan[1], Gowri Sivaramakrishnan[2]

Affiliations expand

- PMID: 38664319

- DOI: 10.1007/s11096-024-01736-8

Abstract

Background: Inhalational corticosteroids (ICS) were observed to increase the pneumonia risk in chronic obstructive pulmonary airway disorder (COPD). However, it is unknown whether any differences exist between the drugs within the ICS class.

Aim: This study aimed to evaluate the risk of pneumonia associated with different ICS and identify factors that predict pneumonia in patients with moderate-to-severe COPD using a network meta-analysis.

Method: Electronic databases (Medline, Cochrane CENTRAL and Google Scholar) were searched for trials comparing ICS in COPD patients. The outcomes were pneumonia and serious pneumonia. Odds ratios (OR) with 95% confidence interval (95% CI) were estimated. Meta-regression was used to identify the predictors. The strength of evidence was graded using the Grading of Recommendations, Assessment, Development, and Evaluations approach.

Results: Sixty-six studies (103,347 participants) were included. Fluticasone (OR: 1.46; 95% CI: 1.26, 1.7), mometasone (OR: 2.2; 95% CI: 1.05, 4.6), and beclometasone (OR: 1.7; 95% CI: 1.1, 2.6) were observed with an increased pneumonia risk compared to placebo. Fluticasone (OR: 1.5; 95% CI: 1.3, 1.7) was observed with an increased risk of serious pneumonia. High doses (OR: 1.2; 95% CI: 1.03, 1.4), BMI ≥ 25 kg/m^2 (OR: 1.6; 95% CI: 1.1, 2.2), and history of exacerbations in the preceding year predicted the pneumonia risk. Evidence strength was moderate.

Conclusion: ICS class differences in pneumonia risk were observed in terms of pooled effect estimates but it is unlikely that any clinically relevant differences exist. Risk-benefit analysis supports ICS use in moderate-severe COPD.

Keywords: Beclometasone; Budesonide; Fluticasone; Mometasone.

- 101 references

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

9

Environ Sci Technol

. 2024 Apr 25.

doi: 10.1021/acs.est.4c00083. Online ahead of print.

Air Pollution and Cardiac Arrest: A More Significant Intermediate Role of COPD than Cardiac Events

Huihuan Luo[1], Qingli Zhang[1], Xia Meng[1], Haidong Kan[1], Renjie Chen[1,2]

Affiliations expand

- PMID: 38664224

- DOI: 10.1021/acs.est.4c00083

Abstract

No prior studies have linked long-term air pollution exposure to incident sudden cardiac arrest (SCA) or its possible development trajectories. We aimed to investigate the association between long-term exposure to air pollution and SCA, as well as possible intermediate diseases. Based on the UK Biobank cohort, Cox proportional hazard model was applied to explore associations between air pollutants and SCA. Chronic obstructive pulmonary disease (COPD) and major adverse cardiovascular events (MACE) were selected as intermediate conditions, and multistate model was fitted for trajectory analysis. During a median follow-up of 13.7 years, 2884 participants developed SCA among 458 237 individuals. The hazard ratios (HRs) for SCA were 1.04-1.12 per interquartile range increment in concentrations of fine particulate matter, inhalable particulate matter, nitrogen dioxide, and nitrogen oxides. Most prominently, air pollutants could induce SCA through promoting transitions from baseline health to COPD (HRs: 1.06-1.24) and then to SCA (HRs: 1.16-1.27). Less importantly, SCA could be developed through transitions from

baseline health to MACE (HRs: 1.02-1.07) and further to SCA (HRs: 1.12-1.16). This study provides novel and compelling evidence that long-term exposure to air pollution could promote the development of SCA, with COPD serving as a more important intermediate condition than MACE.

Keywords: air pollution; cardiovascular diseases; respiratory diseases; sudden cardiac arrest; trajectory analysis.

10

Review

Sheng Li Xue Bao

. 2024 Apr 25;76(2):346-352.

[Research progress of PD-L1 in inflammatory lung diseases]

[Article in Chinese]

A-Guo Li[1,2], Ai-Hua Cai[1,2], Hao-Ji Li[1,3], Qi-Ying Huang[1,2], Yong-Sheng Tu[1,4]

Affiliations expand

- PMID: 38658383

Free article

Abstract

Programmed death-ligand 1 (PD-L1) is important in maintaining central and peripheral immune tolerance in normal tissues, mediating tumor immune escape and keeping the balance between anti- and pro-inflammatory responses. Inflammation plays an important role in inflammatory lung diseases. This article reviews the research progress and potential clinical value of PD-L1 in inflammatory lung diseases, including acute lung injury, chronic obstructive pulmonary disease, asthma and idiopathic pulmonary fibrosis.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

11

J Asthma

. 2024 Apr 25:1-4.

doi: 10.1080/02770903.2024.2344168. Online ahead of print.

Mounier-Kuhn syndrome in poorly controlled asthma

Marta Solís García[1], Carolina Cisneros Serrano[1], Ana Sofía Martín Hernández[1], Jose María Eiros Bachiller[1], Celeste Marcos[1]

Affiliations expand

- PMID: 38639468

- DOI: 10.1080/02770903.2024.2344168

Abstract

Introduction: Mounier-Kuhn syndrome or tracheobronchomegaly, is a rare condition that consists of abnormal dilation of the trachea and main bronchi due to a pathological arrangement of smooth muscle fibers in this area.

Case report: We present the case of a 46-year-old woman with poorly controlled asthma and recurrent infections, who was diagnosed with Mounier-Kuhn syndrome through a computed tomography scan revealing an unusual enlargement of the trachea with associated bronchiectasis.

Results: The diagnosis of Mounier-Kuhn syndrome is radiological, involving measurement of the trachea where a diameter >25 mm in men and >21 mm in women is observed. While diagnosis is sometimes incidental, there is an association with respiratory diseases such as asthma or COPD, hence clinical suspicion is important in patients with poorly controlled underlying conditions who present with recurrent infections, inadequate secretion management, or even hemoptysis.

Conclusions: Despite its rarity, this syndrome significantly impacts patients' quality of life. Diagnosis and management involve comprehensive evaluations including computed tomography, with a multidisciplinary approach including pulmonologists and radiologists. Exploring its clinical features, associations with other respiratory diseases and treatment options is crucial in managing this rare respiratory condition.

Keywords: Asthma; bronchiectasis; computed tomography; hemoptysis; radiologists; tracheobronchomegaly.

12

Heart

. 2024 Apr 25;110(10):702-709.

doi: 10.1136/heartjnl-2023-323487.

Heightened long-term cardiovascular risks after exacerbation of chronic obstructive pulmonary disease

Nathaniel M Hawkins[1], Clementine Nordon[2], Kirsty Rhodes[2], Manisha Talukdar[3], Suzanne McMullen[4], Paul Ekwaru[4], Tram Pham[4], Arsh K Randhawa[3], Don D Sin[5]

Affiliations expand

- PMID: 38182279

- DOI: 10.1136/heartjnl-2023-323487

Free article

Abstract

Objective: To examine the risk of adverse cardiovascular (CV) events following an exacerbation of chronic obstructive pulmonary disease (COPD).

Methods: This retrospective cohort study identified patients with COPD using administrative data from Alberta, Canada from 2014 to 2019. Exposure periods were 12 months following moderate or severe exacerbations; the reference period was time preceding a first exacerbation. The primary outcome was the composite of all-cause death or a first hospitalisation for acute coronary syndrome, heart failure (HF), arrhythmia or cerebral ischaemia. Time-dependent Cox regression models estimated covariate-adjusted risks associated with six exposure subperiods following exacerbation.

Results: Among 1 42 787 patients (mean age 68.1 years and 51.7% men) 61 981 (43.4%) experienced at least one exacerbation and 34 068 (23.9%) died during median follow-up of 64 months. The primary outcome occurred in 43 564 (30.5%) patients with an incidence rate prior to exacerbation of 5.43 (95% CI 5.36 to 5.50) per 100 person-years. This increased to 95.61 per 100 person-years in the 1-7 days postexacerbation (adjusted HR 15.86, 95% CI 15.17 to 16.58) and remained increased for up to 1 year. The risk of both the composite and individual CV events was increased following either a moderate or a severe exacerbation, though greater and more prolonged following severe exacerbation. The highest magnitude of increased risk was observed for HF decompensation (1-7 days, HR 72.34, 95% CI 64.43 to 81.22).

Conclusion: Moderate and severe COPD exacerbations are independent risk factors for adverse CV events, especially HF decompensation. The impact of optimising COPD management on CV outcomes should be evaluated.

Keywords: Arrhythmias, Cardiac; Heart Failure; Risk Factors.

Conflict of interest statement

Competing interests: SM, PE and TP are employed by Medlior Health Outcomes Research Ltd. which received funding for the study from AstraZeneca UK. NMH participated on advisory boards for Bayer, BI, and Servier. He also received honoraria for speakers bureau from AZ, Novartis, and Servier and grants/research support from AZ and Novartis and consulting fees from AZ. DDS received honoraria for speaking engagements on the topic of COPD from AZ, GSK and BI. AKR, MT, CN, KR are the employees of AstraZeneca and may hold shares/stock options.

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Am J Respir Crit Care Med

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. 2024 Apr 24.

doi: 10.1164/rccm.202403-0649ED. Online ahead of print.

The Convoluted Journey to Unveil the Respiratory Syncytial Virus (RSV) in Chronic Obstructive Pulmonary Disease (COPD) Exacerbations: Old Paths and New Traces

Federico Baraldi[1], Marco Contoli[2], Alberto Papi[3]

Affiliations expand

- PMID: 38657157

- DOI: 10.1164/rccm.202403-0649ED

No abstract available

14

Infect Dis Ther

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. 2024 Apr 24.

doi: 10.1007/s40121-024-00963-w. Online ahead of print.

Systematic Literature Review on the Incidence of Herpes Zoster in

Populations at Increased Risk of Disease in the EU/EEA, Switzerland, and the UK

Alen Marijam [1], Nikki Vroom [2], Amit Bhavsar [3], Inga Posiuniene [3], Nicolas Lecrenier [3], Hilde Vroling [2]

Affiliations expand

- PMID: 38656653

- DOI: 10.1007/s40121-024-00963-w

Abstract

Introduction: Older adults and patients with underlying conditions such as immunocompromised (IC) populations (e.g., due to medical conditions or immunosuppressive medication) are at increased risk for herpes zoster (HZ). The first HZ recombinant vaccine for IC patients was approved in 2020. Limited evidence exists to inform decision-makers on HZ incidence in high-risk patients in Europe. This systematic literature review (SLR) assessed HZ incidence across 14 high-risk populations in the European Union/European Economic Area, Switzerland, and the United Kingdom.

Methods: An SLR (Embase, Medline, 2002-2022, observational studies) was performed to identify HZ incidence (i.e., primary outcomes: rate or cumulative; secondary: relative incidence) in type 1 and 2 diabetes mellitus (DM); chronic obstructive pulmonary disease and asthma; depression; rheumatic disorders (RD); multiple sclerosis (MS); inflammatory bowel diseases (IBD); psoriasis; lupus; human immunodeficiency virus (HIV); solid organ transplantation (SOT); solid organ malignancy (SOM); hematologic malignancy (HM); and stem cell transplantation (SCT).

Results: Of 776 unique records screened, 59 studies were included (24 reported incidence rate per 1000 person-years; two, cumulative incidence per 1000 persons; and 33, relative incidence). The highest incidence rates were reported for SOT (12.1-78.8) and SCT (37.2-56.1); HM (2.9-32.0); RD (0.41-21.5); lupus (11.0-16.5); IC mixed population (11.3-15.5); HIV/AIDS (11.8-13.0); chronic respiratory diseases (4.7-11.4); SOM (8.8-11.0); IBD (7.0-10.8); DM (4.3-9.4); depression (7.2-7.6); MS (5.7-6.3); and psoriasis (5.3-6.1). In many high-risk populations, HZ incidence was higher for older age groups, women, and some treatments.

Conclusions: The HZ incidence rate in Europe increased with age and varied across high-risk populations, with high rates for solid organ and stem cell transplants, cancer, and rheumatoid arthritis. Most studies were retrospective with methodological differences

affecting generalizability and comparability. Future studies should stratify data by IC population, age, sex, severity, medication, and study timeframe.

Keywords: Herpes zoster; High-risk populations; Incidence; Shingles; Systematic review.

- 83 references

15

Pulm Pharmacol Ther

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Evaluating the pharmacokinetics of beclometasone dipropionate/formoterol fumarate/glycopyrronium bromide delivered via pressurised metered-dose inhaler using a low global warming potential propellant

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Affiliations expand

- PMID: 38663512

- DOI: 10.1016/j.pupt.2024.102299

Abstract

Introduction: Use of propellants with high global warming potential (such as HFA-134a) for pressurised metered-dose inhalers (pMDIs) is being phased down. Switching to dry-powder inhalers may not be clinically feasible for all patients; an alternative is reformulation using propellants with low global warming potential. The combination of beclometasone dipropionate/formoterol fumarate/glycopyrronium bromide (BDP/FF/GB) is available for asthma or chronic obstructive pulmonary disease via pMDI using HFA-134a as propellant. This is being reformulated using the low global warming potential propellant HFA-152a. This manuscript reports three studies comparing BDP/FF/GB pharmacokinetics delivered via pMDI using HFA-152a vs HFA-134a.

Methods: The studies were four-way crossover, single-dose, randomised, double-blind, in healthy volunteers. In Studies 1 and 2, subjects inhaled four puffs of BDP/FF/GB (Study 1: 100/6/12.5 µg [medium-strength BDP]; Study 2: 200/6/12.5 µg [high-strength]), ingesting activated charcoal in two of the periods (once per propellant). In Study 3, subjects inhaled medium- and high-strength BDP/FF/GB using a spacer. All three studies compared HFA-152a vs HFA-134a in terms of lung availability and total systemic exposure of beclometasone-17-monopropionate (B17MP; active metabolite of BDP), BDP, formoterol and GB. Bioequivalence was concluded if the 90% confidence intervals (CIs) of the ratios between formulations of the geometric mean maximum plasma concentration (C_{max}) and area under the plasma concentration-time curve between time zero and the last quantifiable timepoint (AUC_{0-t}) for the analytes were between 80-125%.

Results: In Studies 1 and 2, systemic exposure bioequivalence (i.e., comparisons without charcoal block) was demonstrated, except for GB C_{max} in Study 2 (upper 90% CI 125.11%). For lung availability (i.e., comparisons with charcoal block), B17MP and formoterol demonstrated bioequivalence in both studies, as did BDP in Study 2; in Study 1, BDP upper CIs were 126.96% for C_{max} and 127.34% for AUC_{0-t}). In Study 1, GB AUC_{0-t} lower CI was 74.54%; in Study 2 upper limits were 135.64% for C_{max} and 129.12% for AUC_{0-t}. In Study 3, the bioequivalence criteria were met for BDP, B17MP and formoterol with both BDP/FF/GB strengths, and were met for GB AUC_{0-t}, although not for C_{max}. Both formulations were similarly well tolerated in all three studies.

Conclusions: Overall, while formal bioequivalence cannot be concluded for all analytes, these data suggest therapeutic equivalence of the new formulation with the existing

BDP/FF/GB pMDI formulation, therefore supporting reformulation using a propellant with low global warming potential.

Keywords: Total systemic exposure; adrenergic beta-2 receptor agonists; inhaled corticosteroids; inhaled triple therapy; lung bioavailability; muscarinic antagonists.

Conflict of interest statement

Declaration of Competing Interest FR, MC, AG, KM, AP and GP are employees of Chiesi, the sponsor of the studies. FV and JK are employees of SGS, the clinical trial site. Both have no conflicts of interest to report.

16

Observational Study

BMC Pulm Med

. 2024 Apr 23;24(1):200.

doi: 10.1186/s12890-024-03002-z.

Longitudinal assessment of interstitial lung abnormalities on CT in patients with COPD using artificial intelligence–

based segmentation: a prospective observational study

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Affiliations expand

- PMID: 38654252

- PMCID: PMC11036664

- DOI: 10.1186/s12890-024-03002-z

Abstract

Background: Interstitial lung abnormalities (ILAs) on CT may affect the clinical outcomes in patients with chronic obstructive pulmonary disease (COPD), but their quantification remains unestablished. This study examined whether artificial intelligence (AI)-based segmentation could be applied to identify ILAs using two COPD cohorts.

Methods: ILAs were diagnosed visually based on the Fleischner Society definition. Using an AI-based method, ground-glass opacities, reticulations, and honeycombing were segmented, and their volumes were summed to obtain the percentage ratio of interstitial lung disease-associated volume to total lung volume (ILDvol%). The optimal ILDvol% threshold for ILA detection was determined in cross-sectional data of the discovery and validation cohorts. The 5-year longitudinal changes in ILDvol% were calculated in discovery cohort patients who underwent baseline and follow-up CT scans.

Results: ILAs were found in 32 (14%) and 15 (10%) patients with COPD in the discovery (n = 234) and validation (n = 153) cohorts, respectively. ILDvol% was higher in patients with ILAs than in those without ILA in both cohorts. The optimal ILDvol% threshold in the discovery cohort was 1.203%, and good sensitivity and specificity (93.3% and 76.3%) were confirmed in the validation cohort. 124 patients took follow-up CT scan during 5 ± 1 years. 8 out of 124 patients (7%) developed ILAs. In a multivariable model, an increase in ILDvol% was associated with ILA development after adjusting for age, sex, BMI, and smoking exposure.

Conclusion: AI-based CT quantification of ILDvol% may be a reproducible method for identifying and monitoring ILAs in patients with COPD.

Keywords: Artificial intelligence; COPD; CT; Interstitial lung abnormality.

Conflict of interest statement

N.T., K.T., T.O., T.Handa and T.Hiari. were supported by grants from FUJIFILM Co., Ltd. And Daiichi Sankyo Company, Ltd. T. Handa is in the employment of the Collaborative Research Laboratory funded by Teijin Pharma Co., Ltd. S.S. received grants from FUJIFILM Co., Ltd., Nippon Boehringer Ingelheim, Philips-Respironics, Fukuda Denshi, Fukuda Lifetec Keiji, and ResMed. None of these companies had a role in the design or analysis of the study or in the writing of the manuscript. The other authors have no conflicts of interest to declare.

- 36 references
- 4 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grants and fundingexpand

FULL TEXT LINKS

UNIMORE

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17

Review

Naunyn Schmiedebergs Arch Pharmacol

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. 2024 Apr 23.

doi: 10.1007/s00210-024-03105-8. Online ahead of print.

Examining the contribution of Notch signaling to lung disease development

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Affiliations expand

- PMID: 38652281

- DOI: 10.1007/s00210-024-03105-8

Abstract

Notch pathway is a widely observed signaling system that holds pivotal functions in regulating various developmental cellular functions and operations. The Notch signaling mechanism is crucial for lung homeostasis, damage, and restoration. Based on increasing evidence, the Notch pathway has been identified, as critical for fibrosis and subsequently, the development of chronic fibroproliferative conditions in various organs and tissues. Recent research indicates that deregulation of Notch signaling correlates with the pathogenesis of significant pulmonary conditions, particularly chronic obstructive pulmonary disease (COPD), pulmonary fibrosis, asthma, pulmonary arterial hypertension (PAH), lung carcinoma, and pulmonary abnormalities in some hereditary disorders. In various cellular and tissue environments, and across both physiological and pathological conditions, multiple consequences of Notch activation have been observed. Studies have ascertained that the Notch signaling cascade exhibits close associations with various other signaling systems. This study provides an updated overview of Notch signaling's role, especially its link to fibrosis and its potential therapeutic implications. This study sheds light on the latest findings regarding the mechanisms and outcomes of irregular or lacking Notch activity in the onset and development of pulmonary diseases. As our insight into this signaling mechanism suggests that modulating Notch signaling might hold potential as a valuable additional therapeutic approach in upcoming research.

Keywords: Chronic obstructive pulmonary disease; Lung cancer; Lung fibrosis; Notch; Pulmonary arterial hypertension.

- 119 references

SUPPLEMENTARY INFO

18

Postgrad Med J

. 2024 Apr 23:qgae054.

doi: 10.1093/postmj/qgae054. Online ahead of print.

Umeclidinium plus vilanterol versus fluticasone propionate plus salmeterol for chronic obstructive pulmonary disease: a meta-analysis of randomized, controlled trials

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Affiliations expand

- PMID: 38652265

- DOI: 10.1093/postmj/qgae054

Abstract

Purpose: Umeclidinium plus vilanterol (UMEC/VI) is an inhaled long-acting muscarinic antagonist/long-acting beta2-agonist (LAMA/LABA), recently approved as once-daily

maintenance therapy for chronic obstructive pulmonary disease (COPD). This meta-analysis aims to assess the efficacy and safety of UMEC/VI compared with fluticasone propionate plus salmeterol (FP/SAL).

Methods: A systematic search was conducted by a trained medical research librarian across MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), and Chinese Biomedical Literature Database (CBM) for randomized controlled trials comparing UMEC/VI with FP/SAL in COPD patients. Two reviewers independently assessed the risk of bias and extracted data. The primary outcome was 0-24 h weighted mean (wm) forced expiratory volume in the first second (FEV1), trough FEV1. The secondary outcomes were other lung functions, symptoms, quality of life, and safety.

Results: Three studies with 2119 patients were included in the meta-analysis. UMEC/VI showed improvement in 0-24 h wm FEV1 (mean difference (MD) 0.08 L, 95% confidence interval (CI) 0.06 to 0.10, P < 0.01, moderate quality) and trough FEV1 (MD 0.09 L, 95% CI 0.07 to 0.11, P < 0.01, moderate quality) in comparison with FP/SAL. UMEC/VI statistically significantly improved all other lung functions compared with FP/SAL. However, there were no significant differences between UMEC/VI and FP/SAL in rescue-medication use, symptomatic endpoints, and health outcomes. UMEC/VI also demonstrated fewer drug-related adverse effects (risk ratio 0.47, 95% CI 0.27 to 0.82, P = 0.01, low quality).

Conclusions: UMEC/VI, when compared with FP/SAL, demonstrated significant improvements in lung functions with fewer drug-related adverse effects. However, the conclusion was limited by the scarcity of studies and long-term trials.

Keywords: COPD; fluticasone/salmeterol; meta-analysis; umeclidinium/vilanterol.

. 2024 Apr 22;24(1):500.

doi: 10.1186/s12913-024-10975-4.

Associations between outpatient care and later hospital admissions for patients with chronic obstructive pulmonary disease – a registry study from Norway

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Affiliations expand

- PMID: 38649963

- PMCID: PMC11036724

- DOI: 10.1186/s12913-024-10975-4

Abstract

Background: Although chronic obstructive pulmonary disease (COPD) admissions put a substantial burden on hospitals, most of the patients' contacts with health services are in outpatient care. Traditionally, outpatient care has been difficult to capture in population-based samples. In this study we describe outpatient service use in COPD patients and assess associations between outpatient care (contact frequency and specific factors) and next-year COPD hospital admissions or 90-day readmissions.

Methods: Patients over 40 years of age residing in Oslo or Trondheim at the time of contact in the period 2009-2018 were identified from the Norwegian Patient Registry (in- and outpatient hospital contacts, rehabilitation) and the KUHR registry (contacts with GPs, contract specialists and physiotherapists). These were linked to the Regular General Practitioner registry (characteristics of the GP practice), long-term care data (home and institutional care, need for assistance), socioeconomic and-demographic data from

Statistics Norway and the Cause of Death registry. Negative binomial models were applied to study associations between combinations of outpatient care, specific care factors and next-year COPD hospital admissions and 90-day readmissions. The sample consisted of 24,074 individuals.

Results: A large variation in the frequency and combination of outpatient service use for respiratory diagnoses (GP, emergency room, physiotherapy, contract specialist and outpatient hospital contacts) was apparent. GP and outpatient hospital contact frequency were strongly associated to an increased number of next-year hospital admissions (1.2-3.2 times higher by increasing GP frequency when no outpatient hospital contacts, 2.4-5 times higher in combination with outpatient hospital contacts). Adjusted for healthcare use, comorbidities and sociodemographics, outpatient care factors associated with lower numbers of next-year hospitalisations were fees indicating interaction between providers (7% reduction), spirometry with GP or specialist (7%), continuity of care with GP (15%), and GP follow-up (8%) or rehabilitation (18%) within 30 days vs. later following any current year hospitalisations. For 90-day readmissions results were less evident, and most variables were non-significant.

Conclusion: As increased use of outpatient care was strongly associated with future hospitalisations, this further stresses the need for good communication between providers when coordinating care for COPD patients. The results indicated possible benefits of care continuity within and interaction between providers.

Keywords: COPD; Hospital admissions; Outpatient care; Readmissions; Registry data.

Conflict of interest statement

The authors declare no competing interests.

- 35 references
- 1 figure

20

Respir Care

. 2024 Apr 22;69(5):557-565.

doi: 10.4187/respcare.11417.

In-Person Versus Remote 6-Minute Walk and Incremental Shuttle Walk Distances in Advanced Lung Disease

Lisa M Wickerson[1 2 3], Manoela de Paula Ferreira[4 2 3], Dmitry Rozenberg[4 5], Sunita Mathur[3 6], Lianne G Singer[4 5]

Affiliations expand

- PMID: 38649272

- DOI: 10.4187/respcare.11417

Abstract

Background: Field-based walk tests conducted remotely may provide an alternative method to a facility-based assessment of exercise capacity for people with advanced lung disease. This prospective study evaluated the level of agreement in the distance walked between a 6-min walk test (6MWT) and an incremental shuttle walk test performed by using standard in-person procedures and test variations and settings.

Methods: Adults with advanced lung disease underwent 4 study visits: (i) one in-person standard 6MWT (30-m corridor) and one in-person treadmill 6MWT, (ii) a remote 6MWT in a home setting (10-m corridor), (iii) 2 in-person standard incremental shuttle walk tests (10-m corridor), and (iv) a remote incremental shuttle walk test in a home setting (10-m corridor). A medical-grade oximeter measured heart rate and oxygen saturation before, during, and for 2 min after the tests.

Results: Twenty-eight participants were included (23 men [82%]; 64 (57-67) y old; 19 with interstitial lung disease [68%] and 9 with COPD [32%]; and 26 used supplemental oxygen (93%) [exertional [Formula: see text] of 0.46 ± 0.1]). There was no agreement between the tests. Greater walking distances were achieved with standard testing procedures: in-person

6MWT versus treadmill 6MWT (355 ± 68 vs *296* ± 97; *P* = .001; *n* = 28), in-person 6MWT versus remote 6MWT (349 ± 68 vs 293 ± 84; *P* = .001; *n* = 24), and in-person incremental shuttle walk test versus remote incremental shuttle walk test (216 ± 62 vs 195 ± 63; *P* = .03; *n* = 22).

Conclusions: Differences in the distance walked may have resulted from different track lengths, widths, and walking surfaces. This should be considered in test interpretation if tests are repeated under different conditions.

Keywords: Field-based walk tests; 6-minute walk test; Incremental Shuttle Walk Test; lung disease; lung transplantation; pulmonary rehabilitation; telerehabilitation.

Conflict of interest statement

The authors have disclosed no conflicts of interest.

21

Med Biol Eng Comput

. 2024 Apr 22.

doi: 10.1007/s11517-024-03099-8. Online ahead of print.

Explicate molecular landscape of combined pulmonary fibrosis and emphysema through explainable artificial intelligence: a comprehensive

analysis of ILD and COPD interactions using RNA from whole lung homogenates

Nakul Tanwar[1], Yasha Hasija[2]

Affiliations expand

- PMID: 38644448

- DOI: 10.1007/s11517-024-03099-8

Abstract

Combined pulmonary fibrosis and emphysema (CPFE) presents a unique challenge in respiratory disorders, merging features of interstitial lung disease (ILD) and chronic obstructive pulmonary disease (COPD). Using the random forest algorithm, our study thoroughly examines the molecular details of CPFE. Analyzing gene expression datasets from GSE47460 (ILD: 254, COPD: 220, control: 108), we identify key genes namely ADRB2, CDH3, IRS2, MATN3, CD38, PDIA4, VEGFC, and among twenty others, crucial in airway regulation, lung function, and apoptosis, shaping the complex pathogenesis of CPFE. Additionally, miRNAs (hsa-mir-101-3p, hsa-mir-1343-3p, hsa-mir-27a-3p, and miR-16-5p) showcase regulatory impacts on CPFE-related molecular pathways. Our machine learning model unveils these intricate interactions, offering a comprehensive insight into CPFE's molecular mechanisms. This research not only pinpoints potential therapeutic targets and biomarkers but also opens avenues for innovative approaches in managing CPFE, linking ILD and COPD within this complex respiratory condition.

Keywords: COPD; CPFE; Explainable artificial intelligence; ILD; SHAP.

- 37 references

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

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Br J Gen Pract

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. 2024 Apr 25;74(742):e307-e314.

doi: 10.3399/BJGP.2023.0114. Print 2024 May.

Predicting anticipated benefit from an extended consultation to personalise care in multimorbidity: a development and internal validation study of a prioritisation algorithm in general practice

Mieke Jl Bogerd[1], Collin Jc Exmann[1], Pauline Slottje[1], Jettie Bont[1], Hein Pj Van Hout[1]

Affiliations expand

- PMID: 38164549

- PMCID: PMC11044021

- DOI: 10.3399/BJGP.2023.0114

Abstract

Background: Persons with multimorbidity may gain from person-centred care compared with the current protocolised chronic-disease management in Dutch general practice. Given time constraints and limited resources, it is essential to prioritise those most in need of an assessment of person-centred chronic-care needs.

Aim: To develop and validate a prioritisation algorithm based on routine electronic medical record (EMR) data that distinguishes between patients with multimorbidity who would, and those who would not, benefit from an extended person-centred consultation to assess person-centred chronic-care needs, as judged by GPs.

Design and setting: A mixed-methods study was conducted in five general practices in the north-west region of the Netherlands. Four out of the five practices were situated in rural areas.

Method: Multivariable logistic regression using EMR data to predict the GPs' judgement on patients' anticipated benefit from an extended consultation, as well as a thematic analysis of a focus group exploring GPs' clinical reasoning for this judgement were conducted. Internal validation was performed using 10-fold cross-validation. Multimorbidity was defined as the presence of ≥3 chronic conditions.

Results: In total, EMRs from 1032 patients were included in the analysis; of these, 352 (34.1%) were judged to have anticipated benefit. The model's cross-validated C-statistic was 0.72 (95% confidence interval = 0.70 to 0.75). Calibration was good. Presence of home visit(s) and history of myocardial infarction were associated with anticipated benefit. Thematic analysis revealed three dimensions feeding anticipated benefit: GPs' cause for concern, patients' mindset regarding their conditions, and balance between received care/expected care needed.

Conclusion: This algorithm may facilitate automated prioritisation, potentially avoiding the need for GPs to personally triage the whole practice population that has multimorbidity. However, external validation of the algorithm and evaluation of actual benefit of consultation is recommended before implementation.

Keywords: general practice; multimorbidity; person-centred care; primary care.

Conflict of interest statement

The authors have declared no competing interests.

- 34 references
- 2 figures

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

2

Eur J Phys Rehabil Med

. 2024 Apr 24.

doi: 10.23736/S1973-9087.24.08486-7. Online ahead of print.

Frailty recommendations and guidelines: an evaluation of the implementability and a critical appraisal of clinical applicability by the ISPRM Frailty Focus Group

Eleftheria Antoniadou[1], Emanuele Giusti[2], Paolo Capodaglio[3,4], Der-Sheng Han[5,6], Francesca Gimigliano[7], Juan M Guzman[8], Mooyeon Oh-Park[9], Walter Frontera[10]; Expert Panel

Collaborators, Affiliations expand

- PMID: 38656081

- DOI: 10.23736/S1973-9087.24.08486-7

Abstract

Introduction: Aging is associated with an increased burden of multi-morbidity and disease related functional loss and disability, widely impacting patients and health care systems. Frailty is a major actor in age-related disability and is an important target for rehabilitation interventions, considering that is a reversible condition.

Evidence acquisition: A working group of members of the ISPRM, responding to WHO 2030 call for action to strengthen rehabilitation, was established to assess the quality and implementability of the existing guidelines for the rehabilitation of frailty. Guidelines were retrieved using a systematic search on Pubmed, Scopus and Web of Science and from the reference lists of screened articles. The included guidelines were evaluated using the AGREE II to assess their quality and using the AGREE-REX to assess their clinical credibility and implementability. Guidelines with a score >4 in the AGREE II item evaluating the overall quality of the guideline were considered for endorsement. Finally, nine external reviewers evaluated the applicability of each recommendation from the endorsed guidelines, providing comments about the barriers and facilitators for their implementation in their country.

Evidence synthesis: Ten guidelines were retrieved and evaluated by the working group, of which four guidelines, i.e. the WHO Guidelines on Integrated Care for Older People, the FOCUS guidelines, the Asia-Pacific Clinical Practice Guidelines for the Management of Frailty and the ICFSR International Clinical Practice Guidelines for Identification and Management of Frailty, were considered for endorsement. All these guidelines were rated as of adequate quality and implementability.

Conclusions: The WHO Guidelines on Integrated Care for Older people (24) the ICFSR International Clinical Practice Guidelines for Identification and management of Frailty (15), the FOCUS guidelines (25) and the Asia Pacific Clinical Practice Guidelines (14) for the Management of Frailty have the best quality and applicability of the existing guidelines on the management of frailty, we suggest that should be employed to define the standards of care for patients with frailty. There are barriers for their implementation, as stated by our experts, to take into account, and some of them are country- or region-specific. Screening for frailty, exercise, nutrition, pharmacological management, social and psychological support, management of incontinence, and an overall comprehensive clinical management are the best tools to face upon frailty.

Review

BMJ Open Respir Res

. 2024 Apr 22;11(1):e002272.

doi: 10.1136/bmjresp-2023-002272.

Modifiable risk factors that may be addressed in routine care to prevent progression to and extension of multimorbidity in people with COPD: a systematic literature review

Andi Orlowski[1,2], Jack Ettinger[3], Alex Bottle[2], Sally Snow[3], Rachel Ashton[3], Jennifer K Quint[2]

Affiliations expand

- PMID: 38653506

- PMCID: PMC11043725

- DOI: 10.1136/bmjresp-2023-002272

Abstract

Chronic obstructive pulmonary disease (COPD) is a multisystem disease, and many patients have multiple conditions. We explored multimorbidity patterns that might inform intervention planning to reduce health-care costs while preserving quality of life for patients. Literature searches up to February 2022 revealed 4419 clinical observational and comparative studies of risk factors for multimorbidity in people with COPD, pulmonary emphysema, or chronic bronchitis at baseline. Of these, 29 met the inclusion criteria for this review. Eight studies were cluster and network analyses, five were regression analyses, and 17 (in 16 papers) were other studies of specific conditions, physical activity and treatment. People with COPD more frequently had multimorbidity and had up to ten times the number of disorders of those without COPD. Disease combinations prominently featured cardiovascular and metabolic diseases, asthma, musculoskeletal and psychiatric disorders. An important risk factor for multimorbidity was low socioeconomic status. One

study showed that many patients were receiving multiple drugs and had increased risk of adverse events, and that 10% of medications prescribed were inappropriate. Many patients with COPD have mainly preventable or modifiable multimorbidity. A proactive multidisciplinary approach to prevention and management could reduce the burden of care.

Keywords: COPD epidemiology.

Conflict of interest statement

Competing interests: None declared.

- 51 references
- 1 figure

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

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

1

Observational Study

Br J Gen Pract

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. 2024 Apr 25;74(742):e347-e354.

doi: 10.3399/BJGP.2023.0211. Print 2024 May.

Continuity and breaches in GP care and their associations with mortality for

patients with chronic disease: an observational study using Norwegian registry data

Sahar Pahlavanyali[1], Øystein Hetlevik[1], Valborg Baste[2], Jesper Blinkenberg[2], Steinar Hunskaar[3]

Affiliations expand

- PMID: 38621803
- PMCID: PMC11044022
- DOI: 10.3399/BJGP.2023.0211

Abstract

Background: Despite many benefits of continuity of care with a named regular GP (RGP), continuity is deteriorating in many countries.

Aim: To investigate the association between RGP continuity and mortality, in a personal list system, in addition to examining how breaches in continuity affect this association for patients with chronic diseases.

Design and setting: A registry-based observational study using Norwegian primary care consultation data for patients with asthma, chronic obstructive pulmonary disease (COPD), diabetes mellitus, or heart failure.

Method: The Usual Provider of Care (UPC, value 0-1) Index was used to measure both disease-related ($UPC^{disease}$) and overall (UPC^{all}) continuity with the RGP at the time of consultation. In most analyses, patients who changed RGP during the study period were excluded. In the combined group of all four chronic conditions, the proportion of consultations with other GPs and out-of-hours services was calculated. Cox regression models calculated the associations between continuity during 2013-2016 and mortality in 2017-2018.

Results: Patients with COPD with $UPC^{disease}$ <0.25 had 47% increased risk of dying within 2 years (hazard ratio 1.47, 95% confidence interval = 1.22 to 1.64) compared with those with $UPC^{disease}$ ≥0.75. Mortality also increased with decreasing $UPC^{disease}$ for patients with heart failure and decreasing UPC^{all} for those with diabetes. In the combined group of chronic

conditions, mortality increased with decreasing UPC_{all}. This latter association was also found for patients who had changed RGP.

Conclusion: Higher disease-related and overall RGP UPC are both associated with lower mortality. However, changing RGP did not significantly affect mortality, indicating a compensatory benefit of informational and management continuity in a patient list system.

Keywords: chronic disease; continuity of care; general practice; mortality; observational study; primary health care.

Conflict of interest statement

The authors have declared no competing interests.

- 35 references
- 3 figures

2

Review

Eur Respir Rev

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. 2024 Apr 24;33(172):230238.

doi: 10.1183/16000617.0238-2023. Print 2024 Apr 30.

Biologic agents licensed for severe asthma: a systematic review and meta-analysis of randomised controlled trials

Christos Kyriakopoulos[1], Athena Gogali[1], Georgios Markozannes[2], Konstantinos Kostikas[3]

Affiliations expand

- PMID: 38657997
- PMCID: PMC11040390
- DOI: 10.1183/16000617.0238-2023

Abstract

Background: Six biologic agents are now approved for patients with severe asthma. This meta-analysis aimed to assess the efficacy and safety of licensed biologic agents in patients with severe asthma, including the recently approved tezepelumab.

Methods: We searched MEDLINE, Embase and CENTRAL to identify randomised controlled trials involving licensed biologics until 31 January 2023. We used random-effects meta-analysis models for efficacy, including subgroup analyses by individual agents and markers of T2-high inflammation (blood eosinophils and fractional exhaled nitric oxide), and assessed safety.

Results: 48 studies with 16 350 patients were included in the meta-analysis. Biologics were associated with a 44% reduction in the annualised rate of asthma exacerbations (rate ratio 0.56, 95% CI 0.51-0.62) and 60% reduction of hospitalisations (rate ratio 0.40, 95% CI 0.27-0.60), a mean increase in the forced expiratory volume in 1 s of 0.11 L (95% CI 0.09-0.14), a reduction in asthma control questionnaire by 0.34 points (95% CI -0.46--0.23) and an increase in asthma quality of life questionnaire by 0.38 points (95% CI 0.26-0.49). There was heterogeneity between different classes of biologics in certain outcomes, with overall greater efficacy in patients with T2 inflammation. Overall, biologics exhibited a favourable safety profile.

Conclusions: This comprehensive meta-analysis demonstrated that licensed asthma biologics reduce exacerbations and hospitalisations, improve lung function, asthma control

and quality of life, and limit the use of systemic corticosteroids, with a favourable safety profile. These effects are more prominent in patients with evidence of T2 inflammation.

Conflict of interest statement

Conflict of interest: A. Gogali has received consulting fees from Boehringer Ingelheim and Chiesi; and payment or honoraria for lectures, presentations or educational events from AstraZeneca, Boehringer Ingelheim, Chiesi, ELPEN, GSK and Novartis. K. Kostikas has received grants from AstraZeneca, Boehringer Ingelheim, Chiesi, Innovis, ELPEN, GSK, Menarini, Novartis and NuvoAir; consulting fees from AstraZeneca, Boehringer Ingelheim, Chiesi, CSL Behring, ELPEN, GSK, Menarini, Novartis, Pfizer and Sanofi Genzyme; and payment or honoraria for lectures, presentations or educational events from AstraZeneca, Boehringer Ingelheim, Chiesi, CSL Behring, ELPEN, GSK, Menarini, Novartis, Pfizer and Sanofi Genzyme. K. Kostikas is a member of the GOLD Assembly. C. Kyriakopoulos and G. Markozannes declare no competing interests.

- 83 references
- 5 figures

3

Allergy

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. 2024 Apr 27.

doi: 10.1111/all.16143. Online ahead of print.

Association between Apgar scores within normal range and development of asthma, allergic rhinitis and eczema in childhood: A Danish nationwide register study

Erik Sören Halvard Hansen[1,2], Hannah Kaiser[3], Kristine Tronier Hansen[4], Klaus Bønnelykke[5], Bo Chawes[5], Vibeke Backer[6], Christian Torp-Pedersen[7], Charlotte Suppli Ulrik[1], Nicklas Brustad[5]

Affiliations expand

- PMID: 38676401

- DOI: 10.1111/all.16143

No abstract available

- 5 references

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

4

Hum Mol Genet

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. 2024 Apr 26:ddae063.

doi: 10.1093/hmg/ddae063. Online ahead of print.

Genetic susceptibility to chronic diseases leads to heart failure among Europeans: the influence of leukocyte telomere length

Jason Y Y Wong[1], Batel Blechter[2], Zhonghua Liu[3], Jianxin Shi[2], Véronique L Roger[1]

Affiliations expand

- PMID: 38676403

- DOI: 10.1093/hmg/ddae063

Abstract

Background: Genetic susceptibility to various chronic diseases has been shown to influence heart failure (HF) risk. However, the underlying biological pathways, particularly the role of leukocyte telomere length (LTL), are largely unknown. We investigated the impact of genetic susceptibility to chronic diseases and various traits on HF risk, and whether LTL mediates or modifies the pathways.

Methods: We conducted prospective cohort analyses on 404 883 European participants from the UK Biobank, including 9989 incident HF cases. Multivariable Cox regression was used to estimate associations between HF risk and 24 polygenic risk scores (PRSs) for various diseases or traits previously generated using a Bayesian approach. We assessed multiplicative interactions between the PRSs and LTL previously measured in the UK Biobank using quantitative PCR. Causal mediation analyses were conducted to estimate the proportion of the total effect of PRSs acting indirectly through LTL, an integrative marker of biological aging.

Results: We identified 9 PRSs associated with HF risk, including those for various cardiovascular diseases or traits, rheumatoid arthritis (P = 1.3E-04), and asthma (P = 1.8E-08). Additionally, longer LTL was strongly associated with decreased HF risk (P-trend = 1.7E-08). Notably, LTL strengthened the asthma-HF relationship significantly (P-interaction = 2.8E-03). However, LTL mediated only 1.13% (P < 0.001) of the total effect of the asthma PRS on HF risk.

Conclusions: Our findings shed light onto the shared genetic susceptibility between HF risk, asthma, rheumatoid arthritis, and other traits. Longer LTL strengthened the genetic effect of asthma in the pathway to HF. These results support consideration of LTL and PRSs in HF risk prediction.

Keywords: asthma; bayesian polygenic risk score; cardiovascular disease; heart failure; leukocyte telomere length.

5

NPJ Prim Care Respir Med

. 2024 Apr 25;34(1):3.

doi: 10.1038/s41533-024-00362-1.

The relationship between prescription rates of oral corticosteroids for respiratory diseases and deprivation in England

Erin Barker [1], Jessica Pocock [2], Joe Moss [2], Nick Hex [2], Jordan Rankin [3], Richard Hudson [3]

Affiliations expand

- PMID: 38664469
- PMCID: PMC11045771
- DOI: 10.1038/s41533-024-00362-1

Abstract

Respiratory diseases, including asthma and chronic obstructive pulmonary disease (COPD), are common in England with the worst respiratory outcomes observed in the most deprived areas. There is limited published research to establish whether the rate of oral corticosteroid (OCS) prescribing for asthma and COPD is linked to levels of deprivation. This study carried out a multivariable regression analysis of publicly available data and found that deprivation is associated with a statistically significant increase in the proportion of patients receiving an OCS prescription for asthma or COPD at a GP practice level ($p < 0.001$). The model estimated that the proportion of prescriptions is 1.88% (95% CI 1.83% to 1.92%) and 2.84% (95% CI 2.70% to 2.98%) for the least deprived GP practice and the most deprived GP practice, respectively. This study lays the groundwork for future research using individual patient level data to consider the impact of variation in OCS prescribing rates.

Conflict of interest statement

Sanofi funded this study. Richard Hudson and Jordin Rankin are employed by Sanofi. All other authors declare no competing interests.

- 32 references
- 1 figure

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

UNIMORE

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Comment

Eur Respir J

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. 2024 Apr 25;63(4):2400554.

doi: 10.1183/13993003.00554-2024. Print 2024 Apr.

Reply: Asthma and cardiovascular disease: the strength of triangulation

Chloe I Bloom[1]

Affiliations expand

- PMID: 38663973

- PMCID: PMC11043613

- DOI: 10.1183/13993003.00554-2024

Abstract

A triangulation approach integrated different epidemiological methods and data sources (large observational study and Mendelian randomisation study) to provide more reliable findings and reveal potential sources of bias in previous asthma–CHD studies https://bit.ly/3IXoK84

Conflict of interest statement

Conflict of interest: C.I. Bloom is the recipient of NIHR Imperial Biomedical Research Council awards, and reports grants from the National Institute for Health and Care Research (NIHR) (advanced fellowship) and Asthma+Lung UK.

Comment on

- Asthma and incident coronary heart disease: an observational and Mendelian randomisation study.
  Valencia-Hernández CA, Del Greco M F, Sundaram V, Portas L, Minelli C, Bloom CI.Eur Respir J. 2023 Nov 29;62(5):2301788. doi: 10.1183/13993003.01788-2023. Print 2023 Nov.PMID: 37945032 **Free PMC article.**

- 7 references

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

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7

Editorial

Eur Respir J

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. 2024 Apr 25;63(4):2400469.

doi: 10.1183/13993003.00469-2024. Print 2024 Apr.

Asthma and cardiovascular disease: embracing disease heterogeneity is required

Matthew C Tattersall[1], Ronald E Gangnon[2,3], Nizar N Jarjour[3]

Affiliations expand

- PMID: 38663972

- DOI: 10.1183/13993003.00469-2024

No abstract available

Conflict of interest statement

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

Comment on

- Asthma and incident coronary heart disease: an observational and Mendelian randomisation study.
  Valencia-Hernández CA, Del Greco M F, Sundaram V, Portas L, Minelli C, Bloom CI.Eur Respir J. 2023 Nov 29;62(5):2301788. doi: 10.1183/13993003.01788-2023. Print 2023 Nov.PMID: 37945032 **Free PMC article.**

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

Mult Scler

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. 2024 Apr 25:13524585241240398.

doi: 10.1177/13524585241240398. Online ahead of print.

Montelukast as a repurposable additive drug for standard-efficacy multiple sclerosis treatment: Emulating clinical trials with retrospective administrative health claims data

Astrid M Manuel[1], Assaf Gottlieb[1], Leorah Freeman[2], Zhongming Zhao[3]

Affiliations expand

- PMID: 38660773

- DOI: 10.1177/13524585241240398

Abstract

Background: Effective and safe treatment options for multiple sclerosis (MS) are still needed. Montelukast, a leukotriene receptor antagonist (LTRA) currently indicated for asthma or allergic rhinitis, may provide an additional therapeutic approach.

Objective: The study aimed to evaluate the effects of montelukast on the relapses of people with MS (pwMS).

Methods: In this retrospective case-control study, two independent longitudinal claims datasets were used to emulate randomized clinical trials (RCTs). We identified pwMS aged 18-65 years, on MS disease-modifying therapies concomitantly, in de-identified claims from Optum's Clinformatics® Data Mart (CDM) and IQVIA PharMetrics® Plus for Academics. Cases included 483 pwMS on montelukast and with medication adherence in CDM and 208 in PharMetrics Plus for Academics. We randomly sampled controls from 35,330 pwMS without montelukast prescriptions in CDM and 10,128 in PharMetrics Plus for Academics. Relapses were measured over a 2-year period through inpatient hospitalization and

corticosteroid claims. A doubly robust causal inference model estimated the effects of montelukast, adjusting for confounders and censored patients.

Results: pwMS treated with montelukast demonstrated a statistically significant 23.6% reduction in relapses compared to non-users in 67.3% of emulated RCTs.

Conclusion: Real-world evidence suggested that montelukast reduces MS relapses, warranting future clinical trials and further research on LTRAs' potential mechanism in MS.

Keywords: Multiple sclerosis; administrative health claims; clinical informatics; doubly robust; drug repurposing; leukotriene receptor antagonist; montelukast.

Conflict of interest statement

Declaration of Conflicting InterestsThe author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: L.F. has received fees for consultancy and advisory board participation from Genentech, Roche, Novartis, Bristol Myers Squibb, EMD Serono, Sanofi, Horizon Therapeutics, and TG Therapeutics; has received honorarium for participation in educational programs from Medscape, Inc., the MS Association of America and Impact Education; has received program sponsorship from EMD Serono and grant support from the National Institutes of Health (NIH)/ the National Institute of Neurological Disorders and Stroke (NINDS), the Patient-Centered Outcomes Research Institute (PCORI), Genentech, and EMD Serono through her institution; currently serves on the Healthcare Advisory Committee of the MS Association of America. Z.Z. received speaker fee from a recent User Group meeting of Illumina, Inc.

9

J Asthma

. 2024 Apr 25:1-4.

doi: 10.1080/02770903.2024.2344168. Online ahead of print.

Mounier-Kuhn syndrome in poorly controlled asthma

Marta Solís García[1], Carolina Cisneros Serrano[1], Ana Sofía Martín Hernández[1], Jose María Eiros Bachiller[1], Celeste Marcos[1]

Affiliations expand

- PMID: 38639468

- DOI: 10.1080/02770903.2024.2344168

Abstract

Introduction: Mounier-Kuhn syndrome or tracheobronchomegaly, is a rare condition that consists of abnormal dilation of the trachea and main bronchi due to a pathological arrangement of smooth muscle fibers in this area.

Case report: We present the case of a 46-year-old woman with poorly controlled asthma and recurrent infections, who was diagnosed with Mounier-Kuhn syndrome through a computed tomography scan revealing an unusual enlargement of the trachea with associated bronchiectasis.

Results: The diagnosis of Mounier-Kuhn syndrome is radiological, involving measurement of the trachea where a diameter >25 mm in men and >21 mm in women is observed. While diagnosis is sometimes incidental, there is an association with respiratory diseases such as asthma or COPD, hence clinical suspicion is important in patients with poorly controlled underlying conditions who present with recurrent infections, inadequate secretion management, or even hemoptysis.

Conclusions: Despite its rarity, this syndrome significantly impacts patients' quality of life. Diagnosis and management involve comprehensive evaluations including computed tomography, with a multidisciplinary approach including pulmonologists and radiologists. Exploring its clinical features, associations with other respiratory diseases and treatment options is crucial in managing this rare respiratory condition.

Keywords: Asthma; bronchiectasis; computed tomography; hemoptysis; radiologists; tracheobronchomegaly.

10

Review

Respir Res

. 2024 Apr 24;25(1):178.

doi: 10.1186/s12931-024-02812-3.

Barriers to clinical remission in severe asthma

Inês Farinha[1], Liam G Heaney[2]

Affiliations expand

- PMID: 38658975
- PMCID: PMC11044532
- DOI: 10.1186/s12931-024-02812-3

Abstract

Severe asthma is associated with an increased risk for exacerbations, reduced lung function, fixed airflow obstruction, and substantial morbidity and mortality. The concept of remission in severe asthma as a new treatment goal has recently gained attention due to the growing use of monoclonal antibody therapies, which target specific pathologic

pathways of inflammation. This review evaluates the current definitions of asthma remission and unveils some of the barriers for achieving this state in the severe asthma population. Although there is no unified definition, the concept of clinical remission in asthma should be based on a sustained period of symptom control, elimination of oral corticosteroid exposure and exacerbations, and stabilization of pulmonary function. The conjugation of these criteria seems a realistic treatment target in a minority of asthmatic patients. Some unmet needs in severe asthma may affect the achievement of clinical remission. Late intervention with targeted therapies in the severe asthma population may increase the risk of corticosteroid exposure and the development of irreversible structural airway changes. Moreover, airway infection is an important component in persistent exacerbations in patients on biologic therapies. Phenotyping exacerbations may be useful to guide therapy decisions and to avoid the liberal use of oral corticosteroids. Another challenge associated with the aim of clinical remission in severe asthma is the multifaceted interaction between the disease and its associated comorbidities. Behavioural factors should be evaluated in case of persistent symptoms despite optimised treatment, and assessing biomarkers and targeting treatable traits may allow for a more objective way of reaching remission. The concept of clinical remission will benefit from an international consensus to establish unifying criteria for its assessment, and it should be addressed in the future management guidelines.

Keywords: Asthma; Biologics; Clinical remission.

Conflict of interest statement

The authors declare no competing interests.

- 52 references
- 1 figure

11

Editorial

J Allergy Clin Immunol

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. 2024 Apr 23:S0091-6749(24)00415-9.

doi: 10.1016/j.jaci.2024.04.013. Online ahead of print.

Can sputum eosinophils predict a poor response to mepolizumab?

Catherine Lemiere[1], James G Martin[2]

Affiliations expand

- PMID: 38663816

- DOI: 10.1016/j.jaci.2024.04.013

No abstract available

Keywords: CD62L expression; Severe asthma; mepolizumab; sputum eosinophils.

J Allergy Clin Immunol

. 2024 Apr 23:S0091-6749(24)00365-8.

doi: 10.1016/j.jaci.2024.03.023. Online ahead of print.

Utility of eosinophil peroxidase as a biomarker of eosinophilic inflammation in asthma

Monica Tang[1], Annabelle R Charbit[1], Mats W Johansson[2], Nizar N Jarjour[2], Loren C Denlinger[2], Wilfred W Raymond[1], Michael C Peters[1], Eleanor M Dunican[3], Mario Castro[4], Kaharu Sumino[5], Serpil C Erzurum[6], Suzy A Comhair[6], Wendy C Moore[7], Bruce D Levy[8], Elliot Israel[8], Wanda Phipatanakul[9], Brenda R Phillips[10], David T Mauger[10], Eugene R Bleecker[11], Sally E Wenzel[12], Merritt L Fajt[12], Prescott G Woodruff[1], Annette T Hastie[7], John V Fahy[13]; National Heart Lung and Blood Institute Severe Asthma Research Program[14]

Affiliations expand

- PMID: 38663815

- DOI: 10.1016/j.jaci.2024.03.023

Abstract

Background: The relative utility of eosinophil peroxidase (EPX) and blood and sputum eosinophil counts as disease biomarkers in asthma is uncertain.

Objective: To determine the utility of EPX as a biomarker of systemic and airway eosinophilic inflammation in asthma.

Methods: EPX protein was measured by immunoassay in serum and sputum in 110 healthy controls to establish a normal reference range and in repeated samples of serum and sputum collected during three years of observation in 480 participants in the Severe Asthma Research Program (SARP)-3.

Results: Over three years, EPX levels in asthma patients were higher than normal in 27-31% of serum samples and 36-53% of sputum samples. Eosinophils and EPX correlated better in blood than in sputum (r_s values of 0.74 and 0.43, respectively), and high sputum EPX levels occurred in 27% of participants with blood eosinophil counts < 150 cells/uL and

42% of participants with blood eosinophil counts 150-299 cells/uL. Patients with persistently high sputum EPX values for three years were characterized by severe airflow obstruction, frequent exacerbations, and high mucus plug scores. In 59 asthma patients who started mepolizumab during observation, serum EPX levels normalized in 96% but sputum EPX normalized in only 49%. Lung function remained abnormal even when sputum EPX normalized.

Conclusion: Serum EPX is a valid protein biomarker of systemic eosinophilic inflammation in asthma, and sputum EPX levels are a more sensitive biomarker of airway eosinophilic inflammation than sputum eosinophil counts. Eosinophil measures in blood frequently miss airway eosinophilic inflammation, and mepolizumab frequently fails to normalize airway eosinophilic inflammation even though it invariably normalizes systemic eosinophilic inflammation.

Keywords: Asthma; eosinophil; eosinophilic inflammation; mepolizumab; mucus plugs; sputum.

13

Pulm Pharmacol Ther

. 2024 Apr 23:102299.

doi: 10.1016/j.pupt.2024.102299. Online ahead of print.

Evaluating the pharmacokinetics of beclometasone dipropionate/formoterol

fumarate/glycopyrronium bromide delivered via pressurised metered-dose inhaler using a low global warming potential propellant

François Rony[1], Mauro Cortellini[2], Alessandro Guasconi[2], Kusum S Mathews[2], Annalisa Piccinno[2], Gianluigi Poli[2], Frédéric Vanhoutte[3], Jelle Klein[3]

Affiliations expand

- PMID: 38663512

- DOI: 10.1016/j.pupt.2024.102299

Abstract

Introduction: Use of propellants with high global warming potential (such as HFA-134a) for pressurised metered-dose inhalers (pMDIs) is being phased down. Switching to dry-powder inhalers may not be clinically feasible for all patients; an alternative is reformulation using propellants with low global warming potential. The combination of beclometasone dipropionate/formoterol fumarate/glycopyrronium bromide (BDP/FF/GB) is available for asthma or chronic obstructive pulmonary disease via pMDI using HFA-134a as propellant. This is being reformulated using the low global warming potential propellant HFA-152a. This manuscript reports three studies comparing BDP/FF/GB pharmacokinetics delivered via pMDI using HFA-152a vs HFA-134a.

Methods: The studies were four-way crossover, single-dose, randomised, double-blind, in healthy volunteers. In Studies 1 and 2, subjects inhaled four puffs of BDP/FF/GB (Study 1: 100/6/12.5 µg [medium-strength BDP]; Study 2: 200/6/12.5 µg [high-strength]), ingesting activated charcoal in two of the periods (once per propellant). In Study 3, subjects inhaled medium- and high-strength BDP/FF/GB using a spacer. All three studies compared HFA-152a vs HFA-134a in terms of lung availability and total systemic exposure of beclometasone-17-monopropionate (B17MP; active metabolite of BDP), BDP, formoterol and GB. Bioequivalence was concluded if the 90% confidence intervals (CIs) of the ratios between formulations of the geometric mean maximum plasma concentration (C_{max}) and area under the plasma concentration-time curve between time zero and the last quantifiable timepoint (AUC_{0-t}) for the analytes were between 80-125%.

Results: In Studies 1 and 2, systemic exposure bioequivalence (i.e., comparisons without charcoal block) was demonstrated, except for GB C_{max} in Study 2 (upper 90% CI 125.11%).

For lung availability (i.e., comparisons with charcoal block), B17MP and formoterol demonstrated bioequivalence in both studies, as did BDP in Study 2; in Study 1, BDP upper CIs were 126.96% for C_{max} and 127.34% for AUC_{0-t}). In Study 1, GB AUC_{0-t} lower CI was 74.54%; in Study 2 upper limits were 135.64% for C_{max} and 129.12% for AUC_{0-t}. In Study 3, the bioequivalence criteria were met for BDP, B17MP and formoterol with both BDP/FF/GB strengths, and were met for GB AUC_{0-t}, although not for C_{max}. Both formulations were similarly well tolerated in all three studies.

Conclusions: Overall, while formal bioequivalence cannot be concluded for all analytes, these data suggest therapeutic equivalence of the new formulation with the existing BDP/FF/GB pMDI formulation, therefore supporting reformulation using a propellant with low global warming potential.

Keywords: Total systemic exposure; adrenergic beta-2 receptor agonists; inhaled corticosteroids; inhaled triple therapy; lung bioavailability; muscarinic antagonists.

Conflict of interest statement

Declaration of Competing Interest FR, MC, AG, KM, AP and GP are employees of Chiesi, the sponsor of the studies. FV and JK are employees of SGS, the clinical trial site. Both have no conflicts of interest to report.

14

J Allergy Clin Immunol Pract

. 2024 Apr 23:S2213-2198(24)00411-2.

doi: 10.1016/j.jaip.2024.04.026. Online ahead of print.

Multivariate Cluster Analyses to Characterize Asthma Heterogeneity and Benralizumab Responsiveness

Xingnan Li[1], Paul Newbold[2], Rohit Katial[3], Ian Hirsch[4], Huashi Li[5], Ubaldo J Martin[6], Deborah A Meyers[7], Eugene R Bleecker[8]

Affiliations expand

- PMID: 38663470

- DOI: 10.1016/j.jaip.2024.04.026

Abstract

Background: An improved understanding of how severe asthma heterogeneity affects response could inform treatment decisions.

Objectives: Characterize heterogeneity and benralizumab responsiveness in patients grouped by predefined Severe Asthma Research Program clusters using a multivariate approach.

Methods: In post-hoc analyses of the randomized, double-blind, placebo-controlled phase III SIROCCO (NCT01928771) and CALIMA (NCT01914757) studies, patients with severe asthma who received benralizumab or placebo were assigned to clusters using an established discriminant function to simultaneously analyze 11 clinical characteristics. Annualized asthma exacerbation rate, exacerbation incidence, and lung function were analyzed across clusters.

Results: Patients (N = 2,281) met criteria for 4 of 5 clusters: Cluster 2 (early-onset moderate asthma, n = 393), Cluster 4 (early-onset severe, n = 386), Cluster 3 (late-onset severe, n = 641), and Cluster 5 (late-onset severe, obstructed, n = 861); no patients met Cluster 1 criteria. Exacerbation rate reductions were significant in late-onset severe (-48% [95% CI: -61%, -31%], P<.0001) and late-onset severe, obstructed asthma (-50% [95% CI: -59%, -38%], P<.0001), with non-significant reductions in early-onset clusters. These differences could not be fully explained by blood eosinophil count differences. Forced expiratory volume in 1 second improvements were significant in late-onset severe (+133 mL [95% CI: 66 mL, 200 mL], P=.0001) and late-onset severe, obstructed asthma (+160 mL [95% CI: 85 mL, 235 mL], P<.0001) while maintaining acute bronchodilator responsiveness.

Conclusions: Benralizumab reduced exacerbations and improved lung function, primarily in late-onset asthma clusters. This multivariate approach to identify subphenotypes, potentially reflecting pathobiological mechanisms, can guide therapy beyond univariate approaches.

Keywords: Anti-Asthmatic Agents; Asthma; Benralizumab; Forced Expiratory Volume; Heterogeneity; Phenotypic Cluster; Respiratory Hypersensitivity; Vital Capacity.

15

Case Reports

Respirol Case Rep

. 2024 Apr 23;12(4):e01359.

doi: 10.1002/rcr2.1359. eCollection 2024 Apr.

Successful ultrathin bronchoscopy with cryobiopsy for diagnosing and removing mucus plugs in allergic bronchopulmonary mycosis mimicking lung cancer

Yuki Takigawa[1], Hiromi Watanabe[1], Ken Sato[1], Mayu Goda[1], Tomoyoshi Inoue[1], Miho Fujiwara[1], Suzuka Matsuoka[1], Kenichiro Kudo[1], Akiko Sato[1], Keiichi Fujiwara[1], Takuo Shibayama[1]

Affiliations expand

- PMID: 38660339
- PMCID: PMC11040176
- DOI: 10.1002/rcr2.1359

Abstract

In patients presenting with abnormal pulmonary nodules, especially those with a history of asthma, allergic bronchopulmonary mycosis should be considered. Eosinophil counts and IgE levels should be checked in such patients.

Keywords: allergic bronchopulmonary mycosis; cryobiopsy; mucus plug; ultrathin bronchoscope.

Conflict of interest statement

None declared.

- 2 references
- 5 figures

16

JMIR Res Protoc

. 2024 Apr 23:13:e54388.

doi: 10.2196/54388.

Leveraging AI and Machine Learning to Develop and Evaluate a Contextualized User-Friendly Cough Audio Classifier for Detecting Respiratory Diseases: Protocol for a Diagnostic Study in Rural Tanzania

Kahabi Ganka Isangula[1], Rogers John Haule[1]

Affiliations expand

- PMID: 38652526

- DOI: 10.2196/54388

Free article

Abstract

Background: Respiratory diseases, including active tuberculosis (TB), asthma, and chronic obstructive pulmonary disease (COPD), constitute substantial global health challenges, necessitating timely and accurate diagnosis for effective treatment and management.

Objective: This research seeks to develop and evaluate a noninvasive user-friendly artificial intelligence (AI)-powered cough audio classifier for detecting these respiratory conditions in rural Tanzania.

Methods: This is a nonexperimental cross-sectional research with the primary objective of collection and analysis of cough sounds from patients with active TB, asthma, and COPD in

outpatient clinics to generate and evaluate a noninvasive cough audio classifier. Specialized cough sound recording devices, designed to be nonintrusive and user-friendly, will facilitate the collection of diverse cough sound samples from patients attending outpatient clinics in 20 health care facilities in the Shinyanga region. The collected cough sound data will undergo rigorous analysis, using advanced AI signal processing and machine learning techniques. By comparing acoustic features and patterns associated with TB, asthma, and COPD, a robust algorithm capable of automated disease discrimination will be generated facilitating the development of a smartphone-based cough sound classifier. The classifier will be evaluated against the calculated reference standards including clinical assessments, sputum smear, GeneXpert, chest x-ray, culture and sensitivity, spirometry and peak expiratory flow, and sensitivity and predictive values.

Results: This research represents a vital step toward enhancing the diagnostic capabilities available in outpatient clinics, with the potential to revolutionize the field of respiratory disease diagnosis. Findings from the 4 phases of the study will be presented as descriptions supported by relevant images, tables, and figures. The anticipated outcome of this research is the creation of a reliable, noninvasive diagnostic cough classifier that empowers health care professionals and patients themselves to identify and differentiate these respiratory diseases based on cough sound patterns.

Conclusions: Cough sound classifiers use advanced technology for early detection and management of respiratory conditions, offering a less invasive and more efficient alternative to traditional diagnostics. This technology promises to ease public health burdens, improve patient outcomes, and enhance health care access in under-resourced areas, potentially transforming respiratory disease management globally.

International registered report identifier (irrid): PRR1-10.2196/54388.

Keywords: Africa; Tanzania; analysis; artificial intelligence; asthma; chronic obstructive pulmonary disease; cough; cough classifiers; cough sound; cross-sectional research; detecting respiratory disease; diagnostic study; machine learning; management; mobile phone; noninvasive; respiratory diseases; rural; treatment; tuberculosis; user-friendly.

17

Review

Naunyn Schmiedebergs Arch Pharmacol

. 2024 Apr 23.

doi: 10.1007/s00210-024-03105-8. Online ahead of print.

Examining the contribution of Notch signaling to lung disease development

Samar A Antar[1,2], Mohamed Kh ElMahdy[3], Ahmed G Darwish[4]

Affiliations expand

- PMID: 38652281

- DOI: 10.1007/s00210-024-03105-8

Abstract

Notch pathway is a widely observed signaling system that holds pivotal functions in regulating various developmental cellular functions and operations. The Notch signaling mechanism is crucial for lung homeostasis, damage, and restoration. Based on increasing evidence, the Notch pathway has been identified, as critical for fibrosis and subsequently, the development of chronic fibroproliferative conditions in various organs and tissues. Recent research indicates that deregulation of Notch signaling correlates with the pathogenesis of significant pulmonary conditions, particularly chronic obstructive pulmonary disease (COPD), pulmonary fibrosis, asthma, pulmonary arterial hypertension (PAH), lung carcinoma, and pulmonary abnormalities in some hereditary disorders. In various cellular and tissue environments, and across both physiological and pathological conditions, multiple consequences of Notch activation have been observed. Studies have ascertained that the Notch signaling cascade exhibits close associations with various other

signaling systems. This study provides an updated overview of Notch signaling's role, especially its link to fibrosis and its potential therapeutic implications. This study sheds light on the latest findings regarding the mechanisms and outcomes of irregular or lacking Notch activity in the onset and development of pulmonary diseases. As our insight into this signaling mechanism suggests that modulating Notch signaling might hold potential as a valuable additional therapeutic approach in upcoming research.

Keywords: Chronic obstructive pulmonary disease; Lung cancer; Lung fibrosis; Notch; Pulmonary arterial hypertension.

- 119 references

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

Proceed to details

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18

Allergy

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. 2024 Apr 23.

doi: 10.1111/all.16131. Online ahead of print.

Response of sputum periostin to anti-T2 biologics treatment in severe asthma

Parameswaran Nair[1], Katherine Radford[1], Satoshi Nunomura[2], Manali Mukherjee[1], Kenji Izuhara[2]

Affiliations expand

- PMID: 38651839

- DOI: 10.1111/all.16131

No abstract available

- 7 references

19

Respirology

.

. 2024 Apr 23.

doi: 10.1111/resp.14729. Online ahead of print.

Asthma-related death trends and biologics use for severe asthma in the super-aged society of Japan

Keiko Kan-O[1]

Affiliations expand

- PMID: 38651273

- DOI: 10.1111/resp.14729

No abstract available

Keywords: Japan; asthma-related deaths; biologics; severe asthma; super-aged society.

- 7 references

20

Med Sci Sports Exerc

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. 2024 Apr 23.

doi: 10.1249/MSS.0000000000003419. Online ahead of print.

Exhaled and Systemic Biomarkers to Aid the Diagnosis of Bronchial Asthma in Elite Water Sports Athletes

Balázs Csoma[1], Nóra Sydó[2], Gergő Szűcs[1], Éva Seres[1], Tamás Erdélyi[1], Gábor Horváth[1], Emese Csulak[2], Béla Merkely[2], Veronika Müller[1]

Affiliations expand

- PMID: 38650115

- DOI: 10.1249/MSS.0000000000003419

Abstract

Purpose: Our aim was to evaluate the accuracy of a combined airway inflammatory biomarker assessment in diagnosing asthma in elite water sports athletes.

Methods: Members of the Hungarian Olympic and Junior Swim Team and elite athletes from other aquatic disciplines were assessed for asthma by objective lung function measurements, and blood eosinophil count (BEC), serum total IgE, FENO measurements, and skin prick testing were performed. A scoring system from BEC, FENO, serum IgE, and skin test positivity was constructed by dichotomising the variables and assigning a score of 1 if the variable is elevated. These scores were summed to produce a final composite score ranging from 0 to 4.

Results: A total of 48 participants were enrolled (age 21 ± 4 years, 42% male), of which 22 were diagnosed with asthma. Serum total IgE and FENO levels were higher in asthmatic individuals (68 [27-176] vs. 24 ([1-44], $p = 0.01$; 20 [17-26] vs. 15 [11-22], $p = 0.02$), and positive prick test was also more frequent (55% vs. 8%, $p < 0.01$). Asthmatic participants had higher composite variable scores (2 ([1-3] vs. 1 [0-1], $p = 0.02$). ROC analysis showed that total IgE, FENO, and the composite variable were suitable for identifying asthmatic participants (AUC 0.72, $p = 0.01$; 0.70, $p = 0.02$, and 0.69, $p = 0.03$). A composite score of >2 reached a specificity of 96.2%, sensitivity of 36.4%, and likelihood ratio of 9.5. Logistic regression model revealed a strong association between the composite variable and the asthma diagnosis (OR 2.71 (95% CI 1.17-6.23), $p = 0.02$).

Conclusions: Our data highlight the diagnostic value of combined assessment of Th2-type inflammation in elite water sports athletes. The proposed scoring system may be helpful in ruling in asthma in this population upon clinical suspicion.

Conflict of interest statement

Conflict of Interest and Funding Source: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. The study was partially funded by the TKP2021-NKTA-46 research grant of the Hungarian National Research, Development and Innovation Office. BC and ET were supported by the research grants of the Hungarian Respiratory Society. BC was also supported by the Semmelweis 250+ Excellence Fellowship of Semmelweis University, the National Talent Program of the Hungarian Prime Ministry, and the Hungarian State Eötvös Scholarship of the Tempus Public Foundation.

Review

Expert Opin Biol Ther

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Advancements in biologic therapy in eosinophilic asthma

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Affiliations expand

- PMID: 38619468

- DOI: 10.1080/14712598.2024.2342527

Abstract

Introduction: Asthma encompasses a spectrum of phenotypes often categorized into two groups- type 2 high (T2 high) and type 2 low (T2 low). T2 high includes atopic and eosinophilic presentations whereas T2 low is non-atopic, non-eosinophilic, and oft associated with neutrophilic inflammation. Eosinophilic asthma is often driven by IgE, IL-4, IL-5, and IL-13 and TSLP. This can lead to eosinophilic inflammatory response in the airways which in turn can be used as target for treatment.

Areas covered: The article will focus on biologic therapy that is currently being used in eosinophilic asthma management in mainly the adult population including clinical trials and co-morbidities that can be treated using the same biologics. A review on asthma biologics for pediatric population has been reviewed elsewhere.

Expert opinion: Biological therapy for asthma targeting the IgE, IL-4, IL-5, IL-13, and TSLP pathways are shown to have benefit for the treatment of eosinophilic asthma, as exemplified in real-world studies. When choosing the right biological agent factors such as phenotype, comorbidities, and cost-effectiveness of the biologic agent must be taken into consideration.

Keywords: IL-13; IL-4; IL-5; IgE; Severe asthma; TSLP; benralizumab; dupilumab; eosinophil; mepolizumab; omalizumab; reslizumab; tezepelumab.

22

Curr Med Res Opin

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Development and validation of a score assessing the risk of severe asthma in primary care

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Affiliations expand

- PMID: 38602488

- DOI: 10.1080/03007995.2024.2341869

Abstract

Objective: To develop and validate the Asthma Severity-Health Search (AS-HScore), predicting severe asthma risk in Italian primary care. According to the current asthma treatment guidelines, the AS-HScore intended to serve as a clinical decision support system (CDSS) for General Practitioners (GPs).

Methods: Using the Health Search Database (HSD), a cohort of 32,917 asthma-diagnosed patients between 2013 and 2021 was identified. The AS-HScore was developed using multivariable Cox regression in a two-part cohort: development and validation. Candidate determinants were estimated and linearly combined to form the score; its predictive accuracy was evaluated in the validation sub-cohort.

Results: AS-HScore performance in the validation cohort revealed a 73% area under the curve (i.e. discrimination power) and a 22% pseudo-R^2 (explained variation). Calibration slope of 1.07 indicated strong calibration without rejecting the equivalence hypothesis (p = 0.157). Estimating a mean 10% (SD: 6.8%) 1-year risk of severe asthma, GPs might be provided with risk thresholds for patient categorization.

Conclusion: The AS-HScore emerges as an accurate tool predicting severe asthma risk in the Italian primary care. It therefore shows promising application to enhance asthma care by early identification of severe cases. Implementing a score-based CDSS for Italian GPs holds potential for significantly improving asthma management and patients' outcomes.

Keywords: Severe asthma; primary care; risk assessment.

BMJ Open Respir Res

. 2024 Apr 22;11(1):e002272.

doi: 10.1136/bmjresp-2023-002272.

Modifiable risk factors that may be addressed in routine care to prevent progression to and extension of multimorbidity in people with COPD: a systematic literature review

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Affiliations expand

- PMID: 38653506

- PMCID: PMC11043725

- DOI: 10.1136/bmjresp-2023-002272

Abstract

Chronic obstructive pulmonary disease (COPD) is a multisystem disease, and many patients have multiple conditions. We explored multimorbidity patterns that might inform intervention planning to reduce health-care costs while preserving quality of life for patients. Literature searches up to February 2022 revealed 4419 clinical observational and comparative studies of risk factors for multimorbidity in people with COPD, pulmonary emphysema, or chronic bronchitis at baseline. Of these, 29 met the inclusion criteria for this review. Eight studies were cluster and network analyses, five were regression analyses, and 17 (in 16 papers) were other studies of specific conditions, physical activity and treatment. People with COPD more frequently had multimorbidity and had up to ten times the number of disorders of those without COPD. Disease combinations prominently featured cardiovascular and metabolic diseases, asthma, musculoskeletal and psychiatric disorders. An important risk factor for multimorbidity was low socioeconomic status. One

study showed that many patients were receiving multiple drugs and had increased risk of adverse events, and that 10% of medications prescribed were inappropriate. Many patients with COPD have mainly preventable or modifiable multimorbidity. A proactive multidisciplinary approach to prevention and management could reduce the burden of care.

Keywords: COPD epidemiology.

Conflict of interest statement

Competing interests: None declared.

- 51 references
- 1 figure

24

ERJ Open Res

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Severe asthma care trajectories: the French RAMSES cohort

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Affiliations expand

- PMID: 38651091

- PMCID: PMC11033728

- DOI: 10.1183/23120541.00837-2023

Abstract

Background: The French RAMSES study is an observational prospective multicentre real-life cohort including severe asthmatic subjects. The objective of the study was to compare the characteristics of patients, in terms of phenotype and asthma care trajectories, between those managed by tertiary referral centres (TRCs) or secondary care centres (SCCs).

Methods: Patients were prospectively recruited and enrolled for a 5-year follow-up. Patients' characteristics were analysed at inclusion and compared between TRCs and SCCs.

Results: 52 centres (24 TRCs and 28 SCCs) included 2046 patients: 1502 (73.4%) were included by a TRC and 544 (26.6%) by a SCC. Patients were mainly women (62%), 53±15 years old, 67% with Asthma Control Test <20; at inclusion, 14% received oral corticosteroids (OCS) and 66% biologics. Compared with the SCC group, the TRC group had more frequent comorbidities and lower blood eosinophil counts (262 *versus* 340 mm^{-3}; p=0.0036). OCS and biologics use did not differ between groups, but patients in the TRC group benefited more frequently from an educational programme (26% *versus* 18%; p=0.0008) and received more frequently two or more sequential lines of biologics (33% *versus* 24%; p=0.0105). In-depth investigations were more frequently performed in the TRC group (allergy tests: 74% *versus* 62%; p<0.0001; exhaled nitric oxide fraction: 56% *versus* 21%; p<0.0001; induced sputum: 6% *versus* 3%; p=0.0390).

Conclusions: Phenotypes and care trajectories differed in the RAMSES cohort between SCCs and TRCs, probably related to different levels of asthma severity and differences in

medical resources and practices among centres. This highlights the need for standardisation of severe asthma care.

Conflict of interest statement

Conflict of interest: J-M. Perotin reports lecture honoraria from AstraZeneca, support for attending meetings from AstraZeneca and Chiesi, and membership of working groups and associations receiving financial support from AstraZeneca, Chiesi, Novartis and Sanofi; outside the submitted work. N. Just participated or participates as an investigator in clinical trials with Chiesi, and reports honoraria from Chiesi and AstraZeneca. G. Devouassoux reports lecture honoraria from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Mundi Pharma, Novartis Pharma, Vivisol, Sanofi, ALK and Menarini; consultancy fees from AGIR Adom, ALK, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Meda, MSD, Novartis Pharma, Orkyn, Takeda, TEVA, Sanofi and Cipla; has served as a principal investigator and/or study coordinator for AB Science, ALK, Amgen, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Lilly, Novartis Pharma, Roche, Regeneron Pharmaceuticals Inc., Sanofi, TEVA, VitalAire, Gossamer and Zambon; and reports research grants from AGIR Adom, ALLP, Chiesi, GlaxoSmithKline, MSD, Novartis Pharma, Orkyn, Takeda and Vivisol. C. Chenivesse reports grants from AstraZeneca, GlaxoSmithKline, Novartis and Santelys, personal fees from ALK-Abello, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline and Sanofi, and congress support from AstraZeneca, Boehringer Ingelheim, Chiesi, Novartis and Sanofi. C. Saint Raymond reports lecture honoraria, support for attending meetings, and membership of working groups and associations receiving financial support from AstraZeneca, Novartis, GlaxoSmithKline and Sanofi. A. Bourdin reports grants from Boehringer Ingelheim, AstraZeneca, GlaxoSmithKline, AB Science, Celltrion, Cipla, Areteia, Novartis, Sanofi Regeneron and Chiesi, consulting fees, lecture fees and support for meetings from Boehringer Ingelheim, AstraZeneca, GlaxoSmithKline, AB Science, Celltrion, Cipla, Novartis, Sanofi Regeneron and Chiesi, and participation on an advisory board for AB Science. G. Garcia reports personal fees from AstraZeneca, Sanofi, Novartis, Chiesi and GlaxoSmithKline, and congress support from Sanofi and Oxyvie. A. Boudjemaa reports personal fees from AstraZeneca, Sanofi, Chiesi and GlaxoSmithKline, and congress support from GlaxoSmithKline and Oxyvie. P. Bonniaud reports research grants from AstraZeneca, personal fees from AstraZeneca, Boehringer Ingelheim, Sanofi, Novartis and GlaxoSmithKline, and congress support from AstraZeneca, Sanofi, Boehringer Ingelheim, Stallergenes and Novartis. P. Chanez reports grants, consulting fees, lectures fees and support for meetings from ALK, AstraZeneca, Biopharm, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Novartis and Sanofi-Aventis. C. Barnig reports support for attending meetings from AstraZeneca, GlaxoSmithKline, Sanofi, ALK and Chiesi. A. Beurnier reports lecture fees from AstraZeneca and Sanofi. N. Freymond reports lecture honoraria from AstraZeneca, Sanofi and GlaxoSmithKline, and support for attending meetings from AstraZeneca and Sanofi; outside the submitted work. C. Tcherakian reports a grant from Air Liquide Foundation, lecture fees from AstraZeneca, GlaxoSmithKline, Chiesi, Novartis and

Sanofi, and meeting support from Sanofi and GlaxoSmithKline. M. Drucbert reports lecture honoraria from GlaxoSmithKline and AstraZeneca, and membership of working group receiving financial support from AstraZeneca; outside the submitted work. S. Guillo reports no personal fees, congress support or research grants with conflicting interests to disclose other than the funding of the RAMSES cohort. C. Estellat reports no personal fees, congress support or research grants with conflicting interests to disclose other than the funding of the RAMSES cohort. C. Taillé reports lecture or advisory board fees and grants from AstraZeneca, Sanofi, GlaxoSmithKline, Chiesi, Stallergenes and Novartis. All other authors have nothing to declare. There are no further conflicting interests to disclose.

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J Asthma

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Machine Learning and Bioinformatics Approaches to Identify the Candidate Biomarkers in Severe Asthma

Fuying Zhang[1], Xiang Weng[2], Jiabao Zhu[2], Qin Tang[1], Mingsheng Lei[1,3], Weimin Zhou[2]

Affiliations expand

- PMID: 38647226

- DOI: 10.1080/02770903.2024.2335562

Abstract

Severe asthma is characterized by a poor level of control that severely affects the patient's life and prognosis. However, the underlying pathogenic mechanisms remain unknown. Here, we identified differentially expressed genes from the microarray datasets(GSE130499 and GSE63142) of severe asthma, and then constructed models to screen the most relevant biomarkers to severe asthma by machine learning algorithms(LASSO and SVM-RFE), with further validation of the results by GSE43696. Three genes (*BCL3*, *DDIT4* and *S100A14*) are considered as biomarkers of severe asthma and had good diagnostic effect. Among them, *BCL3* transcript level was down-regulated in severe asthma, while *S100A14* and *DDIT4* transcript levels were up-regulated. Next, the features of the immune microenvironment in severe asthma were analyzed and single-cell datasets(GSE193816 and GSE227744) were identified for potential biomarker-specific expression and intercellular communication. Infiltration of neutrophils and mast cells were found to be increased in severe asthma and may be associated with bronchial epithelial cells through BMP and NRG signaling. Finally, The expression levels of potential biomarkers were verified with a mouse model of asthma.

Keywords: candidate biomarkers; cellular communication; epithelial cells; immune microenvironment; severe asthma.

26

J Occup Environ Med

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Long-term impairment from irritant-induced occupational asthma

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Affiliations expand

- PMID: 38637911

- DOI: 10.1097/JOM.0000000000003120

Abstract

Objective: To assess the long-term physical condition, health-related quality of life, employment, and work ability of irritant-induced asthma (IIA) patients.

Methods: Forty-three IIA patients completed a follow-up questionnaire a median of eight (interquartile range 4-11) years after asthma diagnosis. We compared their results with those of 43 low-molecular-weight (LMW) sensitizer-induced occupational asthma (OA) patients and those of 206 adult-onset asthmatics in the general population.

Results: Of the IIA patients, 40% reported depressive symptoms. Of the <65-year-olds, 56% were employed, of whom 39% assessed their work ability as limited. IIA patients had more difficulty climbing several flights of stairs than LMW-induced OA patients (70% vs. 47%, OR 4.83 95%CI 1.51-15.47). Most of the IIA patients' outcomes were inferior to those of the adult-onset asthmatics in the general population.

Conclusion: IIA prognosis appeared poor but resembled that of LMW-induced OA.

Conflict of interest statement

Conflicts of interest: NONE DECLARED

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Respir Care

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Noninvasive Respiratory Support for Pediatric Critical Asthma: A Multicenter Cohort Study

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Affiliations expand

- PMID: 38290751

- DOI: 10.4187/respcare.11502

Abstract

Background: Noninvasive respiratory support (NRS) for pediatric critical asthma includes CPAP; bi-level positive airway pressure (BPAP); and heated, humidified, high-flow nasal cannula (HFNC). We used the Virtual Pediatric System database to estimate NRS by prescribing rates for pediatric critical asthma and characterize patient clinical features and in-patient outcomes by the initial NRS device applied.

Methods: We performed a retrospective cohort study from 125 participating pediatric ICUs among children 2-17 years of age hospitalized for critical asthma and prescribed NRS from 2017 through 2021. The primary outcomes were NRS modality prescribing rates and trends. Secondary outcomes were descriptive and included demographics, comorbidities, severity of illness indices, and NRS failure rates (defined as escalation from the initial NRS modality to invasive ventilation, HFNC to BPAP or CPAP, or CPAP to BPAP).

Results: Of the 10,083 encounters studied, the initial NRS modalities prescribed varied widely by hospital center (HFNC: 69.7 ± 29.6%; BPAP: 27.2 ± 7.1%; CPAP: 3.1 ± 5.9%). The mean rates of HFNC use increased from 59.7% in 2017 to 71.9% in 2021 (+2.5%/y). In contrast, BPAP (-1.6%/y) and CPAP (-0.8%/y) utilization declined throughout the study period. Older children who were obese and with a higher Pediatric Risk of Mortality III-Probability of Mortality score were more frequently prescribed BPAP and CPAP compared with HFNC. Those children on HFNC experienced higher noninvasive respiratory support failure rates versus BPAP (7.3% vs 2.4%; $P < .001$) but a lower subsequent invasive ventilation rate versus BPAP (0.8% vs 2.4%; $P < .001$).

Conclusions: In this multi-center cohort study, we observed that children with critical asthma are increasingly exposed to HFNC compared with BPAP and CPAP. Rates of HFNC failure were greater than those of BPAP failure, but a majority were transitioned to BPAP without subsequent invasive ventilation. The next steps include prospective trials, including practical end points such as patient comfort and optimal delivery of nebulized treatments to distinguish device superiority and suitable NRS utilization.

Keywords: Asthma; Bilevel positive airway pressure; Continuous positive airway pressure; Critical asthma; High-flow nasal cannula; Invasive ventilation; Noninvasive respiratory support; Noninvasive ventilation; Pediatric; Status asthmaticus.

Conflict of interest statement

The authors have disclosed no conflicts of interest.

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Allergy

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. 2024 Apr 27.

doi: 10.1111/all.16143. Online ahead of print.

Association between Apgar scores within normal range and development of asthma, allergic rhinitis and eczema in childhood: A Danish nationwide register study

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Affiliations expand

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- DOI: 10.1111/all.16143

No abstract available

- 5 references

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

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Quantitative Comparison of Chatbots on Common Rhinology Pathologies

Jeffrey R Bellinger[1], Minhie W Kwak[1], Gabriel A Ramos[1], Jeffrey S Mella[1], Jose L Mattos[1]

Affiliations expand

- PMID: 38666768

- DOI: 10.1002/lary.31470

Abstract

Objectives: Understanding the strengths and weaknesses of chatbots as a source of patient information is critical for providers in the rising artificial intelligence landscape. This study is the first to quantitatively analyze and compare four of the most used chatbots available regarding treatments of common pathologies in rhinology.

Methods: The treatment of epistaxis, chronic sinusitis, sinus infection, allergic rhinitis, allergies, and nasal polyps was asked to chatbots ChatGPT, ChatGPT Plus, Google Bard, and Microsoft Bing in May 2023. Individual responses were analyzed by reviewers for readability, quality, understandability, and actionability using validated scoring metrics. Accuracy and comprehensiveness were evaluated for each response by two experts in rhinology.

Results: ChatGPT, Plus, Bard, and Bing had FRE readability scores of 33.17, 35.93, 46.50, and 46.32, respectively, indicating higher readability for Bard and Bing compared to ChatGPT ($p = 0.003$, $p = 0.008$) and Plus ($p = 0.025$, $p = 0.048$). ChatGPT, Plus, and Bard had mean DISCERN quality scores of 20.42, 20.89, and 20.61, respectively, which was higher than the score for Bing of 16.97 ($p < 0.001$). For understandability, ChatGPT and Bing had PEMAT scores of 76.67 and 66.61, respectively, which were lower than both Plus at 92.00 ($p < 0.001$, $p < 0.001$) and Bard at 92.67 ($p < 0.001$, $p < 0.001$). ChatGPT Plus had an accuracy score of 4.39 which was higher than ChatGPT (3.97, $p = 0.118$), Bard (3.72, $p = 0.002$), and Bing (3.19, $p < 0.001$).

Conclusion: On aggregate of the tested domains, our results suggest ChatGPT Plus and Google Bard are currently the most patient-friendly chatbots for the treatment of common pathologies in rhinology.

Level of evidence: N/A Laryngoscope, 2024.

Keywords: ChatGPT; chatbots; large language models; otolaryngology; rhinology.

- 45 references

3

Int Arch Allergy Immunol

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. 2024 Apr 25:1-13.

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Low-Level Laser Therapy for Allergic Rhinitis: A Systematic Review and Meta-Analysis

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Affiliations expand

- PMID: 38663361

- DOI: 10.1159/000538049

Abstract

Introduction: Allergic rhinitis (AR) is a common allergic disorder that impairs social and physical functioning as well as quality of life. It is characterized by sneezing, rhinorrhea, congestion, and itching which respond suboptimally to drug therapy. Low-level laser therapy (LLLT) has anti-inflammatory and immunosuppressive properties that have shown promise in some studies. We aimed to systematically review LLLT's effectiveness in treating AR and meta-analyze our findings.

Methods: A systematic search of PubMed, Scopus, and Web of Science was conducted on November 24, 2023. All studies investigating LLLT on AR were included, and a pre-post meta-analysis of nasal symptoms (rhinorrhea, nasal congestion, nasal itching, and sneezing) in the LLLT-treated arm was conducted. Rhinoconjunctivitis quality of life questionnaire (RQLQ) scores before and after LLLT were also meta-analyzed alongside a pairwise meta-analysis of LLLT with placebo, acupuncture, steroids/antihistamines, and ultraviolet lasers. A random-effects model was used with a conservative pre-post correlation of 0.4 and standardized mean difference (SMD) as the effect size.

Results: Sixteen studies were included in this review, and we found that nasal symptoms are alleviated post-LLLT in people with AR (SMD: -1.4, 95 CI: [-2.07 to -1.13], p value <0.001). RQLQ scores were also reduced after LLLT (SMD = -0.72, 95 CI: [-0.94 to -0.50], p value <0.001), and very few adverse events were reported. This meta-analysis, however, had significant publication bias and heterogeneity. When compared to a placebo, LLLT did not significantly improve nasal symptoms (SMD: -0.69, p value = 0.167), which might mean the post-LLLT nasal symptom alleviation is due to a placebo effect. Comparisons to other treatment modalities were too few to deduce anything meaningful, although it does appear that LLLT is less effective than UV lasers.

Conclusion: LLLT is most likely effective at alleviating nasal symptomology and has a low likelihood of adverse event incidence, yet more high-quality studies with larger sample sizes are needed to compare LLLT to a placebo to ensure its superiority to the placebo effect, as well as non-inferiority clinical trials to compare it to standard treatments.

Keywords: Allergic rhinitis; Hay fever; Low-level laser therapy.

4

Mult Scler

. 2024 Apr 25:13524585241240398.

doi: 10.1177/13524585241240398. Online ahead of print.

Montelukast as a repurposable additive drug for standard-efficacy multiple sclerosis treatment: Emulating clinical trials with retrospective administrative health claims data

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Affiliations expand

- PMID: 38660773

- DOI: 10.1177/13524585241240398

Abstract

Background: Effective and safe treatment options for multiple sclerosis (MS) are still needed. Montelukast, a leukotriene receptor antagonist (LTRA) currently indicated for asthma or allergic rhinitis, may provide an additional therapeutic approach.

Objective: The study aimed to evaluate the effects of montelukast on the relapses of people with MS (pwMS).

Methods: In this retrospective case-control study, two independent longitudinal claims datasets were used to emulate randomized clinical trials (RCTs). We identified pwMS aged 18-65 years, on MS disease-modifying therapies concomitantly, in de-identified claims from Optum's Clinformatics® Data Mart (CDM) and IQVIA PharMetrics® Plus for Academics.

Cases included 483 pwMS on montelukast and with medication adherence in CDM and 208 in PharMetrics Plus for Academics. We randomly sampled controls from 35,330 pwMS without montelukast prescriptions in CDM and 10,128 in PharMetrics Plus for Academics. Relapses were measured over a 2-year period through inpatient hospitalization and corticosteroid claims. A doubly robust causal inference model estimated the effects of montelukast, adjusting for confounders and censored patients.

Results: pwMS treated with montelukast demonstrated a statistically significant 23.6% reduction in relapses compared to non-users in 67.3% of emulated RCTs.

Conclusion: Real-world evidence suggested that montelukast reduces MS relapses, warranting future clinical trials and further research on LTRAs' potential mechanism in MS.

Keywords: Multiple sclerosis; administrative health claims; clinical informatics; doubly robust; drug repurposing; leukotriene receptor antagonist; montelukast.

Conflict of interest statement

Declaration of Conflicting InterestsThe author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: L.F. has received fees for consultancy and advisory board participation from Genentech, Roche, Novartis, Bristol Myers Squibb, EMD Serono, Sanofi, Horizon Therapeutics, and TG Therapeutics; has received honorarium for participation in educational programs from Medscape, Inc., the MS Association of America and Impact Education; has received program sponsorship from EMD Serono and grant support from the National Institutes of Health (NIH)/ the National Institute of Neurological Disorders and Stroke (NINDS), the Patient-Centered Outcomes Research Institute (PCORI), Genentech, and EMD Serono through her institution; currently serves on the Healthcare Advisory Committee of the MS Association of America. Z.Z. received speaker fee from a recent User Group meeting of Illumina, Inc.

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The Incidence, Mortality and Medical Expenditure in Patients with Asthma in Taiwan: Ten-year Nationwide Study

Kuang-Ming Liao[1,2], Pei-Jun Chen[3], Yu-Tung Hung[4], Tzu-Ju Hsu[4], Fuu-Jen Tsai[4], Te-Chun Shen[5,6,7]

Affiliations expand

- PMID: 38656730

- DOI: 10.1007/s44197-024-00230-8

Abstract

Background: This study examines incidence, mortality, medical expenditure and prescription patterns for asthma on a national scale, particularly in Asian countries for asthma is limited. Our aim is to investigate incidence, mortality, prescription patterns and provide a comprehensive overview of healthcare utilization trends for asthma from 2009 to 2018.

Methods: We included patients diagnosed with asthma between 2009 and 2018. We excluded patients with missing demographic data. Our analysis covered comorbidities, including diabetes mellitus, hypertension, allergic rhinitis, eczema, atopic dermatitis, coronary artery disease, congestive heart failure, chronic kidney disease, chronic hepatitis, stroke, and cancer. Investigated medications comprised oral and intravenous steroids, short-acting beta-agonists, inhaled corticosteroids (ICS), combinations of ICS and long-acting beta-agonists, long-acting muscarinic antagonists, and leukotriene receptor antagonists montelukast. We also assessed the number of outpatient visits, emergency visits, and hospitalizations per year, as well as the average length of hospitalization and average medical costs.

Results: The study included a final count of 88,244 subjects from 1,998,311 randomly selected samples between 2000 and 2019. Over the past decade, there was a gradual decline in newly diagnosed asthma patients per year, from 10,140 to 6,487. The mean age annually increased from 47.59 in 2009 to 53.41 in 2018. Over 55% of the patients were

female. Eczema was diagnosed in over 55% of the patients. Around 90% of the patients used oral steroids, with a peak of 97.29% in 2018, while the usage of ICS varied between 86.20% and 91.75%. Intravenous steroids use rose from 40.94% in 2009 to 54.14% in 2018. The average annual hospital stay ranged from 9 to 12 days, with a maximum of 12.26 days in 2013. Lastly, the average medical expenses per year ranged from New Taiwan dollars 5558 to 7921.

Conclusions: In summary, both asthma incidence and all-cause mortality rates decreased in Taiwan from 2009 to 2018. Further analysis of medical expenses in patients with asthma who required multiple hospitalizations annually revealed an increase in outpatient and emergency visits and hospitalizations, along with longer hospital stays and higher medical costs.

Keywords: Asthma; Incidence; Medical Expenditure; Mortality.

- 28 references

SUPPLEMENTARY INFO

Grants and fundingexpand

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6

Monaldi Arch Chest Dis

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. 2024 Apr 23.

doi: 10.4081/monaldi.2024.2855. Online ahead of print.

Existence and pattern of sleep-related breathing disorders in patients diagnosed with bronchial asthma

Saroj Kumari Meena[1], Rajnish Gupta[2], Manmohan Puri[3]

Affiliations expand

- PMID: 38656459

- DOI: 10.4081/monaldi.2024.2855

Abstract

Asthma and obstructive sleep apnea (OSA) are commonly prevalent diseases, and both can co-exist to result in an alternate overlap syndrome, where a bidirectional relationship can adversely affect each other. This study aimed to determine the existence and pattern of sleep-related breathing disorders in subjects with bronchial asthma. It was prospectively conducted at the National Institute of Tuberculosis and Respiratory Diseases, New Delhi, in diagnosed cases of bronchial asthma. A subjective assessment of sleepiness was done using the Epworth sleepiness scale (ESS). All subjects underwent overnight polysomnography (PSG) in the Sleep Laboratory of the Institute. A total of 70 subjects were screened, and among them, finally, 30 were enrolled. The mean age of the subjects was 37.53±11.21 years, the mean body mass index (BMI) was 26.4±5.58 kg/m2, the mean ESS score was 3.1, and 80% of the subjects were male. After PSG, OSA (apnea hypopnea index >5/hour) was found in 63% (19/30) of the patients, of whom 43% had mild OSA, 10% had moderate OSA, and 10% had severe OSA. 10% (3/30) had nocturnal oxygen desaturation, while none had sleep hypoventilation. Patients with OSA compared to those without OSA had a higher BMI, more co-morbid allergic rhinitis, severe bronchial asthma, and a worse percentage of predicted forced expiratory volume in the first second. The study showed high detection rates of OSA in bronchial asthma patients. Hence, asthma patients should be evaluated for OSA.

chronic cough

1
Respir Med

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. 2024 Apr 24:107642.

doi: 10.1016/j.rmed.2024.107642. Online ahead of print.

Development of an Italian Version of the Leicester Cough Questionnaire and its Relationship with other Symptom-specific Measures for Patients with Chronic Cough

Alessandra Sorano[1], Carlo Fumagalli[2], Elenia Cinelli[1], Surinder S Birring[3], Giovanni A Fontana[1], Federico Lavorini[4]

Affiliations expand

- PMID: 38670318

- DOI: 10.1016/j.rmed.2024.107642

Abstract

Objective: To implement subjective methods for measuring the impact of chronic cough on patients' daily life, including an Italian version of the symptom-specific, health status measure for patients with chronic cough, i.e. the Leicester Cough Questionnaire (LCQ).

Methods: Sixty-five chronic cough patients attended a tertiary cough clinic on two separate occasions 8 weeks apart. The visual analogue scale for cough severity (VAS), the LCQ and the cough disturbance score (CDS) were administered on both occasions. The LCQ was adapted for Italian conditions following a forward-backward translation

procedure. Concurrent validation, internal consistency, repeatability and responsiveness were determined.

Results: The CDS, VAS and LCQ were correlated (r coefficients ranging from 0.69 to 0.94, p<0.01). The internal consistency for each LCQ domain was high (alpha coefficient range 0.87-0.93), as was the 8-week repeatability of the LCQ in the patients (n=36, 60%) who displayed no change in CDS and VAS (intra-class correlation coefficient = 0.86, p<001) over the same period. Patients who reported an improvement in CDS and VAS after 8 weeks (n=29) also demonstrated significant improvements in each LCQ domain. The mean difference in LCQ total score before and after improvements was 2.26 (95% CI: 1.58-4.47).

Conclusions: The Italian version of the LCQ appears to be just as valid as the other language versions of the questionnaire. In addition, the CDS appears to be a clinically useful, symptom-specific measure of the overall disturbance provoked by cough.

Keywords: Leicester cough questionnaire; VAS; chronic cough; cough disturbance score; validation.

Conflict of interest statement

Declaration of Competing Interest The authors have no conflicts of interest to declare.

2

JMIR Res Protoc

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doi: 10.2196/54388.

Leveraging AI and Machine Learning to Develop and Evaluate a Contextualized User-Friendly Cough Audio Classifier for Detecting Respiratory Diseases: Protocol for a Diagnostic Study in Rural Tanzania

Kahabi Ganka Isangula[1], Rogers John Haule[1]

Affiliations expand

- PMID: 38652526

- DOI: 10.2196/54388

Free article

Abstract

Background: Respiratory diseases, including active tuberculosis (TB), asthma, and chronic obstructive pulmonary disease (COPD), constitute substantial global health challenges, necessitating timely and accurate diagnosis for effective treatment and management.

Objective: This research seeks to develop and evaluate a noninvasive user-friendly artificial intelligence (AI)-powered cough audio classifier for detecting these respiratory conditions in rural Tanzania.

Methods: This is a nonexperimental cross-sectional research with the primary objective of collection and analysis of cough sounds from patients with active TB, asthma, and COPD in outpatient clinics to generate and evaluate a noninvasive cough audio classifier. Specialized cough sound recording devices, designed to be nonintrusive and user-friendly, will facilitate the collection of diverse cough sound samples from patients attending outpatient clinics in 20 health care facilities in the Shinyanga region. The collected cough sound data will undergo rigorous analysis, using advanced AI signal processing and machine learning techniques. By comparing acoustic features and patterns associated with TB, asthma, and COPD, a robust algorithm capable of automated disease discrimination will be generated facilitating the development of a smartphone-based cough sound classifier. The classifier will be evaluated against the calculated reference standards

including clinical assessments, sputum smear, GeneXpert, chest x-ray, culture and sensitivity, spirometry and peak expiratory flow, and sensitivity and predictive values.

Results: This research represents a vital step toward enhancing the diagnostic capabilities available in outpatient clinics, with the potential to revolutionize the field of respiratory disease diagnosis. Findings from the 4 phases of the study will be presented as descriptions supported by relevant images, tables, and figures. The anticipated outcome of this research is the creation of a reliable, noninvasive diagnostic cough classifier that empowers health care professionals and patients themselves to identify and differentiate these respiratory diseases based on cough sound patterns.

Conclusions: Cough sound classifiers use advanced technology for early detection and management of respiratory conditions, offering a less invasive and more efficient alternative to traditional diagnostics. This technology promises to ease public health burdens, improve patient outcomes, and enhance health care access in under-resourced areas, potentially transforming respiratory disease management globally.

International registered report identifier (irrid): PRR1-10.2196/54388.

Keywords: Africa; Tanzania; analysis; artificial intelligence; asthma; chronic obstructive pulmonary disease; cough; cough classifiers; cough sound; cross-sectional research; detecting respiratory disease; diagnostic study; machine learning; management; mobile phone; noninvasive; respiratory diseases; rural; treatment; tuberculosis; user-friendly.

. 2024 Apr 23.

doi: 10.1002/jcph.2442. Online ahead of print.

Single- and Multiple-Dose Pharmacokinetics of Gefapixant (MK-7264), a P2X3 Receptor Antagonist, in Healthy Adults

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Affiliations expand

- PMID: 38651193

- DOI: 10.1002/jcph.2442

Abstract

Gefapixant (MK-7264, RO4926219, AF-219) is a first-in-class P2X3 antagonists being developed to treat refractory or unexplained chronic cough. The initial single- and multiple-dose safety, tolerability, and pharmacokinetics of gefapixant at doses ranging from 7.5 to 1800 mg were assessed in four clinical trials. Following single-dose administration of 10-450 mg, the pharmacokinetic (PK) profile of gefapixant in plasma and urine demonstrated low inter-subject variability and a dose-proportional exposure. Following administration of multiple doses twice daily, the plasma exposures were dose-proportional at doses ranging from 7.5 to 50 mg and less than dose-proportional at doses ranging from 100 to 1800 mg. The time to mean peak drug concentration ranged from 2 to 3 h post-dose, and steady state was achieved by 7 days after dosing, with an accumulation ratio of approximately 2, comparing data from day 1 to steady state. The mean apparent terminal half-life ranged from 8.2 to 9.6 h. Gefapixant was primarily excreted unmodified in urine. Gefapixant was well tolerated following single-dose administration up to 1800 mg and multiple doses up to 1800 mg twice daily; there were no serious adverse events (AEs) reported. The most common AE reported was dysgeusia. The PK profile supports a twice-daily dosing regimen.

Keywords: AF-219; P2X3; RO4926219; antitussives; chronic cough; gefapixant; purinergic receptor.

- 16 references

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

1
Am J Respir Crit Care Med

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. 2024 Apr 26.

doi: 10.1164/rccm.202307-1165OC. Online ahead of print.

Five-Year Outcomes Among U.S. Bronchiectasis and Nontuberculous Mycobacterial Registry Patients

Timothy R Aksamit[1], Nicholas Locantore[2], Doreen Addrizzo-Harris[3], Juzar Ali[4], Alan Barker[5], Ashwin Basavaraj[3], Megan Behrman[6], Amanda E Brunton[2], Sarah Chalmers[7], Radmila Choate[8], Nathan C Dean[9], Angela DiMango[10], David Fraulino[11], Margaret M Johnson[12], Nicole C Lapinel[13], Diego J Maselli[14], Pamela J McShane[15], Mark L Metersky[11], Bruce E Miller[2], Edward T Naureckas[16], Anne E O'Donnell[17], Kenneth N Olivier[18], Elly Prusinowski[19], Marcos I Restrepo[20], Christopher J Richards[21], Gloria Rhyne[22], Andreas Schmid[23], George M Solomon[24], Ruth Tal-Singer[25], Byron Thomashow[26], Gregory Tino[27], Kevin Tsui[19], Sumith Abraham Varghese[19], Heather E Warren[19], Kevin Winthrop[28], Beth Shoshanna Zha[29]

Affiliations expand

- PMID: 38668710

- DOI: 10.1164/rccm.202307-1165OC

Abstract

Rationale: Nontuberculous mycobacteria (NTM) are prevalent among patients with bronchiectasis. However, the long-term natural history of patients with NTM and bronchiectasis is not well described.

Objective: To assess the impact of NTM on 5-year clinical outcomes and mortality in patients with bronchiectasis.

Methods: Patients in the United States Bronchiectasis and Nontuberculous Mycobacteria Research Registry with ≥5 years of follow-up were eligible. Data were collected for all-cause mortality, lung function, exacerbations, hospitalizations, and disease severity. Outcomes were compared between patients with and without NTM at baseline. Mortality was assessed using Cox proportional hazards models and the log-rank test.

Measurements and main results: In total, 2,634 patients were included: 1,549 (58.8%) with and 1,085 (41.2%) without NTM at baseline. All-cause mortality (95% confidence interval) at Year 5 was 12.1% (10.5%, 13.7%) overall, 12.6% (10.5%, 14.8%) in patients with NTM, and 11.5% (9.0%, 13.9%) in patients without NTM. Independent predictors of 5-year mortality were baseline forced expiratory volume in 1 second % predicted, age, hospitalization within 2 years before baseline, body mass index, and gender (all $p<0.01$). The probabilities of acquiring NTM or *Pseudomonas aeruginosa* were approximately 4% and 3% per year, respectively. Spirometry, exacerbations, and hospitalizations were similar irrespective of NTM status, except that annual exacerbations were lower in patients with NTM ($p<0.05$).

Conclusions: Outcomes including exacerbations, hospitalizations, rate of loss of lung function, and mortality rate were similar across 5 years in patients with bronchiectasis with or without NTM.

Keywords: Pseudomonas aeruginosa; exacerbation; hospitalization; mortality; spirometry.

2

J Asthma

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. 2024 Apr 25:1-4.

doi: 10.1080/02770903.2024.2344168. Online ahead of print.

Mounier-Kuhn syndrome in poorly controlled asthma

Marta Solís García[1], Carolina Cisneros Serrano[1], Ana Sofía Martín Hernández[1], Jose María Eiros Bachiller[1], Celeste Marcos[1]

Affiliations expand

- PMID: 38639468

- DOI: 10.1080/02770903.2024.2344168

Abstract

Introduction: Mounier-Kuhn syndrome or tracheobronchomegaly, is a rare condition that consists of abnormal dilation of the trachea and main bronchi due to a pathological arrangement of smooth muscle fibers in this area.

Case report: We present the case of a 46-year-old woman with poorly controlled asthma and recurrent infections, who was diagnosed with Mounier-Kuhn syndrome through a computed tomography scan revealing an unusual enlargement of the trachea with associated bronchiectasis.

Results: The diagnosis of Mounier-Kuhn syndrome is radiological, involving measurement of the trachea where a diameter >25 mm in men and >21 mm in women is observed. While diagnosis is sometimes incidental, there is an association with respiratory diseases such as asthma or COPD, hence clinical suspicion is important in patients with poorly controlled underlying conditions who present with recurrent infections, inadequate secretion management, or even hemoptysis.

Conclusions: Despite its rarity, this syndrome significantly impacts patients' quality of life. Diagnosis and management involve comprehensive evaluations including computed tomography, with a multidisciplinary approach including pulmonologists and radiologists. Exploring its clinical features, associations with other respiratory diseases and treatment options is crucial in managing this rare respiratory condition.

Keywords: Asthma; bronchiectasis; computed tomography; hemoptysis; radiologists; tracheobronchomegaly.

3

Respir Res

. 2024 Apr 24;25(1):177.

doi: 10.1186/s12931-024-02810-5.

Exploring the link between a novel approach for computer aided lung sound analysis and imaging biomarkers: a cross-sectional study

Eline Lauwers[1,2], Toon Stas[3], Ian McLane[4,5], Annemiek Snoeckx[6,7], Kim Van Hoorenbeeck[8,9], Wilfried De Backer[7,10,11], Kris Ides[8,3,9,11], Jan Steckel[3], Stijn Verhulst[8,9]

Affiliations expand

- PMID: 38658980

- PMCID: PMC11044477

- DOI: 10.1186/s12931-024-02810-5

Abstract

Background: Computer Aided Lung Sound Analysis (CALSA) aims to overcome limitations associated with standard lung auscultation by removing the subjective component and allowing quantification of sound characteristics. In this proof-of-concept study, a novel automated approach was evaluated in real patient data by comparing lung sound characteristics to structural and functional imaging biomarkers.

Methods: Patients with cystic fibrosis (CF) aged > 5y were recruited in a prospective cross-sectional study. CT scans were analyzed by the CF-CT scoring method and Functional Respiratory Imaging (FRI). A digital stethoscope was used to record lung sounds at six chest locations. Following sound characteristics were determined: expiration-to-inspiration (E/I) signal power ratios within different frequency ranges, number of crackles per respiratory phase and wheeze parameters. Linear mixed-effects models were computed to relate CALSA parameters to imaging biomarkers on a lobar level.

Results: 222 recordings from 25 CF patients were included. Significant associations were found between E/I ratios and structural abnormalities, of which the ratio between 200 and 400 Hz appeared to be most clinically relevant due to its relation with bronchiectasis, mucus plugging, bronchial wall thickening and air trapping on CT. The number of crackles was also associated with multiple structural abnormalities as well as regional airway resistance determined by FRI. Wheeze parameters were not considered in the statistical analysis, since wheezing was detected in only one recording.

Conclusions: The present study is the first to investigate associations between auscultatory findings and imaging biomarkers, which are considered the gold standard to evaluate the respiratory system. Despite the exploratory nature of this study, the results showed various meaningful associations that highlight the potential value of automated CALSA as a novel non-invasive outcome measure in future research and clinical practice.

Keywords: Chest computed tomography; Computer aided lung sound analysis; Cystic fibrosis; Digital lung auscultation; Functional respiratory imaging.

Conflict of interest statement

IM was Chief Technology Officer at Sonavi Labs at the time the study was executed, which is a medical device and software company that commercialized an advanced digital

stethoscope to record and analyze lung sounds using AI technology. WDB is executive chair of the board of directors at Fluidda NV, and EL is an employee of Fluidda NV, a company that develops and markets the FRI technology described in this paper. The other authors had no financial relationships with any organization or company that might have an interest in the submitted work during the conduct of this study. No direct funding was received from either Sonavi Labs or Fluidda NV.

- 27 references
- 2 figures

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS

4

Comparative Study

BMC Pulm Med

. 2024 Apr 24;24(1):203.

doi: 10.1186/s12890-024-03019-4.

Embosphere microspheres size for bronchial artery embolization in patients with hemoptysis caused by bronchiectasis: a retrospective

comparative analysis of 500–750 versus 700–900 μm microspheres

Hong-Dou Xu[#1], Liang Yang[#1], Shi-Bing Hu[2]

Affiliations expand

- PMID: 38658883
- PMCID: PMC11044458
- DOI: 10.1186/s12890-024-03019-4

Abstract

Background: Bronchial arterial embolization (BAE) has been accepted as an effective treatment for bronchiectasis-related hemoptysis. However, rare clinical trials compare different sizes of specific embolic agents. This study aims to evaluate whether different Embosphere microsphere sizes change the outcome of BAE.

Methods: A retrospective review was conducted on consecutive patients with bronchiectatic hemoptysis who were scheduled to undergo BAE treatment during a period from January 2018 to December 2022. The patients received BAE using microspheres of different sizes: group A patients were treated with 500-750 μm microspheres, and group B patients were treated with 700-900 μm microspheres. The cost of embolic microspheres (Chinese Yuan, CNY), duration of hospitalization, complications, and hemoptysis-free survival were compared between patients in group A and those in group B. A Cox proportional hazards regression model was used to identify predictors of recurrent hemoptysis.

Results: Median follow-up was 30.2 months (range, 20.3-56.5 months). The final analysis included a total of 112 patients (49-77 years of age; 45 men). The patients were divided into two groups: group A (N = 68), which received 500-750 μm Embosphere microspheres, and group B (N = 44), which received 700-900 μm Embosphere microspheres. Except for the cost of embolic microspheres(group A,5314.8 + 1301.5 CNY; group B, 3644.5 + 1192.3 CNY; p = 0.042), there were no statistically significant differences in duration of hospitalization (group A,7.2 + 1.4 days; group B, 8 + 2.4days; p = 0.550), hemoptysis-free survival (group A, 1-year, 2-year, 3-year, 85.9%, 75.8%, 62.9%; group B, 1-year, 2-year, 3-year, 88.4%, 81.2%,59.4%;P = 0.060), and complications(group A,26.5%; group B, 38.6%; p = 0.175) between the two groups. No major complications were observed. The multivariate

analysis results revealed that the presence of cystic bronchiectasis (OR 1.61, 95% CI 1.12-2.83; P = 0.001) and systemic arterial-pulmonary shunts (SPSs) (OR 1.52, 95% CI 1.10-2.72; P = 0.028) were independent risk factors for recurrent bleeding.

Conclusions: For the treatment of BAE in patients with bronchiectasis-related hemoptysis, 500-750 µm diameter Embosphere microspheres have a similar efficacy and safety profile compared to 700-900 µm diameter Embosphere microspheres, especially for those without SPSs or cystic bronchiectasis. Furthermore, the utilization of large-sized (700-900 µm) Embosphere microspheres is associated with the reduced cost of an embolic agent.

Keywords: Bronchiectasis; Embosphere microspheres; Hemoptysis; Hemoptysis recurrence; Size.

Conflict of interest statement

The authors declare no competing interests.

- 21 references
- 4 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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J Med Econ

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. 2024 Apr 22:1-15.

doi: 10.1080/13696998.2024.2340382. Online ahead of print.

Impact of *pseudomonas aeruginosa* on resource utilization and costs in patients with exacerbated non-cystic fibrosis bronchiectasis

Meg Franklin[1,2], Michael E Minshall[3], Federica Pontenani[4], Sunjay Devarajan[5]

Affiliations expand

- PMID: 38646702

- DOI: 10.1080/13696998.2024.2340382

Free article

Abstract

Aims Non-cystic fibrosis bronchiectasis (NCFB) is a chronic progressive respiratory disorder occurring at a rate ranging from 4.2 to 278.1 cases per 100,000 persons, depending on age, in the United States. For many patients with NCFB, the presence of *Pseudomonas aeruginosa* (PA) makes treatment more complicated and typically has worse outcomes. Management of NCFB can be challenging, warranting a better understanding of the burden of illness for NCFB, treatments applied, healthcare resources used, and subsequent treatment costs. Comparing patients diagnosed with exacerbated NCFB, with or without PA on antibiotic utilization, treatments, and healthcare resources utilization and costs, was the purpose of this study.**Materials and Methods** This was a retrospective cohort study of commercial claims from IQVIA's PharMetrics Plus database (01/01/2006-12/31/2020). Study patients with a diagnosis of NCFB were stratified into two groups based on presence or absence of PA, then followed to identify demographic characteristics, comorbid conditions, antibiotic treatment regimen prescribed, healthcare resources utilized, and costs of care.**Results** The results showed that patients with exacerbated NCFB who were PA^+ had significantly more oral antibiotic fills per patient per year, more inpatient admissions with a longer length of stay, and more outpatient encounters than those who were PA^-. For costs, PA^+ patients also had significantly greater total healthcare costs per patient when compared to those who were PA^-.**Conclusion** Exacerbated NCFB with PA^+ was associated with increased antibiotic usage, greater resource utilization, and increased costs. The major contributor to the cost differences was the use of inpatient services. Treatment strategies aimed at reducing the need for inpatient treatment could lessen the disparities observed in patients with NCFB.

Keywords: I; I1; I10; I12; Non-cystic fibrosis bronchiectasis; healthcare resource utilization.