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COPD

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Respir Res

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. 2022 Nov 11;23(1):309.

doi: 10.1186/s12931-022-02113-7.

Subtyping preserved ratio impaired spirometry (PRISm) by using quantitative HRCT imaging characteristics

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Affiliations expand

- PMID: 36369019

- DOI: 10.1186/s12931-022-02113-7

Abstract

Background: Preserved Ratio Impaired Spirometry (PRISm) is defined as FEV1/FVC ≥ 70% and FEV1 < 80%pred by pulmonary function test (PFT). It has highly prevalence and is associated with increased respiratory symptoms, systemic inflammation, and mortality. However, there are few radiological studies related to PRISm. The purpose of this study was to investigate the quantitative high-resolution computed tomography (HRCT) characteristics of PRISm and to evaluate the correlation between quantitative HRCT parameters and pulmonary function parameters, with the goal of establishing a nomogram model for predicting PRISm based on quantitative HRCT.

Methods: A prospective and continuous study was performed in 488 respiratory outpatients from February 2020 to February 2021. All patients underwent both deep inspiratory and expiratory CT examinations, and received pulmonary function test (PFT) within 1 month. According to the exclusion criteria and Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification standard, 94 cases of normal pulmonary function, 51 cases of PRISm and 48 cases of mild to moderate chronic obstructive lung disease (COPD) were included in the study. The lung parenchyma, parametric response mapping (PRM), airway and vessel parameters were measured by automatic segmentation software (Aview). One-way analysis of variance (ANOVA) was used to compare the differences in clinical features, pulmonary function parameters and quantitative CT parameters. Spearman rank correlation analysis was used to evaluate the correlation between CT quantitative index and pulmonary function parameters. The predictors were obtained by binary logistics regression analysis respectively in normal and PRISm as well as PRISm and mild to moderate COPD, and the nomogram model was established.

Results: There were significant differences in pulmonary function parameters among the three groups ($P < 0.001$). The differences in pulmonary parenchyma parameters such as emphysema index (EI), pixel indices-1 (PI-1) and PI-15 were mainly between mild to moderate COPD and the other two groups. The differences of airway parameters and pulmonary vascular parameters were mainly between normal and the other two groups, but were not found between PRISm and mild to moderate COPD. Especially there were significant differences in mean lung density (MLD) and the percent of normal in PRM (PRM^{Normal}) among the three groups. Most of the pulmonary quantitative CT parameters had mild to moderate correlation with pulmonary function parameters. The predictors of the nomogram model using binary logistics regression analysis to distinguish normal from PRISm were smoking, MLD, the percent of functional small airways disease (fSAD) in PRM (PRM^{fSAD}) and Lumen area. It had a good goodness of fit ($\chi^2 = 0.31$, $P < 0.001$) with the area under curve (AUC) value of 0.786. The predictor of distinguishing PRISm from mild to moderate COPD were PRM^{Emph} ($P < 0.001$, AUC = 0.852).

Conclusions: PRISm was significantly different from subjects with normal pulmonary function in small airway and vessel lesions, which was more inclined to mild to moderate COPD, but there was no increase in pulmonary parenchymal attenuation. The nomogram based on quantitative HRCT parameters has good predictive value and provide more objective evidence for the early screening of PRISm.

Keywords: Chronic obstructive pulmonary disease; Computed tomography; Preserved ratio impaired spirometry; Pulmonary function test; Quantitative.

- 35 references

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Viral Immunol

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. 2022 Nov 11.

doi: 10.1089/vim.2022.0135. Online ahead of print.

Persistence of RNA Viruses in the Respiratory Tract: An Overview

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Affiliations expand

- PMID: 36367976

- DOI: 10.1089/vim.2022.0135

Abstract

Respiratory RNA viruses are a major cause of acute lower respiratory tract infections and contribute substantially to hospitalization among infants, elderly, and immunocompromised. Complete viral clearance from acute infections is not always achieved, leading to persistence. Certain chronic respiratory diseases like asthma and chronic obstructive pulmonary disease have been associated with persistent infection by human respiratory syncytial virus and human rhinovirus, but it is still not clear whether RNA

viruses really establish long-term infections as it has been recognized for DNA viruses as human bocavirus and adenoviruses. Herein, we summarize evidence of RNA virus persistence in the human respiratory tract, as well as in some animal models, to highlight how long-term infections might be related to development and/or maintenance of chronic respiratory symptoms.

Keywords: respiratory RNA viruses; respiratory tract; viral persistence.

Nicotine Tob Res

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doi: 10.1093/ntr/ntac257. Online ahead of print.

The impact of the Danish national smoking ban from 2007 on the incidence of eight smoking-related diseases - a nationwide register-based interrupted time series analysis

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- PMID: 36367774

- DOI: 10.1093/ntr/ntac257

Abstract

Background: Previous research has documented the effect of comprehensive smoking bans on preventing various adverse health outcomes in the years post-ban. In 2007, Denmark implemented a national smoking ban that prohibited indoor smoking in workplaces and public settings, although only partial restrictions applied in specific premises such as small bars, one-person offices, and in psychiatric units. We tested the hypothesis that the implementation of the national smoking ban was associated with a decrease in incidence of smoking-related morbidity in the Danish population compared to the pre-ban period.

Methods: Interrupted time series analyses including the entire Danish population (30+ years) was conducted. Information of hospitalizations and cause-specific mortality due to acute myocardial infarction, heart failure, hemorrhagic stroke, ischemic stroke, chronic obstructive pulmonary disease, cancer in bronchus and lung, cancer in lip, mouth, oral cavity, and pharynx, and bladder cancer were obtained from population-based registers. Poisson regression models accounting for seasonal variations and secular trends quantified immediate changes in incidence rates occurring at the time of the smoking ban as well as changes in the post-ban trend compared to pre-ban levels.

Results: Overall, we observed no consistent declines in incidence of cardiovascular diseases, chronic obstructive pulmonary disease, or the specific types of cancer in the post-ban period compared with the pre-ban period.

Conclusion: No consistent reduction in incidence of smoking-related diseases were observed after the smoking ban was introduced in Denmark. This probably reflects that the Danish smoking ban included several exemptions, resulting in a less comprehensive ban compared those introduced in other countries.

Implications: In this study we found that the Danish national smoking ban from 2007 did not consistently reduced the incidence of eight smoking-related outcomes in the post-ban period compared to pre-ban levels. We argue that due to the exemptions in the smoking ban, which for example allowed smoking in specific premises of the care and nursing sector, in one-person offices, and small bars, the ban was not sufficiently comprehensive to influence smoking behavior and thereof the incidence of smoking-related morbidity. Our findings highlight the importance of introducing comprehensive legislative measures in order to yield largest health benefits at a population level.

Intern Emerg Med

. 2022 Nov 10.

doi: 10.1007/s11739-022-03132-4. Online ahead of print.

Predictive value of the hemoglobin-albumin-lymphocyte-platelet (HALP) index for ICU mortality in patients with acute exacerbations of chronic obstructive pulmonary disease (AECOPD)

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- DOI: 10.1007/s11739-022-03132-4

Abstract

The combined index of hemoglobin, albumin, lymphocyte, and platelet (HALP) is a novel indicator reflecting systemic inflammation and nutritional status. To explore the relationship between HALP score and ICU mortality risk in patients with acute exacerbations of chronic obstructive pulmonary disease (AECOPD). A total of 1533 AECOPD patients from the eICU Collaborative Research Database (eICU-CRD) between 2014 and 2015 were included in this retrospective cohort study. Univariate and multivariate Cox proportional hazards models were utilized to investigate the association of HALP score, platelet-to-lymphocyte ratio (PLR) score, and lymphocyte-to-monocyte ratio (LMR) score with the ICU mortality risk in patients with AECOPD. Stratified analyses were

performed based on patients' ICU admission type, body mass index (BMI), and Acute Physiology, Age and Chronic Health Evaluation IV (APACHE IV) score. Of these 1533 AECOPD patients, 123 (8.00%) patients died in the ICU. Low HALP score [hazard ratio (HR) = 1.69; 95% confidence interval (CI) 1.14-2.53] and low LMR score (HR = 1.60; 95% CI 1.07-2.39) were associated with an increased ICU mortality risk in patients with AECOPD after adjusting for all confounders. Stratified analyses indicated that low HALP score were still associated with a higher ICU mortality risk in patients admitted to ICU by emergency (HR = 1.81; 95% CI 1.11-2.96), obese patients (HR = 2.81; 95% CI 1.29-6.10), and patients with low APACHE scores (HR = 2.87; 95% CI 1.75-4.69). Low HALP score was associated with an increased risk of ICU mortality in patients with AECOPD, suggesting that the HALP score may be a novel prognostic predictor in patients with AECOPD.

Keywords: Acute exacerbations of chronic obstructive pulmonary disease; Albumin; Hemoglobin; ICU mortality risk; Inflammation; Lymphocyte; Nutritional status; Platelet index.

- 30 references

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Toxics

. 2022 Nov 6;10(11):667.

doi: 10.3390/toxics10110667.

Impact of Acute Exacerbation and Its Phenotypes on the Clinical Outcomes of Chronic Obstructive Pulmonary Disease

in Hospitalized Patients: A Cross-Sectional Study

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- PMID: 36355958

- DOI: 10.3390/toxics10110667

Abstract

Acute exacerbations of COPD (AECOPD) are clinically significant events having therapeutic and prognostic consequences. However, there is a lot of variation in its clinical manifestations described by phenotypes. The phenotypes of AECOPD were categorized in this study based on pathology and exposure. In our cross-sectional study, conducted between 1 January 2016 to 31 December 2020, the patients were categorized into six groups based on pathology: non-bacterial and non-eosinophilic; bacterial; eosinophilic; bacterial infection with eosinophilia; pneumonia; and bronchiectasis. Further, four groups were classified based on exposure to tobacco smoke (TS), biomass smoke (BMS), both, or no exposure. Cox proportional-hazards regression analyses were performed to assess hazard ratios, and Kaplan-Meier analysis was performed to assess survival, which was then compared using the log-rank test. The odds ratio (OR) and independent predictors of ward admission type and length of hospital stay were assessed using binomial logistic regression analyses. Of the 2236 subjects, 2194 were selected. The median age of the cohort was 67.0 (60.0 to 74.0) and 75.2% were males. Mortality rates were higher in females than in males (6.2% vs. 2.3%). AECOPD-B (bacterial infection) subjects [HR 95% CI 6.42 (3.06-13.46)], followed by AECOPD-P (pneumonia) subjects [HR (95% CI: 4.33 (2.01-9.30)], were at higher mortality risk and had a more extended hospital stay (6.0 (4.0 to 9.5) days; 6.0 (4.0 to 10.0). Subjects with TS and BMS-AECOPD [HR 95% CI 7.24 (1.53-34.29)], followed by BMS-AECOPD [HR 95% CI 5.28 (2.46-11.35)], had higher mortality risk. Different phenotypes have different impacts on AECOPD clinical outcomes. A better understanding of AECOPD phenotypes could contribute to developing an algorithm for the precise management of different phenotypes.

Keywords: AECOPD; COPD; acute exacerbation; biomass; mortality; phenotype; tobacco.

SUPPLEMENTARY INFO

Grant supportexpand

Expert Rev Respir Med

. 2022 Nov 9.

doi: 10.1080/17476348.2022.2145951. Online ahead of print.

Cost-effectiveness of single-inhaler triple therapy for patients with severe COPD: A systematic literature review

Rezwanul Hasan Rana[1,2], Khorshed Alam[3], Syed Afroz Keramat[4], Jeff Gow[3,5,6]

Affiliations expand

- PMID: 36350733

- DOI: 10.1080/17476348.2022.2145951

Abstract

Introduction: Evidence from non-randomised studies shows benefits for single-inhaler users compared with multiple-inhaler users who receive the same medication. As a result, comparative cost-effectiveness studies are required to inform treatment decisions with an increasing choice of medications and devices for chronic obstructive pulmonary disease (COPD). This study conducted a systematic literature review to evaluate the cost-effectiveness of using a single combination inhaler regimen for patients with severe COPD. This review also investigated the health impact on patients in different settings.

Areas covered: A systematic literature search was conducted in PubMed (MEDLINE), EMBASE, Web of Science, Scopus, Cochrane Library, EBSCO Host (including CINAHL and

EconLit), Health Technology Assessment Database, National Institute for Health Research Economic Evaluation Database, Cost-Effectiveness Analysis Registry and Google Scholar.

Expert opinion: Based on the primary findings of 13 included studies: (1) single-inhaler triple therapy was a cost-effective treatment option for patients with severe COPD, and (2) triple therapy also resulted in better health outcomes (reduced exacerbations, life-years gained) and increased QALYs for patients with severe COPD. Eleven out of the thirteen selected studies were funded by the pharmaceutical industry, and none were conducted in least developed countries. Therefore, the results should be interpreted with caution.

Keywords: COPD; Cost-effectiveness; Multiple inhalers; Single inhaler; Systematic review.

BMC Pulm Med

. 2022 Nov 9;22(1):406.

doi: 10.1186/s12890-022-02203-8.

Chronic rhinosinusitis associated with chronic bronchitis in a five-year follow-up: the Telemark study

Joel Bergqvist[1,2], Mogens Bove[3,4], Anders Andersson[5,6], Linus Schiöler[7], Geir Klepaker[8], Regine Abrahamsen[8], Anne Kristin M Fell[8,9], Johan Hellgren[10,3]

Affiliations expand

- PMID: 36348489

- DOI: 10.1186/s12890-022-02203-8

Free article

Abstract

Background: Chronic rhinosinusitis (CRS) is associated with generalised airway inflammation. Few studies have addressed the relationship between CRS and chronic bronchitis (CB).

Methods: This prospective study over a five-year period aims to investigate the risk of developing CB in subjects reporting CRS at the beginning of the study. A random sample of 7393 adult subjects from Telemark County, Norway, answered a comprehensive respiratory questionnaire in 2013 and then 5 years later in 2018. Subjects reporting CB in 2013 were excluded from the analyses. New cases of CB in 2018 were analysed in relation to having CRS in 2013 or not.

Results: The prevalence of new-onset CB in 2018 in the group that reported CRS in 2013 was 11.8%. There was a significant increase in the odds of having CB in 2018 in subjects who reported CRS in 2013 (OR 3.8, 95% CI 2.65-5.40), adjusted for age, sex, BMI, smoking and asthma.

Conclusion: In this large population sample, CRS was associated with increased odds of developing CB during a five-year follow-up. Physicians should be aware of chronic bronchitis in patients with CRS.

Keywords: Chronic bronchitis; Epidemiology; Rhinitis.

- 33 references

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

mSphere

. 2022 Nov 7;e0037722.

doi: 10.1128/msphere.00377-22. Online ahead of print.

Effects of Fluticasone Propionate on *Klebsiella pneumoniae* and Gram-Negative Bacteria Associated with Chronic Airway Disease

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Affiliations expand

- PMID: 36342141

- DOI: 10.1128/msphere.00377-22

Free article

Abstract

Inhaled corticosteroids (ICS) are commonly prescribed first-line treatments for asthma and chronic obstructive pulmonary disease (COPD). Recent evidence has shown that ICS use is associated with changes in the airway microbiome, which may impact clinical outcomes such as potential increased risk for pneumonia in COPD. Although the immunomodulatory effects of corticosteroids are well appreciated, whether ICS could directly influence the behavior of respiratory tract bacteria has been unknown. In this pilot study we explored the

effects of fluticasone proprionate, a commonly prescribed inhaled corticosteroid, on respiratory bacteria with an expanded focus on Klebsiella pneumoniae, a species previously implicated in fluticasone-associated pneumonia in COPD. We observed significant effects of fluticasone proprionate on growth responses of *K. pneumoniae*, as well as other bacterial species isolated from asthmatic patients. Fluticasone-exposed *K. pneumoniae* displayed altered expression of several bacterial genes and reduced the metabolic activity of bronchial epithelial cells and their expression of human β-defensin 2. Targeted assays identified a fluticasone metabolite from fluticasone-exposed *K. pneumoniae* cells, suggesting this species may be capable of metabolizing fluticasone proprionate. Collectively, these observations support the hypothesis that specific members of the airway microbiota possess the functional repertoire to respond to or potentially utilize corticosteroids in their microenvironment. These findings lay a foundation for novel research directions into the potential direct effects of ICS, often prescribed long term to patients, on the broader airway microbial community and on the behavior of specific microbial species implicated in asthma and COPD outcomes. **IMPORTANCE** Inhaled corticosteroids are widely prescribed for many respiratory diseases, including asthma and COPD. While they benefit many patients, corticosteroids can also have negative effects. Some patients do not improve with treatment and even experience adverse side effects. Recent studies have shown that inhaled corticosteroids can change the make-up of bacteria in the human respiratory tract. However, whether these medications can directly impact the behavior of such bacteria has been unknown. Here, we explored the effects of fluticasone propionate, a commonly prescribed inhaled corticosteroid, on Klebsiella pneumoniae and other airway bacteria of interest, including primary species isolated from adult asthma patients. We provide evidence of growth responses to direct fluticasone exposure in culture and further examined fluticasone's effects on K. pneumoniae, including gene expression changes and effects of fluticasone-exposed bacteria on airway cells. These findings indicate that members of the human airway bacterial community possess the functional ability to respond to corticosteroids, which may have implications for the heterogeneity of treatment response observed clinically.

Keywords: COPD; asthma; bacteria; corticosteroids; inhaled corticosteroids; microbiome.

. 2022 Nov 12;24(12):1978-1984.

doi: 10.1093/ntr/ntac137.

Trends in Hospital Admissions for Chronic Obstructive Pulmonary Diseases After Comprehensive Tobacco Control Policies in Beijing, China

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Affiliations expand

- PMID: 35808957

- DOI: 10.1093/ntr/ntac137

Abstract

Introduction: Only a few studies have examined the effectiveness of tobacco control policies on respiratory conditions, and the results were less consistent. The 2015 Beijing tobacco control policy package incorporating all six components of MPOWER has been implemented since Jun 2015. The present study aimed to evaluate the impact of a comprehensive tobacco control policy package on hospital admissions for chronic obstructive pulmonary disease (COPD) in Beijing, China.

Aims and methods: An interrupted time-series study was conducted based on the hospital admission information for about 18 million residents, who were covered by the Beijing Medical Claim Data for Employees from January 2013 to June 2017. The average percentage change of COPD hospital admission rates and reductions in hospital admission numbers were estimated by segmented Poisson regression models.

Results: There were 54 040 COPD hospital admissions with a crude rate of 67.2 per 100 000 residents during the observational period. After the implementation of the policy package, the hospital admission rates of COPD were reduced by -14.7% (95%CI: -17.8%, -11.5%) immediately. The secular trend was slowed down by -3.0% (95% CI: -5.6%, -0.4%) annually. A total of 5 581 reductions in COPD hospital admissions were estimated during

the 25 months post-law period, accounting for 17.5% (95% CI: 12.5%, 22.5%) of overall COPD hospital admissions. More reductions were shown in males and those aged over 65 years old.

Conclusions: The results indicated significant protections against hospitalization of COPD after the 2015 Beijing comprehensive tobacco control policy package. The results provide support for public health benefits for respiratory conditions from WHO-recommended tobacco control measures.

Implications: Only a few studies have examined the effectiveness of tobacco control policies on respiratory conditions, and the results were less consistent. Based on medical records for about 18 million residents, this study showed an association between comprehensive tobacco control policies and significant reductions of hospital admissions for chronic obstructive pulmonary disease. The results provide support for public health benefits for respiratory conditions from WHO-recommended tobacco control measures.

Hum Mol Genet

. 2022 Nov 10;31(22):3873-3885.

doi: 10.1093/hmg/ddac117.

Assessing the contribution of rare genetic variants to phenotypes of

chronic obstructive pulmonary disease using whole-genome sequence data

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Affiliations expand

- PMID: 35766891

- DOI: 10.1093/hmg/ddac117

Abstract

Rationale: Genetic variation has a substantial contribution to chronic obstructive pulmonary disease (COPD) and lung function measurements. Heritability estimates using genome-wide genotyping data can be biased if analyses do not appropriately account for the nonuniform distribution of genetic effects across the allele frequency and linkage disequilibrium (LD) spectrum. In addition, the contribution of rare variants has been unclear.

Objectives: We sought to assess the heritability of COPD and lung function using whole-genome sequence data from the Trans-Omics for Precision Medicine program.

Methods: Using the genome-based restricted maximum likelihood method, we partitioned the genome into bins based on minor allele frequency and LD scores and estimated heritability of COPD, FEV1% predicted and FEV1/FVC ratio in 11 051 European ancestry and 5853 African-American participants.

Measurements and main results: In European ancestry participants, the estimated heritability of COPD, FEV1% predicted and FEV1/FVC ratio were 35.5%, 55.6% and 32.5%, of which 18.8%, 19.7%, 17.8% were from common variants, and 16.6%, 35.8%, and 14.6% were from rare variants. These estimates had wide confidence intervals, with common variants and some sets of rare variants showing a statistically significant contribution (P-value < 0.05). In African-Americans, common variant heritability was similar to European ancestry participants, but lower sample size precluded calculation of rare variant heritability.

Conclusions: Our study provides updated and unbiased estimates of heritability for COPD and lung function, and suggests an important contribution of rare variants. Larger studies of more diverse ancestry will improve accuracy of these estimates.

SUPPLEMENTARY INFO

Grant supportexpand

FULL TEXT LINKS

Multicenter Study

Dtsch Arztebl Int

. 2022 Nov 12;118(45):767-768.

doi: 10.3238/arztebl.m2021.0294.

Quality of Domiciliary Oxygen Therapy in Adults with Chronic Respiratory Diseases- Results of a Multicenter Cross-Sectional Study in Germany

Jens Gottlieb, Hayo Schrepper, Christina Valtin, Tobias Welte, Martin Dierich, Thomas Fühner, Heiko Golpon

- PMID: 35125132

- PMCID: PMC8841639

- DOI: 10.3238/arztebl.m2021.0294

Free PMC article
No abstract available

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

Deutsches Ärzteblatt International

ASTHMA

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Am J Prev Med

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. 2022 Nov 9;S0749-3797(22)00469-X.

doi: 10.1016/j.amepre.2022.09.010. Online ahead of print.

Cardiovascular Disease Among Adults With Work-Related Asthma, 2012-2017

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Affiliations expand

- PMID: 36371324

- DOI: 10.1016/j.amepre.2022.09.010

Abstract

Introduction: Asthma is associated with an increased risk for cardiovascular disease, and adults with persistent, severe asthma have a significantly higher risk of cardiovascular disease than adults with intermittent or no asthma.

Methods: The objective of this cross-sectional study was to assess the association between work-related asthma status and cardiovascular disease among ever-employed adults (aged 18-64 years) with current asthma using data from the 2012-2017 Behavioral Risk Factor Surveillance System Asthma Call-Back Survey from 37 states and the District of Columbia. Weighted prevalence ratios and 95% CIs, adjusted for age, sex, race/ethnicity, education, household income, smoking status, chronic obstructive pulmonary disease, diabetes, and BMI, were calculated. In addition, the associations of cardiovascular disease with adverse asthma outcomes and asthma control among adults with work-related asthma were examined. Analyses were conducted in 2021.

Results: Among an estimated annualized 14.8 million ever-employed adults aged 18-64 years with current asthma, adults with work-related asthma (prevalence ratio=1.5; 95% CI=1.2, 1.8) and possible work-related asthma (prevalence ratio=1.2; 95% CI=1.0, 1.5) were significantly more likely to have cardiovascular disease than adults with non-work-related asthma. Among adults with work-related asthma, those with very poorly controlled asthma (prevalence ratio=1.8; 95% CI=1.3, 2.5) and an asthma-related emergency room visit (prevalence ratio=1.5; 95% CI=1.1, 2.0) were significantly more likely to have cardiovascular disease.

Conclusions: Adults with work-related asthma were more likely to have cardiovascular disease than those with non-work-related asthma. Primary prevention, early diagnosis, and implementation of optimal work-related asthma management are essential for workers' health. Cardiovascular disease should be considered where appropriate when diagnosing and recommending treatment and interventions for adults with work-related asthma.

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Effect of stepping up to high-dose inhaled corticosteroids in patients with asthma: UK Database Study

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Affiliations expand

- PMID: 36371063

- DOI: 10.1016/j.jaip.2022.10.040

Abstract

Background: It is unclear whether patients with asthma benefit from stepping up to high-dose inhaled corticosteroids (ICS).

Objective: To determine the effectiveness of stepping up to high-dose ICS.

Methods: A historic cohort study of asthma patients (≥13 years old), identified from two large UK electronic medical record databases, was conducted. Patients who remained on medium-dose ICS were compared to those who stepped up from medium- to high-dose ICS, while patients who stepped up from low- to medium-dose were compared to those who stepped up from low- to high-dose ICS. Time to first severe exacerbation (primary outcome) between treatment groups was compared using multivariable Cox proportional hazards models, and number of exacerbations and antibiotics courses were analyzed using negative binomial regression. Inverse probability of treatment weighting was used to handle confounding.

Results: The mean follow-up time to first exacerbation was 2.7 (SD 2.7) years for those who remained on stable medium-dose ICS and 2.0 (SD 2.2) years for those who stepped up from medium-to high-dose ICS. A similar pattern was noted for those who stepped-up from low- to medium-ICS dose (2.6 (SD 2.5) years) and from low- to high-dose ICS (2.3 (SD 2.5) years). Patients who stepped up from medium- to high-dose ICS (n=6,879) had a higher risk of exacerbations during follow-up compared to those who remained on

medium-dose ICS (n=51,737; hazard ratio [HR] 1.17, 95% confidence interval 1.12-1.22). This was similar in patients stepping up from low- to high-dose (n=3,232) compared to low- to medium-dose (n=12,659) ICS (HR 1.10 [1.04-1.17]). A step-up to high-dose ICS was also associated with higher number of asthma exacerbations and antibiotics courses. No significant difference in associations was found across subgroups of patients with different blood eosinophil counts (BEC).

Conclusion: We found no evidence that a step-up to high-dose ICS is effective in preventing future asthma exacerbations.

Keywords: asthma; corticosteroids; exacerbations; high dose; step-up.

Clin Immunol

. 2022 Nov 8;109182.

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Natural history of infants with non-SCID T cell lymphopenia identified on newborn screen

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Affiliations expand

- PMID: 36368643

- DOI: 10.1016/j.clim.2022.109182

Abstract

Newborn screening (NBS) for severe combined immunodeficiency (SCID) can identify infants with non-SCID T cell lymphopenia (TCL). The purpose of this study was to characterize the natural history and genetic findings of infants with non-SCID TCL identified on NBS. We analyzed data from 80 infants with non-SCID TCL in the mid-Atlantic region between 2012 and 2019. 66 patients underwent genetic testing and 41 (51%) had identified genetic variant(s). The most common genetic variants were thymic defects (33%), defects with unknown mechanisms (12%) and bone marrow production defects (5%). The genetic cohort had significantly lower median initial CD3+, CD4+, CD8+ and CD4/CD45RA+ T cell counts compared to the non-genetic cohort. Thirty-six (45%) had either viral, bacterial, or fungal infection; only one patient had an opportunistic infection (vaccine strain VZV infection). Twenty-six (31%) of patients had resolution of TCL during the study period.

Keywords: Genetic testing; Newborn screening (NBS); Pneumocystis jirovecii pneumonia (PJP); Severe combined immunodeficiency (SCID); T cell lymphopenia (TCL); T cell receptor excision circle (TREC); Varicella-zoster virus (VZV).

Conflict of interest statement

Declaration of Competing Interest None.
Proceed to details

J Asthma

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. 2022 Nov 11;1-19.

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Sex differences in the association between smoking exposure and prevalence of wheeze and asthma in 3-year-old children

Maoka Yamada[1,2], Keiko Tanaka[2,3,4,5], Chisato Nagata[6], Masashi Arakawa[7,8], Yoshihiro Miyake[2,3,4,5]

Affiliations expand

- PMID: 36368047

- DOI: 10.1080/02770903.2022.2147081

Abstract

Objective: We examined independent and joint associations between prenatal and postnatal smoking exposure and the prevalence of wheeze and asthma among 3-year-old Japanese children. Sex differences were also investigated.

Methods: Smoking exposure, allergic symptoms, and potential confounding factor data were collected using a self-administered questionnaire. Wheeze was defined on the basis of the International Study of Asthma and Allergies in Childhood criteria. Physician-diagnosed asthma was considered to be present if a physician had diagnosed the child with asthma any time before the survey was administered.

Results: There were 6402 pediatric participants in this study. Maternal smoking throughout pregnancy and household smoking exposure during the first year of life were associated with an increased prevalence of wheeze among girls but not boys (adjusted odds ratio (OR) [95% CI] = 2.00 [1.13-3.42] and 1.34 [1.07-1.68], respectively). Girls exposed to both prenatal maternal smoking and postnatal household smoking exposure had a significantly higher prevalence of wheeze and physician-diagnosed asthma compared with girls without these exposures (adjusted OR [95% CI] = 2.06 [1.39-3.01] and 1.86 [1.01-3.26], respectively). No association was observed between perinatal smoking exposure and the prevalence of wheeze or asthma among boys. Significant interactions between sex and smoking exposure affecting wheeze and asthma were also found (*p* for interaction = 0.0003 and 0.01, respectively).

Conclusion: We found a positive association between perinatal smoking exposure and the prevalence of wheeze and asthma only among girls. Effects of perinatal smoking exposure on wheeze and asthma might be sex specific. Further research is required.

Keywords: asthma; child; cross-sectional studies; environmental tobacco smoke; passive smoking; wheeze.

Viral Immunol

. 2022 Nov 11.

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Persistence of RNA Viruses in the Respiratory Tract: An Overview

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Affiliations expand

- PMID: 36367976

- DOI: 10.1089/vim.2022.0135

Abstract

Respiratory RNA viruses are a major cause of acute lower respiratory tract infections and contribute substantially to hospitalization among infants, elderly, and immunocompromised. Complete viral clearance from acute infections is not always achieved, leading to persistence. Certain chronic respiratory diseases like asthma and chronic obstructive pulmonary disease have been associated with persistent infection by human respiratory syncytial virus and human rhinovirus, but it is still not clear whether RNA viruses really establish long-term infections as it has been recognized for DNA viruses as human bocavirus and adenoviruses. Herein, we summarize evidence of RNA virus persistence in the human respiratory tract, as well as in some animal models, to highlight

how long-term infections might be related to development and/or maintenance of chronic respiratory symptoms.

Keywords: respiratory RNA viruses; respiratory tract; viral persistence.

Ann Rheum Dis

. 2022 Nov 10;ard-2022-223044.

doi: 10.1136/ard-2022-223044. Online ahead of print.

Targeting the interleukin-5 pathway in EGPA: evidence, uncertainties and opportunities

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Affiliations expand

- PMID: 36357156

- DOI: 10.1136/ard-2022-223044

Abstract

Only a minority of patients with eosinophilic granulomatosis with polyangiitis (EGPA) can be weaned-off glucocorticoids (GC) using conventional treatment strategies. The development of biological agents specifically inhibiting the IL-5 pathway provided the opportunity to treat EGPA by targeting one of the crucial regulators of eosinophils, reducing the GC dose required to control the disease.The anti-IL-5 antibody mepolizumab

at the dose of 300 mg/4 weeks has proven to be safe and effective in EGPA. While relapsing patients-who often experience recurrent respiratory manifestations-benefit from this treatment, data are not enough to support its use combined with GC alone in remission induction of severe active forms, or in remission maintenance without conventional immunosuppressants in patients with vasculitic manifestations. Ultimately, the profile of the best candidate for mepolizumab is still unclear.Several real-life reports suggest that mepolizumab at the dose of 100 mg/4 weeks, approved for eosinophilic asthma/chronic rhinosinusitis with nasal polyposis (CRSwNP), effectively maintains remission of EGPA-related asthma and, to a lesser extent, CRSwNP. Preliminary data on the IL-5 pathway-inhibitors benralizumab and reslizumab in EGPA as steroid-sparing agents are also accumulating.Overall, it remains to be proven whether targeting the IL-5 pathway could block progression of organ damage in EGPA, on top of reducing relapses and sparing GC. Other disease-related factors further complicate the understanding of the real anti-IL-5 agent efficacy, such as the lack of a clear definition of remission, of an effective tool to measure disease activity, and of well-defined treat-to-target approaches or goals of treatment.

Keywords: Antirheumatic Agents; Autoimmune Diseases; Systemic vasculitis.

Conflict of interest statement

Competing interests: None declared.

Ann Allergy Asthma Immunol

. 2022 Nov 7;S1081-1206(22)01912-3.

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Long-term efficacy of dupilumab in asthma with and without chronic rhinosinusitis and/or nasal polyps

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Affiliations expand

- PMID: 36356712

- DOI: 10.1016/j.anai.2022.11.006

Abstract

Background: Coexisting chronic rhinosinusitis and/or nasal polyps (CRS/NP) substantially increases the disease burden of asthma. Dupilumab, a fully human monoclonal antibody, has established efficacy and an acceptable safety profile in asthma and CRS with NP.

Objective: This post hoc analysis assessed long-term dupilumab efficacy in TRAVERSE (NCT02134028) patients with uncontrolled, moderate-to-severe (QUEST) or oral corticosteroid (OCS)-dependent (VENTURE) asthma with/without coexisting CRS/NP.

Methods: In TRAVERSE, 317/1530 (21%) QUEST and 61/187 (48%) VENTURE patients had self-reported CRS/NP; they received subcutaneous 300 mg dupilumab every 2 weeks up to 96 weeks. Patients were categorized by parent study treatment group (placebo/dupilumab, dupilumab/dupilumab). Endpoints included annualized asthma exacerbation rates and mean change from parent study baseline (PSBL) in pre-bronchodilator forced expiratory volume in one second (FEV 1), asthma control (ACQ-5), quality of life (AQLQ), and OCS dose.

Results: Patients with coexisting CRS/NP had higher OCS dose and a history of more exacerbations. Concluding TRAVERSE, exacerbation rates decreased from 2.39 to 0.32 and 2.32 to 0.35 in dupilumab/dupilumab and 2.36 to 0.41 and 2.36 to 0.45 in placebo/dupilumab by Week 96 from QUEST and VENTURE baselines, respectively. Non-CRS/NP results were similar. Improvements in FEV 1, ACQ-5, and AQLQ during parent studies were maintained in TRAVERSE; placebo/dupilumab patients achieved similar improvements to dupilumab/dupilumab by Week 48. By Week 96, 71% and 39% of OCS-dependent patients with CRS/NP and 83% and 47% without CRS/NP treated with dupilumab/dupilumab and placebo/dupilumab, respectively, stopped OCS.

Conclusion: Long-term dupilumab efficacy was maintained in patients with asthma with/without self-reported coexisting CRS/NP, including OCS-sparing effects observed in OCS-dependent severe asthma.

Keywords: asthma; chronic rhinosinusitis with nasal polyps; dupilumab; efficacy; long-term; oral corticosteroids.

J Appl Physiol (1985)

. 2022 Nov 10.

doi: 10.1152/japplphysiol.00493.2022. Online ahead of print.

Therapeutic response to bronchial thermoplasty – toward feasibility of patient selection based on modelling predictions

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Affiliations expand

- PMID: 36356255

- DOI: 10.1152/japplphysiol.00493.2022

Abstract

Bronchial thermoplasty (BT) is a treatment for moderate-to-severe asthma in which the airway smooth muscle layer is targeted directly using thermal ablation. Although it has been shown to be safe and effective in long-term follow up, questions remain about its mechanism of action, patient selection, and optimization of protocol based on structural phenotype. Using a cohort of 20 subjects who underwent thermoplasty and assessment by computed tomography (CT), we demonstrate that response to BT can be feasibly predicted based on pre-treatment airway dimensions that inform a subject-specific computational model. Analysis revealed the need for CT assessment at total lung capacity, rather than functional residual capacity, which was less sensitive to the effects of BT. Final model predictions compared favorably with observed outcomes in terms of airway calibre and asthma control, suggesting that this approach could form the basis of improved clinical practice.

Keywords: Asthma; airway hyper-responsiveness; airway smooth muscle; computational modelling.

Toxics

. 2022 Nov 6;10(11):667.

doi: 10.3390/toxics10110667.

Impact of Acute Exacerbation and Its Phenotypes on the Clinical Outcomes of Chronic Obstructive Pulmonary Disease in Hospitalized Patients: A Cross-Sectional Study

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- PMID: 36355958

- DOI: 10.3390/toxics10110667

Abstract

Acute exacerbations of COPD (AECOPD) are clinically significant events having therapeutic and prognostic consequences. However, there is a lot of variation in its clinical manifestations described by phenotypes. The phenotypes of AECOPD were categorized in this study based on pathology and exposure. In our cross-sectional study, conducted between 1 January 2016 to 31 December 2020, the patients were categorized into six groups based on pathology: non-bacterial and non-eosinophilic; bacterial; eosinophilic; bacterial infection with eosinophilia; pneumonia; and bronchiectasis. Further, four groups were classified based on exposure to tobacco smoke (TS), biomass smoke (BMS), both, or no exposure. Cox proportional-hazards regression analyses were performed to assess hazard ratios, and Kaplan-Meier analysis was performed to assess survival, which was then compared using the log-rank test. The odds ratio (OR) and independent predictors of ward admission type and length of hospital stay were assessed using binomial logistic regression analyses. Of the 2236 subjects, 2194 were selected. The median age of the cohort was 67.0 (60.0 to 74.0) and 75.2% were males. Mortality rates were higher in females than in males (6.2% vs. 2.3%). AECOPD-B (bacterial infection) subjects [HR 95% CI 6.42 (3.06-13.46)], followed by AECOPD-P (pneumonia) subjects [HR (95% CI: 4.33 (2.01-9.30)], were at higher mortality risk and had a more extended hospital stay (6.0 (4.0 to 9.5) days; 6.0 (4.0 to 10.0). Subjects with TS and BMS-AECOPD [HR 95% CI 7.24 (1.53-34.29)], followed by BMS-AECOPD [HR 95% CI 5.28 (2.46-11.35)], had higher mortality risk. Different phenotypes have different impacts on AECOPD clinical outcomes. A better understanding of AECOPD phenotypes could contribute to developing an algorithm for the precise management of different phenotypes.

Keywords: AECOPD; COPD; acute exacerbation; biomass; mortality; phenotype; tobacco.

SUPPLEMENTARY INFO

Grant supportexpand

Dermatol Ther (Heidelb)

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doi: 10.1007/s13555-022-00851-6. Online ahead of print.

The Combination of Dupilumab with Other Monoclonal Antibodies

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Affiliations expand

- PMID: 36355314

- DOI: 10.1007/s13555-022-00851-6

Abstract

Introduction: Dupilumab is an interleukin-4 (IL-4) receptor alpha antagonist indicated for the treatment of moderate-to-severe atopic dermatitis (AD), which could be associated with atopic and non-atopic comorbidities for which concomitant administration of targeted pharmacotherapy including monoclonal antibodies could be required. However, the safety of combining dupilumab with other monoclonal antibodies for different therapeutic indication may be debated.

Methods: We conducted an extensive search in MEDLINE via PubMed for original articles published from January 1, 2017 to October 22, 2022, reporting clinical cases in which dupilumab has been associated with other monoclonal antibodies.

Results: Four small case series were identified reporting data on a total of 16 patients. To them, we have added other patients (n = 8) derived from our clinical practice, achieving a total of 24 cases followed for a period of 2-22 months. Patients were receiving dupilumab mainly because of AD (except one patient for bullous pemphigoid and one for asthma) and other monoclonal antibodies for psoriasis treated with guselkumab (n = 7) and secukinumab (n = 1), asthma with omalizumab or benralizumab (n = 3), Crohn's disease with adalimumab (n = 3), chronic spontaneous urticaria with omalizumab (n = 3), primary

familial hypercholesterolemia with evolocumab (n = 2), hidradenitis suppurativa with adalimumab (n = 1), psoriatic arthritis with secukinumab (n = 1), rheumatoid arthritis with abatacept (n = 1), ankylosing spondylitis with secukinumab (n = 1) and colorectal carcinoma with cetuximab (n = 1). No adverse events related to the combination of the two monoclonal antibodies were reported except for a mild injection site reaction (n = 1) and arthralgia, which resolved spontaneously within a few weeks (n = 1).

Conclusions: Because the evidence is modest, the question remains open as to whether dupilumab can be safely combined with other monoclonal antibodies. Dupilumab does not exert immunosuppressive effects and does not impair the activity of cytochrome P450 isozymes.

Keywords: Atopic dermatitis; Dupilumab; Monoclonal antibodies; Safety; Targeted pharmacotherapies.

- 12 references

SUPPLEMENTARY INFO

Publication typesexpand

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BMC Pulm Med

. 2022 Nov 9;22(1):407.

doi: 10.1186/s12890-022-02205-6.

Temperature-controlled Laminar Airflow (TLA) in symptomatic severe asthma – a post hoc analysis of severe

exacerbations, quality of life and health economics

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Affiliations expand

- PMID: 36352399

- DOI: 10.1186/s12890-022-02205-6

Abstract

Purpose: Uncontrolled severe asthma constitutes a major economic burden to society. Add-ons to standard inhaled treatments include inexpensive oral corticosteroids and expensive biologics. Nocturnal treatment with Temperature-controlled Laminar Airflow (TLA; Airsonett®) could be an effective, safe and cheaper alternative. The potential of TLA in reducing severe asthma exacerbations was addressed in a recent randomised placebo-controlled trial (RCT) in patients with severe asthma (Global Initiative for Asthma (GINA) step 4/5), but the results were inconclusive. We re-analysed the RCT with severe exacerbations stratified by the level of baseline asthma symptoms and Quality of Life.

Methods: More uncontrolled patients, defined by Asthma Control Questionnaire 7 (ACQ7) > 3, EuroQoL 5-Dimension Questionnaire Visual Analogue Scale (EQ5D-VAS) ≤ 65 and Asthma Quality of Life Questionnaire (AQLQ) ≤ 4 were selected for re-analysis. The rates of severe asthma exacerbations, changes in QoL and health-economics were analysed and compared between TLA and placebo.

Results: The study population included 226 patients (113 TLA / 113 placebo.) The rates of severe asthma exacerbations were reduced by 33, 31 and 25% (p = 0.083, 0.073, 0.180) for TLA compared to placebo, dependent on selected control measures (ACQ7, EQ5D-VAS, AQLQ, respectively). For patients with less control defined by AQLQ≤4, the difference in mean $AQLQ_{0\text{-}12M}$ between TLA and placebo was 0.31, 0.33, 0.26 (p = 0.085, 0.034, 0.150), dependent on selected covariate (AQLQ, EQ5D-VAS, ACQ7, respectively). For patients with poor control defined by ACQ7 > 3, the difference in EQ5D-5 L utility scores between TLA and placebo was significant at 9 and 12 months with a cost-effective ICER. The results from the original study did not demonstrate these differences.

Conclusion: This post hoc analysis demonstrated an effect of TLA over placebo on severe exacerbations, asthma control and health economics in a subgroup of patients with more symptomatic severe allergic asthma. The results are consistent with the present

recommendations for TLA. However, these differences were not demonstrated in the full study. Several explanations for the different outcomes have been outlined, which should be addressed in future studies.

Funding: NIHR Health Technology Assessment Programme and Portsmouth Hospitals NHS Trust.

Keywords: Health economics; Quality of life; Severe asthma; Severe exacerbations; Temperature-controlled laminar airflow.

- 33 references

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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12

Int Arch Allergy Immunol

. 2022 Nov 7;1-12.

doi: 10.1159/000526365. Online ahead of print.

Real-Life Experience of Biologic Treatment for Asthma on Chronic Rhinosinusitis: A Finnish Cohort

Annina Lyly[1,2], Emma Genberg[2,3], Paula Kauppi[3], Paula Virkkula[1], Stella E Lee[4], Tanya M Laidlaw[5], Sanna Toppila-Salmi[2,6], Marie Lundberg[1,2,5]

Affiliations expand

- PMID: 36349770

- DOI: 10.1159/000526365

Abstract

Introduction: Biologics are used in the treatment of severe asthma and chronic rhinosinusitis with nasal polyps (CRSwNP). The purpose of this retrospective study was to evaluate the effects of biologics initiated for asthma on coexistent CRS and the influence of comorbid factors, including aspirin-exacerbated respiratory disease (AERD) and secretory otitis media (SOM).

Methods: A review of electronic health records (2009-2020) at a Finnish tertiary center was conducted to identify CRS patients treated with biologics for their asthma. We identified the type of biologic and treatment response, by comparing nasal polyp score (NPS), sinonasal outcome test (SNOT)-22, need for oral corticosteroids (OCS) and antibiotics, frequency of visits, and endoscopic sinus surgeries (ESS) pretreatment and during treatment.

Results: 55 patients were treated with anti-immunoglobulin E (IgE) (n = 18) or anti-interleukin-5/5-receptor (IL-5/5R) (n = 37) biologics. Treatment lasted for an average of 4.1 years. Seventy-five percent (n = 41) had CRSwNP and 25% (n = 14) had CRSsNP. Of all patients, 24% (n = 13) had comorbid AERD and 22% (n = 12) had SOM. Biologic therapy reduced the need for OCS courses (anti-IgE, n = 17, p = 0.03; anti-IL-5/5R, n = 35, p = 0.01) and for daily OCS in anti-IL-5/5R (n = 35, p = 0.001) but not in anti-IgE patients (n = 16, p = 0.07). Biologics also improved NPS by 0.5 point (n = 32, p = 0.009) and SNOT-22 by 14 points (n = 7, p = 0.02) in CRSwNP patients. The overall discontinuation rate was 37.7% (n = 20) and was independent of type of biologic.

Conclusion: Treatment with anti-IgE and/or anti-IL-5/5R biologics reduced the overall need for OCS medication in individuals with asthma and concomitant CRS, but despite this, the discontinuation rate was high.

Keywords: Aspirin-exacerbated respiratory disease; Asthma; Biologics; Chronic rhinosinusitis with nasal polyps; Nonsteroidal anti-inflammatory drug-exacerbated respiratory disease.

Pediatr Pulmonol

. 2022 Nov 8.

doi: 10.1002/ppul.26240. Online ahead of print.

From neonatal lung function to lung function and respiratory morbidity at 6-year follow-up

Fanny Edit Maria Goth[1,2], Kent Green[1], Bo M Hansen[1,2], Lone Agertoft[3], I Merete Jørgensen[1,2]

Affiliations expand

- PMID: 36349430

- DOI: 10.1002/ppul.26240

Abstract

Background: Lung function is traceable from infancy to adulthood. Only a few studies have examined lung function from birth to childhood longitudinally in children born moderate to late preterm. We aimed to investigate how prematurity and lung function in the neonatal period are related to lung function and respiratory morbidity at age six in former moderate to late preterm children compared with children born at term.

Method: Lung function was measured in a cohort of moderately to late preterm (n = 48) and term-born (n = 53) infants in the neonatal period by FeNO, and tidal breathing flow-volume loops (TBFVL) and at age six (n = 52) by spirometry, whole-body plethysmograph and impulse oscillation combined with a respiratory symptom questionnaire.

Results: Moderate to late preterm children had a higher T_{PEF} /T_E ratio neonatally (42.6 % vs 33.7 %, p = 0.02) and a lower % predicted FEV_1 at age six (94.4 % vs 101.9 %, p = 0.01) compared to term-born children. We found a significant association between the variability

of neonatal tidal volume and effective airway resistance at age six (β = -0.34, p = 0.03). No association between neonatal FeNO or TBFVL and respiratory morbidity at six-year follow-up was shown.

Conclusion: Children born moderate to late preterm had lower lung function at age six than term-born children. We did not find evidence for the use of neonatal tidal breathing parameters as a predictor for subsequent respiratory morbidity or lung function, however sample size was small. This article is protected by copyright. All rights reserved.

Keywords: Asthma & Early Wheeze; Neonatal Pulmonary Medicine; Pulmonary function testing.

Review

Adv Ther

. 2022 Nov 8.

doi: 10.1007/s12325-022-02356-2. Online ahead of print.

Safety of SABA Monotherapy in Asthma Management: a Systematic Review and Meta-analysis

Thitiwat Sriprasart[1], Grant Waterer[2], Gabriel Garcia[3], Adalberto Rubin[4], Marco Antonio Loustaunau Andrade[5], Agnieszka Roguska[6], Abhay Phansalkar[7], Sourabh Fulmali[7], Amber Martin[8], Lalith Mittal[9], Bhumika Aggarwal[10], Gur Levy[11]

Affiliations expand

- PMID: 36348141

- DOI: 10.1007/s12325-022-02356-2

Abstract

Introduction: Short-acting β_2-agonist (SABA) reliever overuse is common in asthma, despite availability of inhaled corticosteroid (ICS)-based maintenance therapies, and may be associated with increased risk of adverse events (AEs). This systematic literature review (SLR) and meta-analysis aimed to investigate the safety and tolerability of SABA reliever monotherapy for adults and adolescents with asthma, through analysis of randomized controlled trials (RCTs) and real-world evidence.

Methods: An SLR of English-language publications between January 1996 and December 2021 included RCTs and observational studies of patients aged ≥ 12 years treated with inhaled SABA reliever monotherapy (fixed dose or as needed) for ≥ 4 weeks. Studies of terbutaline and fenoterol were excluded. Meta-analysis feasibility was dependent on cross-trial data comparability. A random-effects model estimated rates of mortality, serious AEs (SAEs), and discontinuation due to AEs (DAEs) for as-needed and fixed-dose SABA treatment groups. ICS monotherapy and SABA therapy were compared using a fixed-effects model.

Results: Forty-two studies were identified by the SLR for assessment of feasibility. Final meta-analysis included 24 RCTs. Too few observational studies (n = 2) were available for inclusion in the meta-analysis. One death unrelated to treatment was reported in each of the ICS, ICS + LABA, and fixed-dose SABA groups. No other treatment-related deaths were reported. SAE and DAE rates were < 4%. DAEs were reported more frequently in the SABA treatment groups than with ICS, potentially owing to worsening asthma symptoms being classified as an AE. SAE risk was comparable between SABA and ICS treatments.

Conclusions: Meta-analysis of data from RCTs showed that deaths were rare with SABA reliever monotherapy, and rates of SAEs and DAEs were comparable between SABA reliever and ICS treatment groups. When used appropriately within prescribed limits as reliever therapy, SABA does not contribute to excess rates of mortality, SAEs, or DAEs.

Keywords: Adolescents; Adults; Adverse events; Monotherapy; Mortality; Overuse; SABA; Safety.

- 50 references

SUPPLEMENTARY INFO

Publication types, Grant supportexpand

FULL TEXT LINKS

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15

Review

Obes Rev

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. 2022 Nov 7;e13527.

doi: 10.1111/obr.13527. Online ahead of print.

Discontinuation and reduction of asthma medications after metabolic and bariatric surgery: A systematic review and meta-analysis

Luyu Xie[1,2], Aparajita Chandrasekhar[1,2], Stacia M DeSantis[3], Jaime P Almandoz[4], Nestor de la Cruz-Muñoz[5], Sarah E Messiah[1,2]

Affiliations expand

- PMID: 36345564

- DOI: 10.1111/obr.13527

Abstract

Obesity is a risk factor for asthma. Metabolic and bariatric surgery (MBS) is a safe and effective treatment option for obesity. Weight reduction via MBS, in turn, may improve asthma outcomes and decrease the need for asthma medications. The aim of the systematic review and meta-analysis is to explore the available evidence focused on the impact of MBS on the improvement of asthma outcomes via the discontinuation and reduction of asthma medications. After a comprehensive search in the PubMed, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL) databases, 15 studies, including pre-post MBS data on asthma medication use among adults, were eligible for the systematic review. Thirteen studies reported the proportion of patient who discontinued asthma medication post-MBS and was meta-analyzed using random effects. Results showed 54% patients completely discontinued asthma medications (95% confidence interval 42%-67%, I^2 = 86.2%, $p < 0.001$). The average number of asthma medications was also decreased by approximately 22%-46%. MBS provides strong therapeutic benefits for patients with asthma, as evidenced by the complete discontinuation of asthma medications in over 50% of MBS completers. The inference was limited by the small number, variations in follow-up time and rates, and heterogeneity of studies. Studies that include more ethnically diverse participant samples are needed to improve generalizability.

Keywords: asthma; bariatric surgery; medication.

Review

Clin Exp Med

. 2022 Nov 7.

doi: 10.1007/s10238-022-00930-0. Online ahead of print.

A systematic review and meta-analysis of paraoxonase-1 activity in asthma

Stefania Bassu[1], Arduino A Mangoni[2,3], Dario Argiolas[4], Ciriaco Carru[5], Pietro Pirina[4], Alessandro G Fois[4], Angelo Zinellu[5]

Affiliations expand

- PMID: 36344783

- DOI: 10.1007/s10238-022-00930-0

Abstract

Human serum paraoxonase-1 (PON-1) is a critical antioxidant defence system against lipid oxidation. Decreased PON-1 activity has been associated with systemic oxidative stress in several disease states. We conducted a systematic review and meta-analysis of plasma/serum concentrations of PON-1 in asthma, a chronic inflammatory airway disease. The electronic databases PubMed, Web of Science, Scopus and Google Scholar were searched from inception to February 2022. In total, 8 studies in 355 asthmatic patients and 289 healthy controls were included in the meta-analysis. Serum PON-1 concentrations were significantly lower in asthmatic patients (SMD = -1.58, 95% CI -2.53 to -0.63; p = 0.001). The pooled SMD values were not substantially altered in sensitivity analysis. There was no publication bias. There were non-significant differences in PON-1 concentrations in patients with severe vs. mild-to-moderate asthma (SMD = - 0.39, 95% CI - 1.00 to 0.22, p = 0.21). Our meta-analysis has shown that serum PON-1 concentrations are significantly lower in patients with asthma, suggesting the presence of an impaired antioxidant defense in this group.

Keywords: Chronic; Disease; Inflammation; Oxidative stress; PON-1.

- 48 references

SUPPLEMENTARY INFO

Publication typesexpand

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17

Meta-Analysis

Nat Commun

-
-
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. 2022 Nov 7;13(1):6712.

doi: 10.1038/s41467-022-33628-8.

Discerning asthma endotypes through comorbidity mapping

Gengjie Jia[1 2 3], Xue Zhong[4], Hae Kyung Im[1 5], Nathan Schoettler[1], Milton Pividori[1 6], D Kyle Hogarth[1], Anne I Sperling[1], Steven R White[1], Edward T Naureckas[1], Christopher S Lyttle[1], Chikashi Terao[7 8 9], Yoichiro Kamatani[7 10], Masato Akiyama[7 11], Koichi Matsuda[10], Michiaki Kubo[7], Nancy J Cox[4], Carole Ober[12], Andrey Rzhetsky[13 14 15 16], Julian Solway[17]

Affiliations expand

- PMID: 36344522

- DOI: 10.1038/s41467-022-33628-8

Free article

Abstract

Asthma is a heterogeneous, complex syndrome, and identifying asthma endotypes has been challenging. We hypothesize that distinct endotypes of asthma arise in disparate genetic variation and life-time environmental exposure backgrounds, and that disease comorbidity patterns serve as a surrogate for such genetic and exposure variations. Here, we computationally discover 22 distinct comorbid disease patterns among individuals with asthma (asthma comorbidity subgroups) using diagnosis records for >151 M US residents, and re-identify 11 of the 22 subgroups in the much smaller UK Biobank. GWASs to discern asthma risk loci for individuals within each subgroup and in all subgroups combined reveal 109 independent risk loci, of which 52 are replicated in multi-ancestry meta-analysis across different ethnicity subsamples in UK Biobank, US BioVU, and BioBank Japan. Fourteen loci confer asthma risk in multiple subgroups and in all subgroups combined. Importantly, another six loci confer asthma risk in only one subgroup. The strength of association between asthma and each of 44 health-related phenotypes also varies dramatically across subgroups. This work reveals subpopulations of asthma patients distinguished by comorbidity patterns, asthma risk loci, gene expression, and health-related phenotypes, and so reveals different asthma endotypes.

- 144 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

FULL TEXT LINKS

nature publishing group

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Emerg Med J

. 2022 Nov 7;emermed-2022-212642.

doi: 10.1136/emermed-2022-212642. Online ahead of print.

International practice patterns of IV magnesium in paediatric acute asthma

Laura Simone[1], Roger Zemek[2], Damian Roland[3 4], Mark D Lyttle[5], Simon Craig[6], Stuart R Dalziel[7], Jocelyn Gravel[8], Yaron Finkelstein[9], Sarah Curtis[10], Stephen B Freedman[11], Amy C Plint[12], Suzanne Schuh[13], Pediatric Emergency Research Network Group

Collaborators, Affiliations expand

- PMID: 36344238

- DOI: 10.1136/emermed-2022-212642

No abstract available

Keywords: acute care; asthma; pediatric emergency medicine; respiratory.

Conflict of interest statement

Competing interests: None declared.

. 2022 Nov 7.

doi: 10.1164/rccm.202206-1132LE. Online ahead of print.

A Pilot RCT of an Intervention to Improve Perception of Lung Function in Older Adults with Asthma

Jonathan M Feldman[1,2], Jyoti Ankam[3], Michele Barry[3], Natalie Fruchter[4], Jacqueline Becker[5], Sunit Jariwala[6], Chang Shim[7], Juan P Wisnivesky[8], Alex D Federman[8]

Affiliations expand

- PMID: 36343280

- DOI: 10.1164/rccm.202206-1132LE

No abstract available

Keywords: adherence; elderly; motivational interviewing; symptom perception.

mSphere

. 2022 Nov 7;e0037722.

doi: 10.1128/msphere.00377-22. Online ahead of print.

Effects of Fluticasone Propionate on *Klebsiella pneumoniae* and Gram-Negative Bacteria Associated with Chronic Airway Disease

Lesa A Begley[1], Kristopher Opron[1], Guowu Bian[1], Ariangela J Kozik[1], Cai Liu[2], Jeremy Felton[2], Bo Wen[2], Duxin Sun[2], Yvonne J Huang[1,3]

Affiliations expand

- PMID: 36342141

- DOI: 10.1128/msphere.00377-22

Free article

Abstract

Inhaled corticosteroids (ICS) are commonly prescribed first-line treatments for asthma and chronic obstructive pulmonary disease (COPD). Recent evidence has shown that ICS use is associated with changes in the airway microbiome, which may impact clinical outcomes such as potential increased risk for pneumonia in COPD. Although the immunomodulatory effects of corticosteroids are well appreciated, whether ICS could directly influence the behavior of respiratory tract bacteria has been unknown. In this pilot study we explored the effects of fluticasone proprionate, a commonly prescribed inhaled corticosteroid, on respiratory bacteria with an expanded focus on Klebsiella pneumoniae, a species previously implicated in fluticasone-associated pneumonia in COPD. We observed significant effects of fluticasone proprionate on growth responses of *K. pneumoniae*, as well as other bacterial species isolated from asthmatic patients. Fluticasone-exposed *K. pneumoniae* displayed altered expression of several bacterial genes and reduced the metabolic activity of bronchial epithelial cells and their expression of human β-defensin 2. Targeted assays identified a fluticasone metabolite from fluticasone-exposed *K. pneumoniae* cells, suggesting this species may be capable of metabolizing fluticasone proprionate. Collectively, these observations support the hypothesis that specific members of the airway microbiota possess the functional repertoire to respond to or potentially utilize corticosteroids in their microenvironment. These findings lay a foundation for novel research directions into the potential direct effects of ICS, often prescribed long term to patients, on the broader airway microbial community and on the behavior of specific microbial species implicated in asthma and COPD outcomes. **IMPORTANCE** Inhaled corticosteroids are widely prescribed for many respiratory diseases, including asthma and

COPD. While they benefit many patients, corticosteroids can also have negative effects. Some patients do not improve with treatment and even experience adverse side effects. Recent studies have shown that inhaled corticosteroids can change the make-up of bacteria in the human respiratory tract. However, whether these medications can directly impact the behavior of such bacteria has been unknown. Here, we explored the effects of fluticasone propionate, a commonly prescribed inhaled corticosteroid, on Klebsiella pneumoniae and other airway bacteria of interest, including primary species isolated from adult asthma patients. We provide evidence of growth responses to direct fluticasone exposure in culture and further examined fluticasone's effects on K. pneumoniae, including gene expression changes and effects of fluticasone-exposed bacteria on airway cells. These findings indicate that members of the human airway bacterial community possess the functional ability to respond to corticosteroids, which may have implications for the heterogeneity of treatment response observed clinically.

Keywords: COPD; asthma; bacteria; corticosteroids; inhaled corticosteroids; microbiome.

J Asthma

. 2022 Nov 6;1-14.

doi: 10.1080/02770903.2022.2144351. Online ahead of print.

Variables associated with asthma control among adult patients

Walid Al-Qerem [1], Anan Jarab [2 3], Shrouq R Abu Heshmeh [2], Jonathan Ling [4]

Affiliations expand

- PMID: 36336819

- DOI: 10.1080/02770903.2022.2144351

Abstract

Background: Asthma is one of the most prevalent chronic diseases with a substantial impact on the health status of affected patients. Further research is necessary to identify factors contributing to poor asthma control. The current study aimed to investigate the factors associated with poor asthma control among adult asthmatic patients. *Methods*: In this case-control study, the Asthma Control Test (ACT) was translated into Arabic and distributed to adults with asthma attending two hospitals in Jordan to evaluate the degree of asthma control. The following variables were collected for each patient: sociodemographic information, comorbidities, appropriate use of inhaler technique, spirometric measurements, and medications use. Binary regression was used to evaluate factors associated with asthma control. *Results*: A total of 314 participants with a mean age of 51.47 years (± 16.37) completed the study. ACT score had a mean of 16.68 (±4.86). The majority of asthmatic patients had insufficiently controlled asthma (64.6%). Binary regression results showed that previous respiratory infection history (p = 0.014, OR = 0.473 (95%CI 0.261-0.857)), higher exposure to irritants (p = 0.010, OR = 0.747 (95%CI 0.598-0.933)) decreased the odds of being in the controlled asthma group. Patients receiving inhaled corticosteroids (ICS) had higher odds of being in the controlled asthma group (p = 0.039, OR = 2.372 (95%CI 1.043-5.392)). *Conclusion*: The majority of asthma patients had insufficiently managed disease. The main factors that contributed to poor asthma control were respiratory infection history, increased exposure to asthma symptoms triggers, and ICS nonuse.

Keywords: ACT; Asthma; Asthma Control Test; Jordan; inhaler technique.

. 2022 Nov 6.

doi: 10.1111/resp.14400. Online ahead of print.

Contribution of obesity to breathlessness in a large nationally representative sample of Australian adults

Yue Leon Guo[1,2,3,4], Maria R Ampon[1,2], Leanne M Poulos[1,2], Sharon R Davis[1,2], Brett G Toelle[1,2,5], Guy B Marks[1,2,6], Helen K Reddel[1,2]

Affiliations expand

- PMID: 36336647

- DOI: 10.1111/resp.14400

Abstract

Background and objective: Breathlessness is prevalent and associated with medical consequences. Obesity is related to breathlessness. However, the magnitude of its contribution has not been clearly documented. This investigation aimed to determine the contribution of obesity to breathlessness by estimating the population attributable fraction (PAF) in a representative sample of Australian adults.

Methods: A cross-sectional, nationally representative survey of Australian residents aged ≥18 years was conducted in October 2019. Breathlessness was defined as modified Medical Research Council (mMRC) dyspnoea scale grade ≥2. BMI was calculated from self-reported height and weight. Adjusted relative risks (aRRs) were estimated using a generalized linear model with Poisson distribution, adjusted for age group and/or participant-reported diagnosed illnesses. Adjusted PAFs were estimated using aRR and obesity prevalence in Australian adults.

Results: Among those who completed the National Breathlessness Survey, 9769 participants (51.4% female) were included in the analysis; 28.1% of participants were obese. The prevalence of breathlessness was 9.54%. The aRR of obesity for breathlessness was 2.04, adjusted for age. Adjusting for various co-morbid conditions, the aRR was slightly attenuated to around 1.85-1.98. The PAF, adjusted only for age, was 24.6% (95% CI 20.1-

29.1) and after further adjustment for co-morbid conditions, the PAF ranged from 21.1% to 23.6%. Obesity accounted for a higher proportion of breathlessness in women than in men.

Conclusion: Our results demonstrate that obesity accounts for around a quarter of breathlessness symptoms in Australian adults. This has important implications for health policy in light of the global trend in increasing obesity.

Keywords: COPD; asthma; breathlessness; chronic obstructive pulmonary disease; dyspnoea; obesity; population attributable fraction.

- 33 references

SUPPLEMENTARY INFO

Grant supportexpand

FULL TEXT LINKS

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23

J Asthma

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. 2022 Nov 8;1-8.

doi: 10.1080/02770903.2022.2137038. Online ahead of print.

The relationship between general and abdominal obesity, nutrition and

respiratory functions in adult asthmatics

Ümüş Özbey Yücel[1], Aliye Gamze Çalış[2]

Affiliations expand

- PMID: 36239386

- DOI: 10.1080/02770903.2022.2137038

Abstract

Objective: Although obesity is known to have adverse effects on asthma, it is not fully known whether general or abdominal obesity affects asthma symptoms more. In this study, the effects of diet and general/abdominal obesity on respiratory functions were evaluated.

Methods: A total of 204 adult asthmatic individuals participated in the study. Anthropometric measurements, respiratory functions, asthma control test (ACT) scores, and 24-hour food consumption were recorded. The results were compared according to body mass index (BMI), waist circumference (WC), and waist-hip ratio (WHR) classification.

Results: FEV_1, FVC, MEF_{25-75}, MEF_{50}, and MEF_{25} decreased with the increase in BMI, WC, and WHR. FEV_1 showed a negative linear relationship with BMI, WC and WHR and these results were more significant in WC and WHR than BMI. Similarly, the ACT score also showed a negative correlation with BMI (r = -0.372; p = 0.023), WC (r = -0.402; p = 0.001) and WHR (r = -0.387; p = 0.011), and the results were more significant in WC and WHR than BMI. Individuals whose WC (OR: 2.170 CI (1.325-3.182)) and WHR (OR: 2.119 CI (1.246-3.338)) were at risk had higher odds of uncontrolled asthma than those with normal WC and WHR. Each 100-kcal increase in total energy consumption increased the odds of uncontrolled asthma (OR: 1.125 CI (1.086-2.217)) (p < 0.05).

Conclusions: The effects of WC and WHR, which are indicators of abdominal obesity, on respiratory functions and ACT score, were found to be higher than BMI. Obese individuals should be referred to diet clinics to improve their asthma symptoms.

Keywords: Asthma; central obesity; general obesity; nutrition.

J Asthma

. 2022 Nov 8;1-9.

doi: 10.1080/02770903.2022.2134795. Online ahead of print.

Airwave oscillometry and spirometry in children with asthma or wheeze

Shannon Gunawardana[1], Mark Tuazon[2], Lorna Wheatley[2], James Cook[3], Christopher Harris[4], Anne Greenough[1,5]

Affiliations expand

- PMID: 36218195
- PMCID: PMC9612926
- DOI: 10.1080/02770903.2022.2134795

Free PMC article

Abstract

Objective: Lung function testing is used in diagnosing asthma and assessing asthma control. Spirometry is most commonly used, but younger children can find performing this test challenging. Non-volitional tests such as airwave oscillometry (AOS) may be helpful in that population. We compared the success of spirometry and AOS in assessing bronchodilator responsiveness in children.

Methods: AOS was conducted alongside routine lung function testing. Resistance at 5 Hz (R5), the difference between the resistance at 5 and 20 Hz (R5-20) and the area under the reactance curve (AX) were assessed. Patients between 5 and 16 years old attending clinic with wheeze or asthma were assessed. Patients performed AOS, followed by spirometry and were then given 400 µg salbutamol; the tests were repeated 15 minutes later.

Results: Lung function testing was performed in 47 children of whom 46 (98%) and 32 (68%) performed acceptable baseline oscillometry and spirometry, respectively ($p < 0.001$). Children unable to perform acceptable spirometry were younger (7.35, range: 5.4-10.3 years) than those who could (10.4, range: 5.5-16.9 years), $p < 0.001$. The baseline z-scores of AOS R5 correlated with FEV_1 ($r = 0.499$, $p = 0.004$), FEF_{75} ($r = 0.617$, $p < 0.001$), and FEV_1/FVC ($r = 0.618$, $p < 0.001$). There was a positive bronchodilator response assessed by spirometry (change in $FEV_1 \geq 12\%$) in eight children which corresponded to a change in R5 of 36% (range: 30%-50%) and a change in X5 of 39% (range: 15%-54%).

Conclusions: Oscillometry is a useful adjunct to spirometry in assessing young asthmatic children's lung function. The degree of airway obstruction, however, might affect the comparability of the results of the two techniques.

Keywords: Lung function; bronchodilator responsiveness; forced expiratory volume in 1 second (FEV1); pediatrics; resistance at 5Hz (R5).

- 1 figure

Eur Respir J

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. 2022 Nov 10;60(5):2201141.

doi: 10.1183/13993003.01141-2022. Print 2022 Nov.

Early-life respiratory infections and pre-adult asthma: could there be an interaction and differential misclassification?

Jennifer L Perret[1], Shyamali C Dharmage[2], Dinh S Bui[2]

Affiliations expand

- PMID: 35896212

- PMCID: PMC9647072

- DOI: 10.1183/13993003.01141-2022

Free PMC article

Abstract

Further analyses to clarify the clinical and public health messages for early-life upper respiratory tract infections are suggested to better inform parents and the healthcare professionals who look after these children in the general community https://bit.ly/3xAWxz0

Conflict of interest statement

Conflict of interest: J.L. Perret, D.S. Bui and S.C. Dharmage have received an investigator-initiated grant from GlaxoSmithKline for unrelated research, and S.C. Dharmage holds an investigator-initiated grant for unrelated research from AstraZeneca.

Comment on

- Early-life respiratory tract infections and the risk of school-age lower lung function and asthma: a meta-analysis of 150 000 European children.
  van Meel ER, Mensink-Bout SM, den Dekker HT, Ahluwalia TS, Annesi-Maesano I, Arshad SH, Baïz N, Barros H, von Berg A, Bisgaard H, Bønnelykke K, Carlsson CJ, Casas M, Chatzi L, Chevrier C, Dalmeijer G, Dezateux C, Duchen K, Eggesbø M, van

der Ent C, Fantini M, Flexeder C, Frey U, Forastiere F, Gehring U, Gori D, Granell R, Griffiths LJ, Inskip H, Jerzynska J, Karvonen AM, Keil T, Kelleher C, Kogevinas M, Koppen G, Kuehni CE, Lambrechts N, Lau S, Lehmann I, Ludvigsson J, Magnus MC, Mélen E, Mehegan J, Mommers M, Nybo Andersen AM, Nystad W, Pedersen ESL, Pekkanen J, Peltola V, Pike KC, Pinot de Moira A, Pizzi C, Polanska K, Popovic M, Porta D, Roberts G, Santos AC, Schultz ES, Standl M, Sunyer J, Thijs C, Toivonen L, Uphoff E, Usemann J, Vafeidi M, Wright J, de Jongste JC, Jaddoe VWV, Duijts L.Eur Respir J. 2022 Oct 6;60(4):2102395. doi: 10.1183/13993003.02395-2021. Print 2022 Oct.PMID: 35487537 **Free PMC article.**

- 5 references

Eur Respir J

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. 2022 Nov 10;60(5):2201384.

doi: 10.1183/13993003.01384-2022. Print 2022 Nov.

Reply to: Early-life respiratory infections and pre-adult asthma: could

there be an interaction and differential misclassification?

Evelien R van Meel[1,2], Liesbeth Duijts[2,3], participating authors of the meta-analysis "Early-life respiratory tract infections and the risk of school-age lower lung function and asthma"

Affiliations expand

- PMID: 35896205
- PMCID: PMC9647075
- DOI: 10.1183/13993003.01384-2022

Free PMC article

Abstract

Upper respiratory tract infections solely in early life are associated with school-age asthma as well, although not as strongly as lower respiratory tract infections solely or both combined https://bit.ly/3ocwwAD

Conflict of interest statement

Conflict of interest: L. Duijts declares support from the European Union's Horizon 2020 research and innovation programme (LIFECYCLE, grant agreement number 733206, 2016; EUCAN-Connect grant agreement number 824989; ATHLETE, grant agreement number 874583), related to the current manuscript; as well as a research grant from Stichting Vrienden van Sophia; a speaker fee (paid to their institution) from Hong Kong University; and roles as the Vice-chair of the Dutch Pediatric Respiratory Society and as a Member of the Science Committee for the Global Initiative for Asthma (GINA) for developing annual reports on strategies for asthma management. E.R. van Meel has nothing to disclose.

Comment on

- Early-life respiratory tract infections and the risk of school-age lower lung function and asthma: a meta-analysis of 150 000 European children.
  van Meel ER, Mensink-Bout SM, den Dekker HT, Ahluwalia TS, Annesi-Maesano I, Arshad SH, Baïz N, Barros H, von Berg A, Bisgaard H, Bønnelykke K, Carlsson CJ, Casas M, Chatzi L, Chevrier C, Dalmeijer G, Dezateux C, Duchen K, Eggesbø M, van der Ent C, Fantini M, Flexeder C, Frey U, Forastiere F, Gehring U, Gori D, Granell R,

Griffiths LJ, Inskip H, Jerzynska J, Karvonen AM, Keil T, Kelleher C, Kogevinas M, Koppen G, Kuehni CE, Lambrechts N, Lau S, Lehmann I, Ludvigsson J, Magnus MC, Mélen E, Mehegan J, Mommers M, Nybo Andersen AM, Nystad W, Pedersen ESL, Pekkanen J, Peltola V, Pike KC, Pinot de Moira A, Pizzi C, Polanska K, Popovic M, Porta D, Roberts G, Santos AC, Schultz ES, Standl M, Sunyer J, Thijs C, Toivonen L, Uphoff E, Usemann J, Vafeidi M, Wright J, de Jongste JC, Jaddoe VWV, Duijts L.Eur Respir J. 2022 Oct 6;60(4):2102395. doi: 10.1183/13993003.02395-2021. Print 2022 Oct.PMID: 35487537 **Free PMC article.**

- 3 references

SUPPLEMENTARY INFO

Publication typesexpand

RHINITIS

Review

Allergy

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. 2022 Nov 10.

doi: 10.1111/all.15578. Online ahead of print.

Biomarkers associated with the development of comorbidities in patients with atopic dermatitis: a systematic review

Conor Broderick[1], Stefanie Ziehfreund[2], Karin van Bart[3], Bernd Arents[4], Kilian Eyerich[2,5], Stephan Weidinger[6], Joseph Rastrick[7], Alexander Zink[2,5], Carsten Flohr[1], BIOMAP Consortium

Affiliations expand

- PMID: 36366871

- DOI: 10.1111/all.15578

Abstract

Biomarkers associated with the development of comorbidities in atopic dermatitis (AD) patients have been reported, but have not yet been systematically reviewed. Seven electronic databases were searched, from database inception to September 2021. English language randomized controlled trials, prospective and retrospective cohort, and case-control studies that investigated the association between a biomarker and the development of comorbidities in AD patients were included. Two authors independently screened the records for eligibility, one extracted all data and critically appraised the quality of studies and risk of bias. 56 articles met the inclusion criteria, evaluating 146 candidate biomarkers. The most frequently reported biomarkers were filaggrin mutations and allergen specific-IgE. Promising biomarkers include specific-IgE and/or skin prick tests predicting the development of asthma, and genetic polymorphisms predicting the occurrence of eczema herpeticum. The identified studies and biomarkers were highly heterogeneous, and associated with predominately moderate-to-high risk of bias across multiple domains. Overall, findings were inconsistent. High-quality studies assessing biomarkers associated with the development of comorbidities in people with AD are lacking. Harmonized datasets and independent validation studies are urgently needed. Systematic review registration: PROSPERO CRD42020193294.

Keywords: allergic rhinitis; asthma; atopic dermatitis; biomarker; comorbidities.

Review

Pathogens

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. 2022 Nov 9;11(11):1313.

doi: 10.3390/pathogens11111313.

Sublingual Immunotherapy for Japanese Cedar Pollinosis: Current Clinical and Research Status

Daiju Sakurai[1], Hiroki Ishii[1], Ayumi Shimamura[1], Daisuke Watanabe[1], Takaaki Yonaga[1], Tomokazu Matsuoka[1]

Affiliations expand

- PMID: 36365064

- DOI: 10.3390/pathogens11111313

Abstract

The incidence of Japanese cedar pollinosis is increasing significantly in Japan, and a recent survey suggested that about 40% of the population will develop this disease. However, spontaneous remission is rare. The increased incident rate of Japanese cedar pollinosis is a huge issue in Japan. Allergen immunotherapy is the only fundamental treatment that modifies the natural course of allergic rhinitis and provides long-term remission that cannot be induced by general drug therapy. Sublingual immunotherapy for Japanese cedar pollinosis has been developed and has been covered by health insurance since 2014 in Japan. The indication for children was expanded in 2018. Clinical trials of sublingual immunotherapy for Japanese cedar pollinosis have demonstrated its long-term efficacy and safety. It is recommended for patients who wish to undergo fundamental treatment regardless of the severity of the practical guidelines for the management of allergic rhinitis in Japan. For sublingual immunotherapy, a long-term treatment period of 3 years or longer is recommended to obtain stable therapeutic effects. In recent years, evidence based on basic research and clinical trials has demonstrated sublingual immunotherapy-induced immunological changes and efficacy in patients; however, biomarkers that objectively predict and judge these therapeutic effects need to be established.

Keywords: Japanese cedar pollen; allergen immunotherapy; allergic rhinitis; pollinosis; sublingual immunotherapy.

SUPPLEMENTARY INFO

Publication typesexpand

Int J Environ Res Public Health

. 2022 Nov 6;19(21):14551.

doi: 10.3390/ijerph192114551.

Investigating the Relationship between Parental Education, Asthma and Rhinitis in Children Using Path Analysis

Ilaria Rocco[1], Giovanna Cilluffo[2], Giuliana Ferrante[3], Fabio Cibella[4], Alessandro Marcon[5], Pierpaolo Marchetti[5], Paolo Ricci[6], Nadia Minicuci[1], Stefania La Grutta[7], Barbara Corso[1]

Affiliations expand

- PMID: 36361431

- DOI: 10.3390/ijerph192114551

Abstract

Parental socioeconomic position (SEP) is a known determinant of a child's health. We aimed to investigate whether a low parental education, as proxy of SEP, has a direct effect on physician-diagnosed asthma, current asthma and current allergic rhinitis in children, or whether associations are mediated by exposure to other personal or environmental risk factors. This study was a secondary data analysis of two cross-sectional studies conducted in Italy in 2006. Data from 2687 adolescents (10-14 years) were analyzed by a path analysis model using generalized structural equation modelling. Significant direct effects were found between parental education and family characteristics (number of children (coefficient = 0.6229, *p* < 0.001) and crowding index (1.1263, *p* < 0.001)) as well as with exposure to passive smoke: during pregnancy (maternal: 0.4697, *p* < 0.001; paternal:

0.4854, *p* < 0.001), during the first two years of children's life (0.5897, *p* < 0.001) and currently (0.6998, *p* < 0.001). An indirect effect of parental education was found on physician-diagnosed asthma in children mediated by maternal smoking during pregnancy (0.2350, *p* < 0.05) and on current allergic rhinitis mediated by early environmental tobacco smoke (0.2002; *p* < 0.05). These results suggest the importance of promotion of ad-hoc health policies for promoting smoking cessation, especially during pregnancy.

Keywords: asthma; children; prenatal education; rhinitis; structural equation modelling.

BMC Pulm Med

. 2022 Nov 9;22(1):406.

doi: 10.1186/s12890-022-02203-8.

Chronic rhinosinusitis associated with chronic bronchitis in a five-year follow-up: the Telemark study

Joel Bergqvist[1,2], Mogens Bove[3,4], Anders Andersson[5,6], Linus Schiöler[7], Geir Klepaker[8], Regine Abrahamsen[8], Anne Kristin M Fell[8,9], Johan Hellgren[10,3]

Affiliations expand

- PMID: 36348489

- DOI: 10.1186/s12890-022-02203-8

Free article

Abstract

Background: Chronic rhinosinusitis (CRS) is associated with generalised airway inflammation. Few studies have addressed the relationship between CRS and chronic bronchitis (CB).

Methods: This prospective study over a five-year period aims to investigate the risk of developing CB in subjects reporting CRS at the beginning of the study. A random sample of 7393 adult subjects from Telemark County, Norway, answered a comprehensive respiratory questionnaire in 2013 and then 5 years later in 2018. Subjects reporting CB in 2013 were excluded from the analyses. New cases of CB in 2018 were analysed in relation to having CRS in 2013 or not.

Results: The prevalence of new-onset CB in 2018 in the group that reported CRS in 2013 was 11.8%. There was a significant increase in the odds of having CB in 2018 in subjects who reported CRS in 2013 (OR 3.8, 95% CI 2.65-5.40), adjusted for age, sex, BMI, smoking and asthma.

Conclusion: In this large population sample, CRS was associated with increased odds of developing CB during a five-year follow-up. Physicians should be aware of chronic bronchitis in patients with CRS.

Keywords: Chronic bronchitis; Epidemiology; Rhinitis.

- 33 references

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

. 2022 Nov 8;15(1):80.

doi: 10.1186/s40545-022-00477-1.

The management of allergic rhinitis by pharmacists in public services: a proposed PhaRmacISt-led Education Model (AR-PRISE)

Chii-Chii Chew[1], Chee-Tao Chang[2], Xin-Jie Lim[3], Wai-Yin Yong[4], Doris George[4], Pathma Letchumanan[5], Philip Rajan[6,5], Chee Ping Chong[1]

Affiliations expand

- PMID: 36348443

- DOI: 10.1186/s40545-022-00477-1

Free article

Abstract

Allergic rhinitis has been identified as a major respiratory disease that places a significant burden on patients and the healthcare system. Nevertheless, the management of allergic rhinitis is challenging for both patients and practitioners. Pharmacists have been recognised as strategic in providing advice for allergic avoidance, disease information, and pharmacological care for allergic rhinitis management. This role has been underutilised in the public health service sector in Malaysia due to variation in practice, regulation, and health system structures when compared to the international guidelines. This article proposed a PhaRmacISt-led Education Model (AR-PRISE) that includes explicit patient education materials and an algorithm for structured counselling by pharmacists in the management of patients with allergic rhinitis.

Keywords: Allergic rhinitis; Educational model; Patient education; Pharmacist; Public health service.

- 29 references

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

Int J Environ Health Res

. 2022 Nov 6;1-12.

doi: 10.1080/09603123.2022.2143482. Online ahead of print.

Fractional exhaled nitric oxide (FeNO) and respiratory symptoms in junior high school students in Penang, Malaysia: the role of household exposure

Dan Norbäck[1], Jamal Hisham Hashim[2], Zailina Hashim[3], Gunilla Wieslander[1]

Affiliations expand

- PMID: 36335594

- DOI: 10.1080/09603123.2022.2143482

Abstract

We studied associations between fractional exhaled nitric oxide (FeNO), health and household exposure among school children (N = 348) in Penang, Malaysia. Multiple logistic regression and linear mixed models were applied. Overall, 46.0% had elevated FeNO (>20 ppb) and 10.6% diagnosed asthma. Male gender (p = 0.002), parental asthma or allergy (p = 0.047), cat allergy (p = 0.009) and seafood allergy (p < 0.001), diagnosed asthma (p = 0.001), wheeze (p = 0.001), ocular symptoms (p = 0.001), rhinitis (p = 0.002) and respiratory infections (p = 0.004) were all associated with FeNO. Students exposed to ETS had lower FeNO (p = 0.05). Dampness and mould was associated with wheeze (p = 0.038), especially in wooden homes (interaction p = 0.042) and among students with elevated FeNO (interaction p = 0.024). Cat keeping increased rhinitis (p = 0.041) and respiratory infections (p = 0.008) and modified the dampness associations. In conclusion, FeNO can be associated with ocular and respiratory symptoms. Elevated FeNO, cat keeping and a wooden house can enhance the risk of wheeze when exposed to dampness and mould.

Keywords: Asthma; Malaysia; allergy; rhinitis; tropical country.

BRONCHIECTASIS

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Toxics

. 2022 Nov 6;10(11):667.

doi: 10.3390/toxics10110667.

Impact of Acute Exacerbation and Its Phenotypes on the Clinical Outcomes of Chronic Obstructive Pulmonary Disease in Hospitalized Patients: A Cross-Sectional Study

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Affiliations expand

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Abstract

Acute exacerbations of COPD (AECOPD) are clinically significant events having therapeutic and prognostic consequences. However, there is a lot of variation in its clinical manifestations described by phenotypes. The phenotypes of AECOPD were categorized in this study based on pathology and exposure. In our cross-sectional study, conducted between 1 January 2016 to 31 December 2020, the patients were categorized into six groups based on pathology: non-bacterial and non-eosinophilic; bacterial; eosinophilic; bacterial infection with eosinophilia; pneumonia; and bronchiectasis. Further, four groups were classified based on exposure to tobacco smoke (TS), biomass smoke (BMS), both, or no exposure. Cox proportional-hazards regression analyses were performed to assess hazard ratios, and Kaplan-Meier analysis was performed to assess survival, which was then compared using the log-rank test. The odds ratio (OR) and independent predictors of ward admission type and length of hospital stay were assessed using binomial logistic regression analyses. Of the 2236 subjects, 2194 were selected. The median age of the cohort was 67.0 (60.0 to 74.0) and 75.2% were males. Mortality rates were higher in females than in males (6.2% vs. 2.3%). AECOPD-B (bacterial infection) subjects [HR 95% CI 6.42 (3.06-13.46)], followed by AECOPD-P (pneumonia) subjects [HR (95% CI: 4.33 (2.01-9.30)], were at higher mortality risk and had a more extended hospital stay (6.0 (4.0 to 9.5) days; 6.0 (4.0 to 10.0). Subjects with TS and BMS-AECOPD [HR 95% CI 7.24 (1.53-34.29)], followed by BMS-AECOPD [HR 95% CI 5.28 (2.46-11.35)], had higher mortality risk. Different phenotypes have different impacts on AECOPD clinical outcomes. A better understanding of AECOPD phenotypes could contribute to developing an algorithm for the precise management of different phenotypes.

Keywords: AECOPD; COPD; acute exacerbation; biomass; mortality; phenotype; tobacco.

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Review

Cystic Fibrosis

Adrienne Savant[1], Benjamin Lyman[2], Christine Bojanowski[3], Jariya Upadia[1]

Margaret P Adam, David B Everman, Ghayda M Mirzaa, Roberta A Pagon, Stephanie E Wallace, Lora JH Bean, Karen W Gripp, Anne Amemiya

, editors.

In: GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993.

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Affiliations expand

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Excerpt

Clinical characteristics: Cystic fibrosis (CF) is a multisystem disease affecting epithelia of the respiratory tract, exocrine pancreas, intestine, hepatobiliary system, and exocrine sweat glands. Morbidities include recurrent sinusitis and bronchitis, progressive obstructive pulmonary disease with bronchiectasis, exocrine pancreatic deficiency and malnutrition, pancreatitis, gastrointestinal manifestations (meconium ileus, rectal prolapse, distal intestinal obstructive syndrome), liver disease, diabetes, male infertility due to hypoplasia or aplasia of the vas deferens, and reduced fertility or infertility in some women. Pulmonary disease is the major cause of morbidity and mortality in CF.

Diagnosis/testing: The diagnosis of CF is established in a proband with:

- Elevated immunoreactive trypsinogen on newborn screen, signs and/or symptoms suggestive of CF, or family history of CF; AND
- Evidence of an abnormality in cystic fibrosis transmembrane conductance regulator (CFTR) function: sweat chloride ≥60 mmol/L on sweat chloride testing, biallelic *CFTR* CF-causing pathogenic variants, or nasal transmembrane epithelial potential difference measurement consistent with CF.

Management: *Treatment of manifestations – targeted therapy:* CFTR modulator therapy is available for individuals with responsive *CFTR* variants.

Supportive care: Newborns: management by a CF specialist or CF care center; airway clearance instruction; encouraging feeding with breast milk; routine vaccinations; contact precautions with every encounter; antibiotics for bacterial suppression and treatment; nutrition management; pancreatic enzyme replacement; nutrient-dense food and supplements; fat-soluble vitamin supplements; laxative treatment as needed with surgical management for bowel obstruction; and salt and water supplementation.

After the newborn period: airway clearance; pulmonary treatment (bronchodilator, hypertonic saline, dornase alfa, airway clearance, inhaled corticosteroids and/or long-acting beta agonist, and aerosolized antibiotic); standard treatments for pneumothorax or hemoptysis; double lung transplant for those with advanced lung disease; routine vaccinations including influenza; contact precautions; antibiotics for bacterial suppression and treatment; antibiotics and/or surgical intervention for nasal/sinus symptoms; nutrition management; pancreatic enzyme replacement; nutrient-dense food and supplements; fat-soluble vitamin supplements; laxative treatment as needed with surgical management for bowel obstruction; standard treatments for gastroesophageal reflux disease; oral ursodiol for biliary sludging/obstruction; liver transplant when indicated; management of CF-related diabetes mellitus by an endocrinologist; assisted reproductive technologies (ART) for infertility; salt and water supplementation; standard treatments for associated mental health issues.

Surveillance: Frequent assessment by a CF specialist to monitor for new or worsening manifestations; pulmonary function testing frequently after age five years; chest x-ray or chest CT examination to assess for bronchiectasis every two years or as needed; cultures of respiratory tract secretions at least every three months; non-tuberculosis mycobacterium culture and serum IgE annually or as indicated; annual CBC with differential; annual ENT assessment; monitoring growth and GI manifestations at each visit; fecal elastase as needed; annual serum vitamin A, D, E, and PT (as a marker of vitamin K); annual liver function tests; annual random glucose, annual two-hour glucose tolerance test beginning at age ten years; DXA scan as needed in adolescence; infertility assessment as needed; annual electrolytes, BUN, and creatinine; annual assessment of depression and anxiety.

Agents/circumstances to avoid: Environmental smoke, exposure to respiratory infections, dehydration.

Evaluation of relatives at risk: Molecular genetic testing of at-risk sibs (if the pathogenic variants in the family are known) or sweat chloride testing of at-risk sibs (if the pathogenic variants in the family are not known) to identify as early as possible those who should be referred to a CF center for initiation of early treatment.

Genetic counseling: CF is inherited in an autosomal recessive manner. If both parents are known to be heterozygous for a *CFTR* pathogenic variant, each sib of an affected individual

has at conception a 25% chance of being affected, a 50% chance of being heterozygous, and a 25% chance of inheriting neither of the familial pathogenic variants. Once the *CFTR* pathogenic variants have been identified in an affected family member, targeted heterozygote testing for at-risk relatives and prenatal/preimplantation genetic testing for CF are possible.

- 117 references

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Review

Ugeskr Laeger

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. 2022 Nov 7;184(45):V04220252.

[Pulmonary manifestations in rheumatoid arthritis]

[Article in Danish]

Charlotte Hyldgaard[1], Saher Burhan Shaker[2], Jesper Rømhild Davidsen[3 4], Torkell Ellingsen[3 5], Elisabeth Bendstrup[6 7]

Affiliations expand

- PMID: 36345900

Free article

Abstract

Rheumatoid arthritis (RA) affects more than 30,000 Danes. In this review, we discuss RA in connection with chronic obstructive pulmonary disease (COPD), bronchiectasis and interstitial lung disease (ILD) which are among the most common lung manifestations and are associated with increased mortality. Early suspicion based upon respiratory symptoms should prompt imaging and pulmonary function test. Smoking cessation, vaccination, and rehabilitation are important. COPD and bronchiectasis are treated according to guidelines. Multidisciplinary collaboration in RA-ILD is important and treatment decisions are based on clinical experience and imaging suggesting an inflammatory or fibrotic phenotype.

BMC Pulm Med

. 2022 Nov 7;22(1):401.

doi: 10.1186/s12890-022-02202-9.

The effect of N-acetylcysteine in patients with non-cystic fibrosis bronchiectasis (NINCFB): study protocol for a multicentre, double-blind, randomised, placebo-controlled trial

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Affiliations expand

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- DOI: 10.1186/s12890-022-02202-9

Free PMC article

Abstract

Background: N-acetylcysteine (NAC), which is specifically involved in airway mucus clearance and antioxidation, is recommended by the treatment guideline for non-cystic fibrosis bronchiectasis (NCFB). However, there is little clinical evidence of its long-term efficacy concerning quality of life (QoL) and exacerbation in patients with NCFB. In addition, the influences of NAC on airway bacterial colonization, chronic inflammation and oxidative stress in NCFB are also unclear.

Methods: NINCFB is a prospective, multicentre, double-blind, randomised, placebo-controlled trial that will recruit 119 patients with NCFB and randomly divide them into an NAC group (n = 79) and a control group (n = 40). Participants in the NAC group will receive 600 mg oral NAC twice daily for 52 weeks, while patients in the control group will receive 600 mg placebo twice daily for 52 weeks. The information at baseline will be collected once participants are enrolled. The primary endpoints are the changes in St George's Respiratory Questionnaire scores and the number of exacerbations in 52 weeks. The secondary endpoints are the 16S rRNA of sputum and the levels of inflammatory

factors and oxidative stressors in sputum and serum. Other data related to radiography, lung function tests, number of oral and/or intravenous antibiotic therapies and adverse events (AEs) will also be analysed. Further subgroup analysis distinguished by the severity of disease, severity of lung function, airway bacterial colonization and exacerbation frequency will be performed.

Discussion: The objective of this study is to determine the long-term efficacy of NAC on QoL and exacerbation of NCFB and to explore the effectiveness of NAC for antibiosis, anti-inflammation and antioxidation in NCFB. The study results will provide high-quality clinical proof for the revision and optimization of treatment guidelines and for expert consensus on NCFB treatment.

Trial registration: The trial was registered on the Chinese Clinical Trial Register at April 11, 2020 (chictr.org.cn , ChiCTR2000031817).

Keywords: Bacterial colonization; Chronic inflammation; Clinical trial; Exacerbation; N-acetylcysteine; Non-cystic fibrosis bronchiectasis; Oxidative stress; Quality of life.

Conflict of interest statement

The authors have no competing interests to declare.

- 42 references
- 1 figure

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

CHRONIC COUGH

1

Case Reports

J Voice

. 2022 Nov 7;S0892-1997(22)00298-3.

doi: 10.1016/j.jvoice.2022.09.021. Online ahead of print.

The Diagnosis and Time of Onset of Voice Disorders in Patients with Chronic Cough

Jessica F Kim[1], WayAnne Watson[2], Benjamin J Becerra[3], Brianna K Crawley[2], Rim Saab[4], Priya Krishna[2], Thomas Murry[5]

Affiliations expand

- PMID: 36357238

- DOI: 10.1016/j.jvoice.2022.09.021

Abstract

Objectives: Chronic cough is a complaint of up to 46% of patients referred to specialist clinics. Patients with cough often report hoarseness at the time of the cough diagnosis. When the cough fails to resolve with standard medications, referrals to other specialists including otolaryngologists are made. This is the first study to report the specific diagnosis and length of time it took to obtain a specific voice disorder diagnosis in patients with chronic cough.

Study design: Case Series METHODS: The charts of 105 patients referred to the Loma Linda Voice and Swallowing Center were reviewed. The first complaint of cough and/or hoarseness and the specific voice disorder diagnosis following otolaryngologic evaluation were identified. Voice disorders were divided into neurogenic or other/functional disorders and common comorbidities were identified. Statistical analysis between diagnostic groups, gender, and age were obtained.

Results: The specific voice disorders in the cohort were identified. There was a high prevalence of neurogenic voice disorders (n = 85, 81%). There were significant relationships between chronic cough and the two most common neurogenic voice disorders, vocal fold paresis and vocal fold atrophy. The average length of time between complaint of hoarseness and the specific voice disorder diagnosis was 32.3 months. Most patients (86%) complained of voice problems after diagnosis of chronic cough. A

significant association was found in prevalence of asthma (OR = 4.52, P = 0.02) and dyspnea (OR = 4.24, P = 0.02) in the cohort who presented first with voice complaints and later developed chronic cough.

Conclusions: There is a high incidence of neurogenic voice disorders accompanying patients with chronic cough. Understanding the relationship between chronic cough and hoarseness provides the clinician with specific diagnostic information in the treatment of both disorders.

Keywords: Chronic cough; Chronic refractory cough; Hoarseness; Neurogenic voice disorders.

Conflict of interest statement

Declaration of interest None for all authors

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Lung

. 2022 Nov 8.

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Validation and Meaningful Change Thresholds for an Objective Cough Frequency Measurement in Chronic Cough

Jonathan Schelfhout[1], Allison Martin Nguyen[1], Surinder S Birring[2], Elizabeth D Bacci[3], Margaret Vernon[4], David R Muccino[1], Carmen La Rosa[1], Jaclyn A Smith[5]

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Abstract

Purpose: Objective cough frequency is used to assess efficacy of chronic cough (CC) treatments. The objective of this study was to explore the relationship between objective cough frequency and cough-specific patient-reported outcomes (PROs) and estimate a clinically meaningful change threshold (MCT) for objective cough frequency.

Methods: Data collected in a phase 2b study in participants with refractory or unexplained CC were used to investigate the relationship between 24-h cough frequency (measured using an ambulatory cough monitor) and cough-specific PROs (i.e., cough severity visual analog scale, cough severity diary, Leicester Cough Questionnaire). Convergent validity was assessed using Spearman ρ. An MCT for 24-h cough frequency was estimated using the patient global impression of change (PGIC) scale as an anchor.

Results: Correlations between 24-h cough frequency and cough-specific PROs at baseline, Week 4, and Week 12 were significant ($P < 0.0001$) but low to moderate in strength ($\rho = 0.30$-0.58). Participants categorized as very much improved/much improved (i.e., PGIC of 1 or 2) or minimally improved (i.e., PGIC of 3) had mean 24-h cough frequency reductions of 55% and 30%, respectively. Receiver operating characteristic curve analysis suggested that a 24-h cough frequency reduction of 38% optimizes sensitivity and specificity for predicting a PGIC score of 1-3.

Conclusion: Objective 24-h cough frequency is significantly associated with cough-specific PROs, but cough frequency and PROs most likely capture distinct aspects of CC. A ≥ 30% reduction in 24-h cough frequency is a reasonable MCT to define treatment response in CC clinical trials.

Keywords: Chronic cough; Clinically meaningful change; Cough monitoring; Cough severity; Objective cough frequency; Patient-reported outcomes.

- 34 references