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CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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1

Respir Res

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. 2022 Nov 19;23(1):321.

doi: 10.1186/s12931-022-02246-9.

Analysis of sputum microbial metagenome in COPD based on

exacerbation frequency and lung function: a case control study

Wei Li[#1], Bingbing Wang[#2], Min Tan[2], Xiaolian Song[2], Shuanshuan Xie[2], Changhui Wang[3]

Affiliations expand

- PMID: 36403054

- DOI: 10.1186/s12931-022-02246-9

Abstract

Background: The role of the sputum microbiome in chronic obstructive pulmonary disease (COPD) progression remains elusive. As the advent of the new culture-independent microbial sequencing technique makes it possible to disclose the complex microbiome community of the respiratory tract. The aim of this study was to use metagenomic next-generation sequencing (mNGS) to confirm whether there are differences in sputum microbiome of COPD between different exacerbation frequencies and lung function.

Methods: Thirty-nine COPD patients were divided into a frequent exacerbators (FE) group (n = 20) and a non-frequent exacerbators (NFE) (n = 19) group according to their exacerbation history, or a mild group (FEV_1/pre ≥ 50%, n = 20) and a severe group (FEV_1/pre < 50%, n = 19) according to the lung function. Sputum was collected during their stable phase, followed by DNA extraction, untargeted metagenomic next-generation sequencing (mNGS) and bioinformatic analysis.

Results: mNGS identified 3355 bacteria, 71 viruses and 22 fungi at the specie level. It was found that Shannon index and Simpson index in FE group was lower than that in NFE group (p = 0.005, 0.008, respectively) but similar between mild and severe groups. Out of top 10 bacteria taxa, Veillonella, Fusobacterium and Prevotella jejuni had a higher abundance in NFE group, Rothia had a higher abundance in mild group. Linear discriminant analysis revealed that many bacterial taxa were more abundant in NFE group, and they mostly belonged to Actinobacteria, Bacteroidetes and Fusobacteria phyla. Frequency of exacerbations was also found to be negatively correlated with alpha diversity (with Shannon index, r = - 0.423, p = 0.009; with Simpson index, r = - 0.482, p = 0.002). No significant correlation was observed between alpha diversity and FEV_1/pre.

Conclusions: Microbiome diversity in FE group was lower than that in NFE group. There was a significant difference in microbiome taxa abundance between FE and NFE groups, or mild and severe groups. These findings demonstrated that sputum microbiome community dysbiosis was associated with different exacerbation frequencies and lung function in stable COPD.

Keywords: Chronic obstructive pulmonary disease (COPD); Exacerbation frequency; Lung function; Metagenomic next-generation sequencing; Microbiome; Sputum.

- 25 references

SUPPLEMENTARY INFO

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Medicine (Baltimore)

. 2022 Nov 18;101(46):e31857.

doi: 10.1097/MD.0000000000031857.

Application of improved Glasgow coma scale score as switching point for sequential invasive-noninvasive mechanical ventilation on chronic obstructive pulmonary disease (COPD) with respiratory failure

Jin-Bo Zhang[1], Li-Hong Li[2], Jin-Qiang Zhu[1], Shi-Fang Zhou[3], Ji-Hong Ma[4], Zhi-Qiang Li[5], Xiao-Hong Jin[1], Xiao-Qin Lin[6]

Affiliations expand

- PMID: 36401492

- DOI: 10.1097/MD.0000000000031857

Abstract

Background: To compare the efficacy and feasibility of using a modified Glasgow coma scale (GCS) score of 13 or 15 as the criterion for switching chronic obstructive pulmonary disease (COPD) patients with respiratory failure to sequential invasive-noninvasive ventilation.

Methods: COPD patients with respiratory failure who had undergone endotracheal intubation and invasive mechanical ventilation (IMV) between June 2017 and June 2020 at 4 different hospitals in China were included. A total of 296 patients were randomly divided into 2 groups. In group A, the patients were extubated and immediately placed on noninvasive ventilation (NIV) when the modified GCS score reached 13. In group B, the same was done when the modified GCS score reached 15.

Results: No significant differences in the mean blood pressure, oxygenation index, arterial partial pressure of oxygen, and arterial partial pressure of carbon dioxide were seen between groups A and B before extubation and 3 hours after NIV. The re-intubation times were also similar in the 2 groups. Compared to group B, the length of hospital stay, incidence of ventilator associated pneumonia, and time of invasive ventilation were all significantly lower in group A (P = .041, .001, <.001).

Conclusion: Using a modified GCS score of 13 as the criterion for switching from IMV to NIV can significantly reduce the duration of IMV, length of hospital stay, and incidence of ventilator associated pneumonia in COPD patients with respiratory failure.

Conflict of interest statement

The authors have no conflicts of interest to disclose.

- 26 references

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Intensive Care Med

. 2022 Nov 18.

doi: 10.1007/s00134-022-06919-3. Online ahead of print.

Effect of postextubation noninvasive ventilation with active humidification vs high-flow nasal cannula on reintubation in patients at very high risk for extubation failure: a randomized trial

Gonzalo Hernández[1,2], Irene Paredes[3], Francisco Moran[3], Marcos Buj[3,4], Laura Colinas[3], María Luisa Rodríguez[3], Alfonso Velasco[3], Patricia Rodríguez[3], María José Pérez-Pedrero[3], Fernando Suarez-Sipmann[5], Alfonso Canabal[5,6], Rafael Cuena[7], Lluis Blanch[8,9], Oriol Roca[8,9]

Affiliations expand

- PMID: 36400984

- DOI: 10.1007/s00134-022-06919-3

Abstract

Purpose: High-flow nasal cannula (HFNC) oxygen therapy was noninferior to noninvasive ventilation (NIV) for preventing reintubation in a heterogeneous population at high-risk for extubation failure. However, outcomes might differ in certain subgroups of patients. Thus, we aimed to determine whether NIV with active humidification is superior to HFNC in preventing reintubation in patients with ≥ 4 risk factors (very high risk for extubation failure).

Methods: Randomized controlled trial in two intensive care units in Spain (June 2020–June 2021). Patients ready for planned extubation with ≥ 4 of the following risk factors for reintubation were included: age > 65 years, Acute Physiology and Chronic Health Evaluation II score > 12 on extubation day, body mass index > 30, inadequate secretions management, difficult or prolonged weaning, ≥ 2 comorbidities, acute heart failure indicating mechanical ventilation, moderate-to-severe chronic obstructive pulmonary disease, airway patency problems, prolonged mechanical ventilation, or hypercapnia on finishing the spontaneous breathing trial. Patients were randomized to undergo NIV with active humidification or HFNC for 48 h after extubation. The primary outcome was reintubation rate within 7 days after extubation. Secondary outcomes included postextubation respiratory failure, respiratory infection, sepsis, multiorgan failure, length of stay, mortality, adverse events, and time to reintubation.

Results: Of 182 patients (mean age, 60 [standard deviation (SD), 15] years; 117 [64%] men), 92 received NIV and 90 HFNC. Reintubation was required in 21 (23.3%) patients receiving NIV vs 35 (38.8%) of those receiving HFNC (difference -15.5%; 95% confidence interval (CI) -28.3 to -1%). Hospital length of stay was lower in those patients treated with NIV (20 [12–36.7] days vs 26.5

[15–45] days, difference 6.5 [95%CI 0.5-21.1]). No additional differences in the other secondary outcomes were observed.

Conclusions: Among adult critically ill patients at very high-risk for extubation failure, NIV with active humidification was superior to HFNC for preventing reintubation.

Trial registration: ClinicalTrials.gov NCT04125342.

Keywords: Active humidification; High-flow nasal cannula; Noninvasive ventilation; Outcome; Reintubation; Weaning.

- 26 references

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Associated dataexpand

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BMC Complement Med Ther

. 2022 Nov 17;22(1):296.

doi: 10.1186/s12906-022-03789-6.

Effect of Liuzijue on pulmonary rehabilitation in patients with chronic obstructive pulmonary disease: study protocol for a multicenter, non-randomized, prospective study

Jiaming Hu[#1], Rundi Gao[#2,3], Yiting Wang[1], Yan Li[1], Yaqin Wang[1], Zhen Wang[4], Junchao Yang[5]

Affiliations expand

- PMID: 36397066

- PMCID: PMC9670448

- DOI: 10.1186/s12906-022-03789-6

Free PMC article

Abstract

Background: Traditional Chinese exercise as a new pulmonary rehabilitation technique has been increasingly used and achieved good results in pulmonary rehabilitation of chronic obstructive pulmonary disease (COPD). The aim of this study is to investigate the protective effects of Liuzijue on exercise tolerance, lung function, and quality of life in patients with COPD.

Methods: This study is a multicenter, non-randomized, prospective study. Patients will be divided into a control group (CG) and a Liuzijue group (LG) based on their willingness to learn Liuzijue. None of the outcome assessors will know the grouping of patients. Participants in this study will be collected from stable COPD patients who are outpatients or inpatients in 3 centers in China since September 2021. Patients will meet the diagnostic criteria for GOLD stage I-II COPD ($FEV_1\% \geq 0.5$ and $FEV_1/FVC < 0.7$) and be aged 40 years or older. Patients voluntarily will take part in the clinical study and sign an informed consent form. All participants will follow their existing medication. For LG patients, Liuzijue training has been added. Patients will practice Liuzijue for more than 30 minutes a day, more than 5 days a week, and adhere to the training for 3 months. Outcome indicators are 6-minute walk test (6MWT), lung function ($FEV_1\%$, FEV_1/FVC, MMEF, PEF), modified British Medical Research Council (mMRC) score, COPD assessment test score (CAT), acute exacerbations and changes in drug treatment.

Discussion: This study quantified the effect of Liuzijue on the pulmonary rehabilitation of COPD patients in the stable phase of the disease, and provided a basis for the use of Liuzijue in COPD patients.

Trial registration: Chinese clinical trial registry, ChiCTR2100048945. Date: 2021-07-19. http://www.chictr.org.cn/showproj.aspx?proj=129094.

Keywords: Chronic obstructive pulmonary disease; Liuzijue; Pulmonary rehabilitation.

Conflict of interest statement

The authors declare that they have no competing interests. This study protocol has undergone peer-review by the funding body.

- 37 references
- 2 figures

SUPPLEMENTARY INFO

Grant supportexpand

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Eur J Intern Med

. 2022 Nov 14;S0953-6205(22)00392-2.

doi: 10.1016/j.ejim.2022.11.011. Online ahead of print.

Airflow grades, outcome measures and response to pulmonary rehabilitation in individuals after an exacerbation of severe chronic obstructive pulmonary disease

Michele Vitacca[1], Mara Paneroni[2], Beatrice Salvi[2], Antonio Spanevello[3], Piero Ceriana[4], Claudio Bruschi[5], Bruno Balbi[6], Maria Aliani[7], Nicolino Ambrosino[5]

Affiliations expand

- PMID: 36396523

- DOI: 10.1016/j.ejim.2022.11.011

Abstract

Background: Individuals with COPD may be staged according to symptoms and exacerbation history (GOLD groups: A-D) and on airflow obstruction (GOLD grades: 1-4). Guidelines recommend pulmonary rehabilitation (PR) for these individuals, including those recovering from an exacerbation (ECOPD) OBJECTIVE: To evaluate whether in individuals with clinically severe COPD, recovering from an ECOPD, the effect size of an in-hospital PR program would be affected by airflow severity grades and assessed outcome measures.

Methods: Retrospective, multicentre study. Participants were compared according to different GOLD airflow grades. In addition to the MRC dyspnoea scale, six-minute walking distance test and COPD assessment test (CAT), Barthel dyspnoea index (Bid), and Short Physical Performance Battery (SPPB) were assessed, evaluating the proportion of individuals reaching the minimum clinically important difference (MCID) (responders).

Results: Data of 479 individuals, completing the program were evaluated. Most of the participants were allocated in GOLD grades 4, (57.6%) and 3 (22.1%). All outcome measures significantly improved after PR ($p < 0.05$), without any significant difference in the proportion of responders in any measure.

Conclusions: in individuals with severe COPD, recovering from ECOPD the success rate of PR does not depend on airflow severity, or outcome measure assessed. In addition to the most used outcome measures, also Bid and SPPB are sensitive to PR.

Keywords: Disease impact; Dyspnoea; Exercise capacity; Exercise training; Physical performance.

Conflict of interest statement

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

PLoS One

. 2022 Nov 17;17(11):e0277632.

doi: 10.1371/journal.pone.0277632. eCollection 2022.

Effects of exercise-based home pulmonary rehabilitation on patients with chronic obstructive pulmonary disease: An overview of systematic review

Jiang Zheng[1], Zhi Zhang[2], Ruijuan Han[1], Hongxia Zhang[3], Jie Deng[4], Meimei Chai[3]

Affiliations expand

- PMID: 36395170
- PMCID: PMC9671331
- DOI: 10.1371/journal.pone.0277632

Free PMC article

Abstract

Background: Clinical research on exercise-based home pulmonary rehabilitation (HPR) effectiveness in chronic obstructive pulmonary disease (COPD) treatment is rising, as are associated systematic reviews/meta-analyses (SRs/MAs). However, different SRs/MAs vary in outcome indicators, analysis methodologies, literature quality, and findings. This overview aimed to describe the findings of these SRs/MAs and assess their methodological quality.

Methods: From inception until April 2022, we searched PubMed, Web of Science, Cochrane Library, EMBASE, China National Knowledge Infrastructure (CNKI), and Wan Fang. Two researchers searched these SRs/MAs separately, collected the data, and cross-checked it using predetermined rules. The Assessing the Methodological Quality of Systematic Reviews 2 (AMSTAR 2) was used to evaluate the methodological quality of each contained SR/MA. The evidence was assessed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2009 (PRISMA-2009). The Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) was used to determine the validity of the results.

Results: A total of 433 records were found, with 44 chosen for full-text review. There were 11 SRs/MAs that matched the inclusion criteria. Our overview included studies published from 2010 to 2022. According to the AMSTAR 2 tool, one had low methodological quality, while the other 10 SRs/MAs had very low quality. The PRISMA statement revealed a low rate of complete reporting for eight items. The GRADE tool, on the other hand, revealed that the evidence quality for most outcomes was very low to moderate.

Conclusion: According to current research, exercise-based HPR may benefit COPD patients. Nevertheless, this finding is restricted by the low quality of the included SRs/MAs. And more high-quality and large-sample studies are needed in the future.

Prospero: ID: CRD42022322768. https://www.crd.york.ac.uk/prospero/#recordDetails.

Conflict of interest statement

The authors have declared that no competing interests exist.

- 45 references
- 2 figures

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Eur Heart J Qual Care Clin Outcomes

. 2022 Nov 17;qcac078.

doi: 10.1093/ehjqcco/qcac078. Online ahead of print.

Correspondence to the European Heart Journal-Quality of Care and Clinical Outcomes in response to the paper by

Warming et al. 2022: Atrial fibrillation and chronic obstructive pulmonary disease: diagnostic sequence and mortality risk

Lily Snell[1], Mahmood Ahmad[2], Jin Un Kim[2]

Affiliations expand

- PMID: 36385644

- DOI: 10.1093/ehjqcco/qcac078

No abstract available

Eur Heart J Qual Care Clin Outcomes

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. 2022 Nov 17;qcac079.

doi: 10.1093/ehjqcco/qcac079. Online ahead of print.

Response to the letter to the editor: The association of temporal sequence in atrial fibrillation and chronic

obstructive pulmonary disease diagnosis and mortality risk

Peder Emil Warming[1], Rodrigue Garcia[1,2,3], Carl Johann Hansen[1], Sami Olavi Simons[4], Christian Torp-Pedersen[5,6], Dominik Linz[7,8,9], Jacob Tfelt-Hansen[1,10]

Affiliations expand

- PMID: 36385353

- DOI: 10.1093/ehjqcco/qcac079

No abstract available

J Am Heart Assoc

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. 2022 Nov 16;e025730.

doi: 10.1161/JAHA.122.025730. Online ahead of print.

Do Not Attempt Resuscitation Order Rates in Hospitalized Patients With Heart Failure, Acute Myocardial Infarction, Chronic Obstructive Pulmonary Disease, and Pneumonia

Supriya Shore[1,2], Michael O'Leary[1,2], Neil Kamdar[1,2], Molly Harrod[3], Maria J Silveira[1,4], Scott L Hummel[1,2,3], Brahmajee K Nallamothu[1,2,3]

Affiliations expand

- PMID: 36382963

- DOI: 10.1161/JAHA.122.025730

Free article

Abstract

Background Descriptions of do not attempt resuscitation (DNAR) orders in heart failure (HF) are limited. We describe use of DNAR orders in HF hospitalizations relative to other common conditions, focusing on race. Methods and Results This was a retrospective study of all adult hospitalizations for HF, acute myocardial infarction (AMI), chronic obstructive pulmonary disease (COPD), and pneumonia from 2010 to 2016 using the California State Inpatient Dataset. Using a hierarchical multivariable logistic regression model with random effects for the hospital, we identified factors associated with DNAR orders for each condition. For racial variation, hospitals were divided into quintiles based on proportion of Black patients cared for. Our cohort comprised 399 816 HF, 190 802 AMI, 192 640 COPD, and 269 262 pneumonia hospitalizations. DNAR orders were most prevalent in HF (11.9%), followed by pneumonia (11.1%), COPD (7.9%), and AMI (7.1%). Prevalence of DNAR orders did not change from 2010 to 2016 for each condition. For all conditions, DNAR orders were more common in elderly people, women, and White people with significant site-level variation across 472 hospitals. For HF and COPD, hospitalizations at sites that cared for a higher proportion of Black patients were less likely associated with DNAR orders. For AMI and pneumonia, conditions such as dementia and malignancy were strongly associated with DNAR orders. Conclusions DNAR orders were present in 12% of HF hospitalizations, similar to pneumonia but higher than AMI and COPD. For HF, we noted significant variability across sites when stratified by proportion of Black patients cared for, suggesting geographic and racial differences in end-of-life care.

Keywords: acute myocardial infarction; chronic obstructive pulmonary disease; do not attempt resuscitation; heart failure; pneumonia.

Respir Res

. 2022 Nov 14;23(1):310.

doi: 10.1186/s12931-022-02225-0.

Black carbon content in airway macrophages is associated with increased severe exacerbations and worse COPD morbidity in SPIROMICS

Vickram Tejwani[1,2], Han Woo[3], Chen Liu[3], Anna K Tillery[4], Amanda J Gassett[5], Richard E Kanner[6], Eric A Hoffman[7], Fernando J Martinez[8], Prescott G Woodruff[9], R Graham Barr[10], Ashraf Fawzy[3], Kirsten Koehler[11], Jeffrey L Curtis[12,13], Christine M Freeman[12,13], Christopher B Cooper[14], Alejandro P Comellas[15], Cheryl Pirozzi[16], Robert Paine[16], Donald Tashkin[14], Jerry A Krishnan[17], Coralynn Sack[5], Nirupama Putcha[3], Laura M Paulin[18], Marina Zusman[5], Joel D Kaufman[5], Neil E Alexis[4], Nadia N Hansel[3]

Affiliations expand

- PMID: 36376879

- PMCID: PMC9664618

- DOI: 10.1186/s12931-022-02225-0

Free PMC article

Abstract

Background: Airway macrophages (AM), crucial for the immune response in chronic obstructive pulmonary disease (COPD), are exposed to environmental particulate matter (PM), which they retain in their cytoplasm as black carbon (BC). However, whether AM BC accurately reflects environmental $PM_{2.5}$ exposure, and can serve as a biomarker of COPD outcomes, is unknown.

Methods: We analyzed induced sputum from participants at 7 of 12 sites SPIROMICS sites for AM BC content, which we related to exposures and to lung function and respiratory outcomes. Models were adjusted for batch (first vs. second), age, race (white vs. non-white), income (<$35,000, $35,000~$74,999, ≥$75,000, decline to answer), BMI, and use of long-acting beta-agonist/long-acting muscarinic antagonists, with sensitivity analysis performed with inclusion of urinary cotinine and lung function as covariates.

Results: Of 324 participants, 143 were current smokers and 201 had spirometric-confirmed COPD. Modeled indoor fine (< 2.5 μm in aerodynamic diameter) particulate matter ($PM_{2.5}$) and urinary cotinine were associated with higher AM BC. Other assessed indoor and ambient pollutant exposures were not associated with higher AM BC. Higher AM BC was associated with worse lung function and odds of severe exacerbation, as well as worse functional status, respiratory symptoms and quality of life.

Conclusion: Indoor $PM_{2.5}$ and cigarette smoke exposure may lead to increased AM BC deposition. Black carbon content in AMs is associated with worse COPD morbidity in current and former smokers, which remained after sensitivity analysis adjusting for cigarette smoke burden. Airway macrophage BC, which may alter macrophage function, could serve as a predictor of experiencing worse respiratory symptoms and impaired lung function.

Keywords: Black carbon; COPD; Macrophage.

Conflict of interest statement

There are no competing interests for any author

- 40 references
- 3 figures

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MeSH terms, Substances, Grant supportexpand

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Respir Res

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. 2022 Nov 15;23(1):311.

doi: 10.1186/s12931-022-02237-w.

Increased chest CT derived bone and muscle measures capture markers of improved morbidity and mortality in COPD

Ava C Wilson[1,2], Jessica M Bon[3,4], Stephanie Mason[5], Alejandro A Diaz[5], Sharon M Lutz[5], Raul San Jose Estepar[6], Gregory L Kinney[7], John E Hokanson[7], Stephen I Rennard[8], Richard Casaburi[9], Surya P Bhatt[2], Marguerite R Irvin[1], Craig P Hersh[5,10], Mark T Dransfield[2], George R Washko[5], Elizabeth A Regan[#,11], Merry-Lynn McDonald[#,12,13,14]

Affiliations expand

- PMID: 36376854

- PMCID: PMC9664607

- DOI: 10.1186/s12931-022-02237-w

Free PMC article

Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a disease of accelerated aging and is associated with comorbid conditions including osteoporosis and sarcopenia. These extrapulmonary conditions are highly prevalent yet frequently underdiagnosed and overlooked by pulmonologists in COPD treatment and management. There is evidence supporting a role for bone-muscle crosstalk which may compound osteoporosis and sarcopenia risk in COPD. Chest CT is commonly utilized in COPD management, and we evaluated its utility to identify low bone mineral density (BMD) and reduced pectoralis muscle area (PMA) as surrogates for osteoporosis and sarcopenia. We then tested whether BMD and PMA were associated with morbidity and mortality in COPD.

Methods: BMD and PMA were analyzed from chest CT scans of 8468 COPDGene participants with COPD and controls (smoking and non-smoking). Multivariable regression models tested the relationship of BMD and PMA with measures of function (6-min walk distance (6MWD), handgrip strength) and disease severity (percent emphysema and lung function). Multivariable Cox proportional hazards models were used to evaluate the relationship between sex-specific quartiles of BMD and/or PMA derived from non-smoking controls with all-cause mortality.

Results: COPD subjects had significantly lower BMD and PMA compared with controls. Higher BMD and PMA were associated with increased physical function and less disease severity.

Participants with the highest BMD and PMA quartiles had a significantly reduced mortality risk (36% and 46%) compared to the lowest quartiles.

Conclusions: These findings highlight the potential for CT-derived BMD and PMA to characterize osteoporosis and sarcopenia using equipment available in the pulmonary setting.

Keywords: COPD; Osteoporosis; Sarcopenia; Screening.

Conflict of interest statement

S.P.B. reports personal fees from GlaxoSmithKline and Sunovion, and grants from the NIH (R01HL151421, R21EB027891, and K23HL133438). S.M.L. reports funding from the NIH (R01MH129337). S.M. reports grants from the Chest Foundation. R.S.J.E. reports personal fees from Chiesi, Leuko Labs, Lung Biotechnology, Boehringer Ingelheim, and is a founder and equity holder of Quantitative Imaging Solutions. G.W. reports grants and other support from GlaxcoSmithKline, Novartis, Boehringer Ingelheim, Quantitative Imaging Solutions, PulmonX, Janssen Pharmacueticals, Vertex, and CSL Behring, and the spouse of G.W. is an employee of Biogen. S.I.R. reports personal fees and other support from AstraZeneca, GlaxcoSmithKline, Verona Pharma, NovoVentures, and Bergenbio. C.P.H. reports grants from the NHLBI, Bayer, Boehringer Ingelheim, Novartis, and Vertex, and personal fees from Takeda. M.T.D. reports personal fees and other support from Boehringer Ingelheim, GlaxoSmithKline, AstraZeneca, Gala, Yungjin, PneumRx/BTG, Pulmonx, Boston Scientific, Quark Pharaceuticals, Nuvaira, Teva, CSA Medical, Mereo, and grants from the American Lung Association, Department of Veterans Affairs, and Department of Defense. M.L.M. reports funding from the Parker B. Francis Foundation. A.A.D. reports funding from the NIH (R01HL133137 and R01HL149861). A.C.W., J.M.B, M.R.I, E.R., R.C., and J.E.H. report no conflicts of interest.

Expert Rev Respir Med

. 2022 Nov 16;1-18.

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[3,4], Syed Afroz Keramat[3,5], Jeff Gow[3,6]

Affiliations expand

- PMID: 36350733

- DOI: 10.1080/17476348.2022.2145951

Abstract

Introduction: Evidence from non-randomized 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. Nonetheless, eleven out of the thirteen selected studies were funded by the pharmaceutical industry, and none were conducted in the least developed countries. Therefore, the results should be interpreted with caution.

Keywords: COPD; Cost-effectiveness; multiple inhalers; single inhaler; systematic review.

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Am J Respir Crit Care Med

. 2022 Nov 15;206(10):1201-1207.

doi: 10.1164/rccm.202205-1000PP.

Pharmacotherapy and Mortality in Chronic Obstructive Pulmonary Disease

David M G Halpin[1], Fernando J Martinez[2]

Affiliations expand

- PMID: 35901121

- DOI: 10.1164/rccm.202205-1000PP

No abstract available

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MeSH termsexpand

FULL TEXT LINKS

AJRCCM Final Version

ASTHMA

1
Respir Res

. 2022 Nov 19;23(1):316.

doi: 10.1186/s12931-022-02240-1.

Preclinical development of a long-acting trivalent bispecific nanobody targeting IL-5 for the treatment of eosinophilic asthma

Linlin Ma[#1], Min Zhu[#2], Guanghui Li[#2], Junwei Gai[2], Yanfei Li[1], Huaiyu Gu[2], Peng Qiao[2], Xiaofei Li[2], Weiwei Ji[2], Rui Zhao[3], Yue Wu[1], Yakun Wan[4]

Affiliations expand

- PMID: 36403040

- DOI: 10.1186/s12931-022-02240-1

Abstract

Background: Eosinophilic asthma is a common subtype of severe asthma with high morbidity and mortality. The cytokine IL-5 has been shown to be a key driver of the development and progression of disease. Although approved monoclonal antibodies (mAbs) targeting IL-5/IL-5R have shown good safety and efficacy, some patients have inadequate responses and frequent dosing results in medication nonadherence.

Results: We constructed a novel trivalent bispecific nanobody (Nb) consisting of 3 VHHs that bind to 2 different epitopes of IL-5 and 1 epitope of albumin derived from immunized phage display libraries. This trivalent IL-5-HSA Nb exhibited similar IL-5/IL-5R blocking activities to mepolizumab (Nucala), an approved targeting IL-5 mAb. Surprisingly, this trivalent Nb was 58 times more active than mepolizumab in inhibiting TF-1-cell

proliferation. In primate studies, the trivalent IL-5-HSA Nb showed excellent pharmacokinetic properties, and peripheral blood eosinophil levels remained significantly suppressed for two months after a single dose. In addition, the trivalent IL-5-HSA Nb could be produced on a large scale in a P. pastoris X-33 yeast system with high purity and good thermal stability.

Conclusions: These findings suggest that the trivalent bispecific IL-5-HSA Nb has the potential to be a next-generation therapeutic agent targeting IL-5 for the treatment of severe eosinophilic asthma.

Keywords: Eosinophilic asthma; IL-5; Long-acting; Trivalent nanobody.

- 40 references

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. 2022 Nov 16;S1323-8930(22)00124-1.

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Differential role of mucus plugs in asthma: Effects of smoking and association with airway inflammation

Akira Oguma[1], Kaoruko Shimizu[2], Hirokazu Kimura[1], Naoya Tanabe[3], Susumu Sato[3], Isao Yokota[4], Michiko Takimoto-Sato[1], Machiko Matsumoto-Sasaki[1], Yuki Abe[1], Nozomu

Takei[1], Houman Goudarzi[1], Masaru Suzuki[1], Hironi Makita[5], Toyohiro Hirai[3], Masaharu Nishimura[5], Satoshi Konno[1], Hi-CARAT investigators

Affiliations expand

- PMID: 36402674

- DOI: 10.1016/j.alit.2022.10.007

Abstract

Background: The physiological importance of mucus plugs in computed tomography (CT) imaging is being increasingly recognized. However, whether airway inflammation and smoking affect the association between mucus plugs and clinical-physiological outcomes in asthma remains to be elucidated. The objective of this study is to examine how airway inflammation and/or smoking affect the correlation of CT-based mucus plug scores with exacerbation frequency and airflow limitation indices in asthma.

Methods: A total of 168 patients with asthma who underwent chest CT and sputum evaluation were enrolled and classified in eosinophilic asthma (EA; n = 103) and non-eosinophilic asthma (NEA; n = 65) groups based on sputum eosinophil percentage (cut-off: 3%). The mucus plug score was defined as the number of lung segments with mucus plugs seen on CT.

Results: More mucus plugs were detected on CT scans in the EA group than in the NEA group, regardless of smoking status. Mucus plug score and exacerbation frequency during one year after enrollment were significantly associated in the EA group but not in the NEA group after adjusting for demographics, blood eosinophil count, and fractional exhaled nitric oxide. Mucus plug score was associated with percentage of predicted forced expiratory volume in 1 s in non-smoking individuals in the EA and NEA group and in smoking individuals in the EA group but not in the NEA group after adjusting for demographics.

Conclusions: The association of mucus plug score with exacerbation frequency and reduced lung function may vary due to airway inflammatory profile and smoking status in asthma.

Keywords: Airflow limitation; Eosinophilic asthma; Exacerbation; Mucus plug; Smoking.

Eur Arch Otorhinolaryngol

. 2022 Nov 18.

doi: 10.1007/s00405-022-07746-4. Online ahead of print.

Diagnostic value of serum and tissue eosinophil in diagnosis of asthma among patients with chronic rhinosinusitis

Che Mohd Hilmi Che Mat[1,2], Norasnieda Md Shukri[3], Sakinah Mohamad[1], Sharifah Emilia Tuan Sharif[4], Rosdi Ramli[2], Murni Hartini Jais[5], Mat Zuki Mat Jaeb[6], Najib Majdi Yaacob[7], Mohd Yusran Yusoff[8], Siti Muhamad Nur Husna[9], Baharudin Abdullah[1]

Affiliations expand

- PMID: 36401099

- DOI: 10.1007/s00405-022-07746-4

Abstract

Background: Chronic rhinosinusitis (CRS) is one of the most common chronic inflammatory diseases of sinonasal mucosa. Asthma among CRS patients is often underdiagnosed which makes the management of CRS more challenging. Therefore, using serum and tissue eosinophil as an indicator and predictor of asthma in CRS patients is vital for further preventing recurrent and increasing the effectiveness of treatment for CRS.

Objective: To determine the association and diagnostic ability of serum and tissue eosinophils in the diagnosis of asthma among CRS patients.

Methods: A cross-sectional study was conducted involving 24 CRS patients with asthma and without asthma, respectively, from the Otorhinolaryngology clinic of two tertiary

hospitals located on the East Coast of Peninsular Malaysia. Serum and tissue eosinophils (obtained from nasal polyp) levels between both groups were compared. Association between serum and tissue eosinophils with asthma was evaluated using logistic regression analysis, adjusting for important sociodemographic characteristics. The diagnostic ability of serum and tissue eosinophil was then evaluated by assessing the receiver operating characteristic curve.

Results: A total of 48 CRS patients with a mean [SD] age of 47.50 [14.99] years were included. Patients with asthma had significantly higher serum [0.48 vs 0.35 × 10^9/L] and tissue eosinophil [100 vs 8.5 per HPF] levels. Tissue eosinophils were found to be an independent predictor of asthma with adjusted OR 1.05, $p < 0.001$, after adjusting for age and serum eosinophils. The area under the receiver operating characteristic curve for serum eosinophil was 69.0%. At optimal cut-off value (0.375 × 10^9/L), the sensitivity and specificity for serum eosinophil was 75.0% and 70.8%. The area under the receiver operating characteristic curve for tissue eosinophil was 93.4%. At the optimal cut-off value (58.0 per HPF), the sensitivity and specificity for tissue eosinophils were 79.2% and 91.7%, respectively.

Conclusion: This study indicates a significantly higher level of serum and tissue eosinophils in CRS with asthma. However, there was no correlation between serum and tissue eosinophils in both group. Based on this study, the CRS patient needs to be screened for asthma if the level of serum eosinophil is > 0.375 × 10^9/L and tissue eosinophil > 58 per HPF.

Keywords: Asthma; Chronic rhinosinusitis; Endoscopic; Nasal polyp; Serum eosinophil; Tissue eosinophil.

- 36 references

SUPPLEMENTARY INFO

Grant supportexpand

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BMJ Open

. 2022 Nov 18;12(11):e062222.

doi: 10.1136/bmjopen-2022-062222.

Chronic non-communicable diseases: Hainan prospective cohort study

Xingbo Gu[#1], Liuting Lin[#2,3], Chanjuan Zhao[1], Ling Wu[1], Yumei Liu[2], Limin He[2], Guotian Lin[2], Yingzi Lin[4], Fan Zhang[4]

Affiliations expand

- PMID: 36400728

- DOI: 10.1136/bmjopen-2022-062222

Abstract

Purpose: The Hainan Cohort was established to investigate the incidence, morbidity and mortality of non-communicable diseases and their risk factors in the community population.

Participants: The baseline investigation of the Hainan Cohort study was initiated in five main areas of Hainan, China, from June 2018 to October 2020. A multistage cluster random-sampling method was used to obtain samples from the general population. Baseline assessments included a questionnaire survey, physical examination, blood and urine sample collection, and laboratory measurements, and outdoor environmental data were obtained.

Findings to data: A total of 14 443 participants aged 35-74 years were recruited at baseline, with a participation rate of 90.1%. The mean age of the participants was 48.8 years; 51.8% were men, and 83.7% had a secondary school or higher education. The crude prevalence of diabetes, coronary heart disease, stroke, hypertension, hyperuricaemia, chronic bronchitis, pulmonary tuberculosis, asthma, cancer, chronic hepatitis and metabolic syndrome were 8.6%, 9.2%, 2.0%, 37.1%, 7.1%, 2.3%, 1.4%, 2.1%, 4.1%, 2.2% and 14.5%, respectively.

Future plans: The Hainan Cohort is a dynamic cohort with no end date. All participants will be monitored annually for cause-specific mortality and morbidity until death. Long-term

follow-up will be conducted every 5 years. The baseline population is considered to expand in the next wave of follow-up, depending on the availability of funding support.

Keywords: EPIDEMIOLOGY; PREVENTIVE MEDICINE; PUBLIC HEALTH.

Conflict of interest statement

Competing interests: None declared.

Editorial

Thorax

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. 2022 Nov 18;thorax-2022-219459.

doi: 10.1136/thorax-2022-219459. Online ahead of print.

Leveraging genetic ancestry to study severe asthma exacerbations in an admixed population

Yadu Gautam [1], Tesfaye B Mersha [2]

Affiliations expand

- PMID: 36400457

- DOI: 10.1136/thorax-2022-219459

No abstract available

Keywords: Asthma; Asthma Genetics.

Conflict of interest statement

Competing interests: None declared.

SUPPLEMENTARY INFO

Publication typesexpand

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Ann Allergy Asthma Immunol

. 2022 Nov 15;S1081-1206(22)01917-2.

doi: 10.1016/j.anai.2022.11.011. Online ahead of print.

User-centered mobile health applications for asthma

Sara L Hantgan[1], Sunit P Jariwala[2]

Affiliations expand

- PMID: 36400353
- PMCID: PMC9663378
- DOI: 10.1016/j.anai.2022.11.011

Free PMC article

No abstract available

Conflict of interest statement

Conflict of Interest Dr.Jariwala has received grant support from the NIH, AHRQ, Stony Wold-Herbert Fund, PCORI, American Lung Association, Price Family Fund, Genentech, AstraZeneca, Sonde Health, and Einstein CTSA/National Center for Advancing Translational Sciences; and has served as a consultant and/or member of a scientific advisory board for Teva and Sanofi.

- 1 figure

J Allergy Clin Immunol

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. 2022 Nov 15;S0091-6749(22)01510-X.

doi: 10.1016/j.jaci.2022.10.028. Online ahead of print.

Eosinophil depletion with benralizumab is associated with attenuated mannitol airway hyperresponsiveness in severe uncontrolled eosinophilic asthma

Rory Chan [1], Chris RuiWen Kuo [1], Sunny Jabbal [1], Brian Lipworth [2]

Affiliations expand

- PMID: 36400178

- DOI: 10.1016/j.jaci.2022.10.028

Abstract

Background: Airway hyperresponsiveness (AHR) and eosinophilia are hallmarks of persistent asthma.

Objective: We investigated whether eosinophil depletion with benralizumab (Benra) might attenuate indirect mannitol AHR in severe uncontrolled asthma using a pragmatic open label design.

Methods: After a 4-week run-in period on usual ICS/LABA (baseline), adults with mannitol responsive uncontrolled severe eosinophilic asthma received 3 doses of open label Benra 30mg every 4 weeks followed by 16 weeks washout after the last dose. The primary outcome was doubling difference (DD) in mannitol PD_{10} at end point after 12 weeks, powered at 90% with n=18 patients required to detect 1 DD. Secondary outcomes included asthma control questionnaire (ACQ) and mini asthma quality of life questionnaire (mini-AQLQ).

Results: 21 patients completed 12 weeks with Benra at end point at week 12. Mean (SEM) age was 53 (4) years, FEV_1 80.2 (4.1) %, ICS dose 1895 (59)µg, n=12 on LAMA, n=13 on LTRA. Improvement in AHR was significant by 8 weeks with a mean 2.1 DD (95%CI 1.0, 3.3; $p<0.01$) change in PD_{10} at week 12, while mean changes in ACQ and mini-AQLQ were significant by week 2 and sustained over 12 weeks both exceeding the minimal important difference. Peripheral blood eosinophils were depleted by 2 weeks (439 to 6 cells/µl). No significant improvements occurred in lung function after 12 weeks. Domiciliary peak flow and symptoms were also improved with Benra.

Conclusion: Eosinophil depletion results in clinically meaningful attenuated AHR in severe uncontrolled asthma patients.

Keywords: airway hyperresponsiveness; asthma control; benralizumab; mannitol; quality of life; severe asthma.

J Allergy Clin Immunol

. 2022 Nov 15;S0091-6749(22)01513-5.

doi: 10.1016/j.jaci.2022.10.031. Online ahead of print.

Do upper respiratory viruses contribute to racial and ethnic disparities in emergency department visits for asthma?

Darlene Bhavnani[1], Matthew Wilkinson[2], Rebecca A Zárate[3], Susan Balcer-Whaley[3], Daniel S W Katz[3], Paul J Rathouz[3], Elizabeth C Matsui[3]

Affiliations expand

- PMID: 36400176

- DOI: 10.1016/j.jaci.2022.10.031

Abstract

Background: There are marked disparities in asthma-related emergency department (ED) visit rates among children by race and ethnicity. Following the implementation of COVID-19 prevention measures, asthma-related ED visits rates declined substantially. The decline has been attributed to the reduced circulation of upper respiratory viruses, a common trigger of asthma exacerbations in children.

Objectives: To better understand the contribution of respiratory viruses to racial and ethnic disparities in ED visit rates, we investigated whether the reduction in ED visit rates affected Black, Latinx and White children with asthma equally.

Methods: Asthma-related ED visits were extracted from electronic medical records at Dell Children's Medical Center (DCMC) in Travis County, Texas. ED visit rates among children with asthma were derived by race/ethnicity. Incidence rate ratios (IRRs) and 95% confidence intervals (95% CI) were estimated by year (2019-2021) and season.

Results: In Spring of 2019, ED visit IRRs comparing Black to White children and Latinx to White children were 6.67 (95% CI = 4.92-9.05) and 2.10 (95% CI = 1.57-2.80), respectively. In Spring of 2020, when infection prevention measures were implemented, corresponding IRRs decreased to 1.73 (95% CI = 0.90-3.32) and 0.68 (95% CI = 0.38-1.23), respectively.

Discussion: The striking reduction of disparities in ED visits suggests that respiratory viruses contribute to the excess burden of asthma-related ED visits among Black and Latinx children with asthma during non-pandemic periods. While further investigation is needed to test this hypothesis, this finding raises the question of whether Black and Latinx children with asthma are more vulnerable to upper respiratory viral infections.

Am J Respir Crit Care Med

. 2022 Nov 18.

doi: 10.1164/rccm.202111-2634OC. Online ahead of print.

Heterogeneity of Airway Smooth Muscle Remodelling in Asthma

Alan L James[1,2], Graham M Donovan[3], Francis H Y Green[4], Thais Mauad[5], Michael J Abramson[6], Alvenia Cairncross[7], Peter B Noble[8], John G Elliot[9]

Affiliations expand

- PMID: 36399661

- DOI: 10.1164/rccm.202111-2634OC

Abstract

Rationale: Ventilatory defects in asthma are heterogeneous and may represent the distribution of airway smooth muscle (ASM) remodelling.

Objectives: To determine the distribution of ASM remodelling in mild-severe asthma.

Methods: The ASM area was measured in 9 airway levels in 3 bronchial pathways in cases of nonfatal (n=30) and fatal asthma (n=20) and compared with controls without asthma (n=30). Correlations of ASM area within and between bronchial pathways were calculated. Asthma cases with 12 large and 12 small airways available (n=42) were classified based on the presence or absence of ASM remodelling (>2SD of mean ASM area of controls n=86) in the large or small airways or both.

Main measurements and results: ASM remodelling varied widely within and between cases of nonfatal asthma and was more widespread and confluent, and more marked, in fatal cases. There were weak correlations of ASM between levels within the same or separate bronchial pathways however, predictable patterns of remodelling were not observed. Using mean data, 44% of all asthma cases were classified as having no ASM remodelling in either the large or small airways, despite a 3-10 fold increase in the number of airways with ASM remodelling and 81% of asthma cases having ASM remodelling in at least 1 large and small airway.

Conclusion: ASM remodelling is related to asthma severity but is heterogenous within and between individuals and may contribute to the heterogenous functional defects observed in asthma. These findings support the need for patient-specific targeting of ASM remodelling.

Keywords: Airway remodeling; Airway smooth muscle; Asthma.

Editorial

Eur Respir J

. 2022 Nov 17;60(5):2201639.

doi: 10.1183/13993003.01639-2022. Print 2022 Nov.

Randomised controlled trials utilising F_{ENO} to manage asthma: is it time to acknowledge that "one size does not fit all"?

Helen Petsky[1]

Affiliations expand

- PMID: 36396158

- DOI: 10.1183/13993003.01639-2022

No abstract available

Conflict of interest statement

Conflict of interest: H. Petsky reports grants from the Children's Hospital Foundation and Asthma Australia.

Comment on

- Effect of asthma management with exhaled nitric oxide *versus* usual care on perinatal outcomes.

Murphy VE, Jensen ME, Holliday EG, Giles WB, Barrett HL, Callaway LK, Bisits A, Peek MJ, Seeho SK, Abbott A, Robijn AL, Colditz PB, Searles A, Attia J, McCaffery K, Hensley MJ, Mattes J, Gibson PG.Eur Respir J. 2022 Nov 17;60(5):2200298. doi: 10.1183/13993003.00298-2022. Print 2022 Nov.PMID: 35777773 **Free PMC article.**

SUPPLEMENTARY INFO

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Editorial

Eur Respir J

. 2022 Nov 17;60(5):2201686.

doi: 10.1183/13993003.01686-2022. Print 2022 Nov.

Is it time to consider allergen immunotherapy earlier in the management of allergic asthma?

Graham Roberts[1][2][3]

Affiliations expand

- PMID: 36396157

- DOI: 10.1183/13993003.01686-2022

No abstract available

Conflict of interest statement

Conflict of interest: G. Roberts reports grants, advisory board consulting fees and lecture honoraria from ALK-Abello, and data safety board participation with Merck, outside the submitted work; and is president of the British Society of Allergy and Clinical Immunology.

Comment on

- Allergen immunotherapy effectively reduces the risk of exacerbations and lower respiratory tract infections in both seasonal and perennial allergic asthma: a nationwide epidemiological study.
  Woehlk C, Von Bülow A, Ghanizada M, Søndergaard MB, Hansen S, Porsbjerg C.Eur Respir J. 2022 Nov 17;60(5):2200446. doi: 10.1183/13993003.00446-2022. Print 2022 Nov.PMID: 35618279

Eur Respir J

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. 2022 Nov 17;2201194.

doi: 10.1183/13993003.01194-2022. Online ahead of print.

Airway inflammation and hyperresponsiveness in subjects with respiratory symptoms and normal spirometry

Louis-Philippe Boulet[1], Marie-Ève Boulay[2], Andréanne Côté[2], J Mark FitzGerald[3], Céline Bergeron[3], Catherine Lemière[4], M Diane Lougheed[5], Katherine L Vandemheen[6], Shawn D Aaron[6]

Affiliations expand

- PMID: 36396140

- DOI: 10.1183/13993003.01194-2022

Abstract

Background: Subjects without a previous history of asthma, presenting with unexplained respiratory symptoms and normal spirometry, may exhibit airway hyperresponsiveness in association with underlying eosinophilic (T2) inflammation, consistent with undiagnosed asthma. However, the prevalence of undiagnosed asthma in these subjects is unknown.

Methods: In this observational study, inhaled corticosteroid-naïve adults without previously diagnosed lung disease reporting current respiratory symptoms and showing normal pre and post bronchodilator spirometry underwent FeNO measurement, methacholine challenge test, and induced sputum analysis. Airway hyperresponsiveness was defined as a provocative concentration of methacholine inducing a 20% fall in forced expiratory volume in one second (PC_{20}) <16 mg·mL^{-1}, and T2 inflammation was defined as sputum eosinophils >2% and/or FeNO >25 ppb.

Results: Out of 132 subjects (mean age±sd: 57.6±14.2 years, 52% women), 47 (36%; 95%CI: 28%-44%) showed airway hyperresponsiveness; 20 (15%; 9%-21%) with PC_{20} <4 mg·mL^{-1} and 27 (21%; 14%-28%) with PC_{20} 4-15.9 mg·mL^{-1}. Of 130 participants for whom sputum eosinophils, FeNO or both results were obtained, 45 (35%; 27%-43%) had T2 inflammation. Fourteen participants (11%; 6%-16%) had sputum eosinophils >2% and a PC_{20} ≥16 mg·mL^{-1}, suggesting eosinophilic bronchitis. The prevalence of T2 inflammation was significantly higher in subjects with a PC_{20} <4 mg·mL^{-1} (60%) than in those with a PC_{20} 4-16 mg·mL^{-1} (30%) or PC_{20} >16 mg·mL^{-1} ((29%), p=0.01).

Conclusions: Asthma, underlying T2 airway inflammation and eosinophilic bronchitis may remain undiagnosed in a high proportion of symptomatic subjects in the community who have normal pre- and post-bronchodilator spirometry.

Contemp Clin Trials

. 2022 Nov 14;107011.

doi: 10.1016/j.cct.2022.107011. Online ahead of print.

AIM2ACT: Randomized controlled trial protocol for a mobile health intervention for early adolescents with asthma

David A Fedele[1], J Graham Thomas[2], Elizabeth L McQuaid[2], Matthew Gurka[3], Cynthia A Berg[4], Sreekala Prabhakaran[3]

Affiliations expand

- PMID: 36396068

- DOI: 10.1016/j.cct.2022.107011

Abstract

Early adolescents diagnosed with asthma have difficulties consistently performing disease self-management behaviors, placing them at-risk for poor asthma control, morbidity, and reduced quality of life. Helpful caregiver support is pivotal in determining whether early adolescents develop and master asthma self-management behaviors. We developed Applying Interactive Mobile health to Asthma Care in Teens (AIM2ACT), a mobile health intervention to facilitate helpful caregiver support in early adolescents (12-15 year-olds) with poorly controlled asthma. AIM2ACT is a dyadic smartphone intervention that contains three components: 1) ecological momentary assessment to identify personalized strengths and weaknesses in asthma self-management behaviors; 2) collaborative identification and tracking of goals that help early adolescents to become increasingly independent in managing their asthma; and 3) a suite of skills training videos. This paper describes our plans to test the efficacy of AIM2ACT and evaluate long-term maintenance of treatment effects in a fully powered randomized controlled trial with 160 early adolescents with poorly controlled persistent asthma, ages 12-15 years, and a caregiver. Families will be randomly assigned to receive AIM2ACT (n = 80) or a mHealth attention control condition (n = 80) that accounts for attention and novelty of a technology-based intervention for 6 months. Assessments will occur at baseline, post-intervention, and 3-, 6-, and 12-month follow-up time points. We will collect patient-reported and objectively monitored (e.g., spirometry, adherence) outcomes. Given the timing of the trial, a secondary exploratory goal is to evaluate the perceived impact of COVID-19 on family functioning and parental control of their adolescent's asthma in the context of our intervention.

Keywords: Adolescent; Asthma; Mobile health; Mobile phone; Self-management.

. 2022 Nov 14;S0091-6749(22)01515-9.

doi: 10.1016/j.jaci.2022.08.032. Online ahead of print.

Indoor environmental exposures and obstructive lung disease phenotypes among asthmatic children living in poor, urban neighborhoods

Torie Grant, Travis Lilley, Meredith C McCormack, Paul J Rathouz, Roger Peng, Corinne A Keet, Ana Rule, Meghan Davis, Susan Balcer-Whaley, Michelle Newman, Elizabeth C Matsui

- PMID: 36395986

- DOI: 10.1016/j.jaci.2022.08.032

Abstract

Background: Air trapping is an obstructive phenotype that has been associated with more severe and unstable asthma in children. Recently, air trapping has been defined using pre- and post-bronchodilator spirometry. The causes of air trapping are not completely understood. It is possible that environmental exposures could be implicated in air trapping in asthmatic children.

Objective: To investigate the association between indoor exposures and air trapping in urban children with asthma.

Methods: Children with asthma ages 5-17 years living in Baltimore enrolled in the Environmental Control as Add-on Therapy for Childhood Asthma study were evaluated for air trapping using spirometry. Aeroallergen sensitization was assessed at baseline and spirometry was performed at 0, 3, and 6 months. Air trapping was defined as a force vital capacity (FVC) z-score <-1.64 or a change in FVC with bronchodilation of ≥10 %predicted. Logistic normal random effects models were used to evaluate associations of air trapping and indoor exposures.

Results: Airborne and bedroom floor mouse allergen concentrations were associated with air trapping, but not airflow limitation: OR 1.19 (1.02-1.37), p=0.02 per 2-fold increase in airborne mouse allergen, OR 1.23 (1.07-1.41), p=0.003 per 2-fold increase in bedroom floor mouse allergen. Other indoor exposures (cockroach, cat, dog, dust mite, PM, nicotine) were not associated with air trapping or airflow limitation.

Conclusion: Mouse allergen exposure, but not other indoor exposures, was associated with air trapping in urban children with asthma.

Clinical implication: Mouse allergen exposure may contribute to the excess asthma burden in urban populations via air trapping.

Keywords: Air trapping; Indoor environmental exposures; Mouse allergen exposure; Pediatric asthma; Urban asthma.

Chest

. 2022 Nov 14;S0012-3692(22)04077-6.

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Bronchodilator Responsiveness in Tobacco-Exposed Persons with or without COPD

Spyridon Fortis[1], Pedro M Quibrera[2], Alejandro P Comellas[3], Surya P Bhatt[4], Donald P Tashkin[5], Eric A Hoffman[6], Gerard J Criner[7], MeiLan K Han[8], R Graham Barr[9], Mehrdad Arjomandi[10], Mark B Dransfield[11], Stephen P Peters[12], Brett A Dolezal[5], Victor Kim[7], Nirupama Putcha[13], Stephen I Rennard[14], Robert Paine 3rd[15], Richard E Kanner[15], Jeffrey L Curtis[16], Russell P Bowler[17], Fernando J Martinez[18], Nadia N Hansel[13], Jerry A Krishnan[19], Prescott G Woodruff[20], Igor Z Barjaktarevic[5], David Couper[2], Wayne H Anderson[21], Christopher B Cooper[5]

Affiliations expand

- PMID: 36395858

- DOI: 10.1016/j.chest.2022.11.009

Abstract

Background: Bronchodilator responsiveness (BDR), in obstructive lung disease varies over time and may be associated with distinct clinical features.

Research question: Is consistent BDR over time (always present) differentially associated with obstructive lung disease features relative to inconsistent (sometimes present) or never (never present) BDR in tobacco-exposed people with or without COPD.

Study design and methods: We retrospectively analyzed data of 2,269 tobacco-exposed participants in SPIROMICS with or without COPD. We used various BDR definitions: change ≥200ml and ≥12% in FEV_1 (FEV_1-BDR), in FVC (FVC-BDR), and in FEV_1 and/or FVC (ATS-BDR). Using generalized linear models adjusted for demographics, smoking history, post-bronchodilator FEV_1 %predicted, and number of visits that the participant completed, we assess the association of BDR group: i) consistent BDR, ii) inconsistent BDR, and iii) never BDR with asthma, CT features, blood eosinophils, and FEV_1 decline in participants without COPD (GOLD0) and the entire cohort (participants with or without COPD).

Results: Both consistent and inconsistent ATS-BDR were associated with asthma history and greater small airway disease ($\%PRM^{fSAD}$) relative to never ATS-BDR in GOLD0 participants and the entire cohort. We observed similar findings using FEV_1-BDR and FVC-BDR definitions. Eosinophils did not consistently vary between BDR groups. Consistent BDR was associated with FEV1 decline over time relative to never BDR in the entire cohort. In GOLD0, both inconsistent (OR=3.20;95%CI 2.21 to 4.66;P<0.001) and consistent ATS-BDR group (OR=9.48;95%CI 3.77 to 29.12;P<0.001) were associated with progression to COPD relative to never ATS-BDR group.

Interpretation: Demonstration of BDR, even once, describes an obstructive lung disease phenotype with history of asthma, and greater small airway disease. Consistent demonstration of BDR indicates a high risk for lung function decline over time in the entire cohort and was associated with higher risk for progression to COPD in GOLD0.

Keywords: COPD; bronchodilator; bronchodilator response; bronchodilator responsiveness; bronchodilator reversibility.

BMJ

. 2022 Nov 16;379:e071932.

doi: 10.1136/bmj-2022-071932.

Comparative effectiveness of sotrovimab and molnupiravir for prevention of severe covid-19 outcomes in patients in the community: observational cohort study with the OpenSAFELY platform

Bang Zheng[1], Amelia C A Green[2], John Tazare[1], Helen J Curtis[2], Louis Fisher[2], Linda Nab[2], Anna Schultze[1], Viyaasan Mahalingasivam[1], Edward P K Parker[1], William J Hulme[2], Sebastian C J Bacon[2], Nicholas J DeVito[2], Christopher Bates[3], David Evans[2], Peter Inglesby[2], Henry Drysdale[2], Simon Davy[2], Jonathan Cockburn[3], Caroline E Morton[2], George Hickman[2], Tom Ward[2], Rebecca M Smith[2], John Parry[3], Frank Hester[3], Sam Harper[3], Amir Mehrkar[2], Rosalind M Eggo[1], Alex J Walker[2], Stephen J W Evans[1], Ian J Douglas[1], Brian MacKenna[2], Ben Goldacre[2], Laurie A Tomlinson[1]

Affiliations expand

- PMID: 36384890

- PMCID: PMC9667468

- DOI: 10.1136/bmj-2022-071932

Free PMC article

Abstract

Objective: To compare the effectiveness of sotrovimab (a neutralising monoclonal antibody) with molnupiravir (an antiviral) in preventing severe outcomes of covid-19 in adult patients infected with SARS-CoV-2 in the community and at high risk of severe outcomes from covid-19.

Design: Observational cohort study with the OpenSAFELY platform.

Setting: With the approval of NHS England, a real world cohort study was conducted with the OpenSAFELY-TPP platform (a secure, transparent, open source software platform for analysis of NHS electronic health records), and patient level electronic health record data were obtained from 24 million people registered with a general practice in England that uses TPP software. The primary care data were securely linked with data on SARS-CoV-2 infection and treatments, hospital admission, and death, over a period when both drug treatments were frequently prescribed in community settings.

Participants: Adult patients with covid-19 in the community at high risk of severe outcomes from covid-19, treated with sotrovimab or molnupiravir from 16 December 2021.

Interventions: Sotrovimab or molnupiravir given in the community by covid-19 medicine delivery units.

Main outcome measures: Admission to hospital with covid-19 (ie, with covid-19 as the primary diagnosis) or death from covid-19 (ie, with covid-19 as the underlying or contributing cause of death) within 28 days of the start of treatment.

Results: Between 16 December 2021 and 10 February 2022, 3331 and 2689 patients were treated with sotrovimab and molnupiravir, respectively, with no substantial differences in baseline characteristics. Mean age of all 6020 patients was 52 (standard deviation 16) years; 59% were women, 89% were white, and 88% had received three or more covid-19 vaccinations. Within 28 days of the start of treatment, 87 (1.4%) patients were admitted to hospital or died of infection from SARS-CoV-2 (32 treated with sotrovimab and 55 with molnupiravir). Cox proportional hazards models stratified by area showed that after adjusting for demographic information, high risk cohort categories, vaccination status, calendar time, body mass index, and other comorbidities, treatment with sotrovimab was associated with a substantially lower risk than treatment with molnupiravir (hazard ratio 0.54, 95% confidence interval 0.33 to 0.88, P=0.01). Consistent results were found from propensity score weighted Cox models (0.50, 0.31 to 0.81, P=0.005) and when restricted to

people who were fully vaccinated (0.53, 0.31 to 0.90, P=0.02). No substantial effect modifications by other characteristics were detected (all P values for interaction >0.10). The findings were similar in an exploratory analysis of patients treated between 16 February and 1 May 2022 when omicron BA.2 was the predominant variant in England.

Conclusions: In routine care of adult patients in England with covid-19 in the community, at high risk of severe outcomes from covid-19, those who received sotrovimab were at lower risk of severe outcomes of covid-19 than those treated with molnupiravir.

Conflict of interest statement

Competing interests: All authors have completed the ICMJE uniform disclosure form at https://www.icmje.org/disclosure-of-interest/ and declare: support from UK Research and Innovation (UKRI), National Institute for Health Research (NIHR), and Asthma UK-British Lung Foundation (BLF) for the submitted work; BG has received research funding from the Laura and John Arnold Foundation, NHS NIHR, NIHR School of Primary Care Research, NHS England, NIHR Oxford Biomedical Research Centre, Mohn-Westlake Foundation, NIHR Applied Research Collaboration Oxford and Thames Valley, Wellcome Trust, Good Thinking Foundation, Health Data Research UK, Health Foundation, World Health Organization, UKRI MRC, Asthma UK, British Lung Foundation, and Longitudinal Health and Wellbeing strand of the National Core Studies programme; BG is a non-executive director at NHS Digital; BG also receives personal income from speaking and writing for lay audiences on the misuse of science; IJD has received unrestricted research grants and holds shares in GlaxoSmithKline (GSK); LAT has received funding from Medical Research Council (MRC), Wellcome, NIHR, consulted for Bayer in relation to an observational study of chronic kidney disease (unpaid), and is a member of four non-industry funded (NIHR/MRC) trial advisory committees (unpaid) and Medicines and Healthcare products Regulatory Agency (MHRA) expert advisory group (Women's Health); NJD has received funding for covid meta-research from the Federal Ministry of Education and Research (BMBF, Germany); JT is funded at the London School of Hygiene and Tropical Medicine (LSHTM) through an unrestricted grant from GSK; AM was a former employee and interim chief medical officer of NHS Digital and is a member of Royal College of General Practitioners (RCGP) health informatics group and the NHS Digital GP data Professional Advisory Group; AS is employed by LSHTM on a fellowship sponsored by GSK; VM has received funding from National Institute for Health and Care Research (NIHR301535); RME has received funding from HDR UK (MR/S003975/1); no other relationships or activities that could appear to have influenced the submitted work.

- 30 references
- 2 figures

Review

Eur Respir Rev

. 2022 Nov 15;31(166):220094.

doi: 10.1183/16000617.0094-2022. Print 2022 Dec 31.

The role of gene–ambient air pollution interactions in paediatric asthma

Jelte Kelchtermans[1 2 3], Hakon Hakonarson[4 2 3]

Affiliations expand

- PMID: 36384702

- DOI: 10.1183/16000617.0094-2022

Free article

Abstract

Globally, asthma prevention and treatment remain a challenge. Ambient air pollution (AAP) is an environmental risk factor of special interest in asthma research. AAP is poorly defined and has been subdivided either by the origin of the air pollution or by the specific bioactive compounds. The link between AAP exposure and asthma exacerbations is well established and has been extensively reviewed. In this narrative review, we discuss the specific genetic variants that have been associated with increased AAP sensitivity and

impact in paediatric asthma. We highlight the relative importance of variants associated with genes with a role in oxidant defences and the nuclear factor-κB pathway supporting a potential central role for these pathways in AAP sensitivity.

Conflict of interest statement

Conflict of interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

SUPPLEMENTARY INFO

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Pneumologie

. 2022 Nov 16.

doi: 10.1055/a-1956-8800. Online ahead of print.

Impact of short-term pausing of oral corticosteroids on blood eosinophil count in patients with severe asthma

Leonie Biener[1], Katrin Milger[2,3], Hendrik Suhling[4], Stephanie Korn[5,6], Carmen Pizarro[1], Dirk Skowasch[1]

Affiliations expand

- PMID: 36384226

- DOI: 10.1055/a-1956-8800

Abstract

in English, German

Background: The peripheral blood eosinophil count (BEC) is a well-established and easily accessible biomarker for asthma patients and crucial for the therapeutic decision regarding monoclonal antibody (mAB) therapy. Oral corticosteroid therapy frequently hinders the correct evaluation of BEC in patients with severe asthma, but a discontinuation of such therapy frequently comes along with severe side effects. Therefore, we examined the effect of a short 24-hour pause of OCS treatment on BEC in patients with severe asthma and followed-up whether patients with a then increased eosinophil count benefited from mAB-therapy, as expected.

Methods: In this multicentre study we retrospectively included 24 patients with severe asthma and OCS therapy and determined their BEC count. Ten patients, where BEC count was obtained in the morning before taking medication (a de-facto 24-hour OCS pause), were assigned to group 1. Fourteen patients, where BEC was obtained after OCS tapering were assigned to group 2. Those who then received mAB treatment were followed up for treatment response (OCS dose, annual acute exacerbations, increase in forced expiratory volume in one second [FEV_1] and asthma control test [ACT]) after ≥3 months.

Results: We included 24 patients with a median age of 60.5 [IQR: 17.3] years. Regarding all baseline characteristics except FEV_1 (l), both groups did not differ significantly.Among all 24 patients, after pausing OCS therapy for 2 [5.5] days the BEC increased significantly from 125.0/µl [125] to 300/µl [232.5] ($p<0.001$). In both individual groups BEC increased significantly as well (150 [123] to 325 [305], $p=0.005$ and 70 [150] to 280 [255], $p<0.001$), with no significant difference for increase (BEC +170/µl [205.0] vs. +195 [222.5], $p=0.886$). Of all 24 patients, 13 (54.2%) reached eosinophil levels ≥300/µl, while 12 of them had not exceeded this threshold before.Subsequently, 20 patients (83.3%) received mAB-therapy with 55.5% demonstrating a good treatment response within 6 [1.5] months. The response rate in patients with BEC count ≥300/µl was even higher (75.0%). There was no difference in the treatment response rate between group 1 and 2 ($p=0.092$).

Conclusion: After just a short 24-hour pause of OCS therapy it was possible to demask a relevant eosinophilia in asthma patients, without risking severe side effects. In this manner, we enabled the possibility of achieving successful targeted mAB-therapy, according to the patient's individual asthma phenotype.

Conflict of interest statement

The authors declare that they have no conflict of interest.

J Allergy Clin Immunol Pract

. 2022 Nov 13;S2213-2198(22)01193-X.

doi: 10.1016/j.jaip.2022.10.047. Online ahead of print.

Switch patterns in a cohort of individuals with asthma who received omalizumab or mepolizumab therapy

Ayobami Akenroye[1], Tessa Ryan[2], Alanna McGill[2], Guohai Zhou[3], Jerome Shier[4], Jodi Segal[5]

Affiliations expand

- PMID: 36384205

- DOI: 10.1016/j.jaip.2022.10.047

No abstract available

Keywords: asthma; biologics; discontinuations; effectiveness; mepolizumab; omalizumab; safety; switches; utilization.

Sci Transl Med

. 2022 Nov 16;14(671):eabl5849.

doi: 10.1126/scitranslmed.abl5849. Epub 2022 Nov 16.

Visualization of exhaled breath metabolites reveals distinct diagnostic signatures for acute cardiorespiratory breathlessness

Wadah Ibrahim[1], Michael J Wilde[2 3], Rebecca L Cordell[2], Matthew Richardson[1], Dahlia Salman[4], Robert C Free[1], Bo Zhao[5 6], Amisha Singapuri[1], Beverley Hargadon[1], Erol A Gaillard[1], Toru Suzuki[7 8], Leong L Ng[7], Tim Coats[9], Paul Thomas[4], Paul S Monks[2], Christopher E Brightling[1], Neil J Greening[1], Salman Siddiqui[1 10], EMBER Consortium; Rachel Munton, John Le Quesne, Alison H Goodall, Hitesh C Pandya, James C Reynolds, Martha R J Clokie, Nilesh J Samani, Michael R Barer, Jacqueline A Shaw

Affiliations expand

- PMID: 36383685

- DOI: 10.1126/scitranslmed.abl5849

Abstract

Acute cardiorespiratory breathlessness accounts for one in eight of all emergency hospitalizations. Early, noninvasive diagnostic testing is a clinical priority that allows rapid triage and treatment. Here, we sought to find and replicate diagnostic breath volatile organic compound (VOC) biomarkers of acute cardiorespiratory disease and understand breath metabolite network enrichment in acute disease, with a view to gaining mechanistic insight of breath biochemical derangements. We collected and analyzed exhaled breath samples from 277 participants presenting acute cardiorespiratory exacerbations and aged-matched healthy volunteers. Topological data analysis phenotypes differentiated acute disease from health and acute cardiorespiratory exacerbation subtypes (acute heart failure, acute asthma, acute chronic obstructive pulmonary disease, and community-acquired pneumonia). A multibiomarker score (101 breath biomarkers) demonstrated good diagnostic sensitivity and specificity (≥80%) in both discovery and replication sets and was associated with all-cause mortality at 2 years. In addition, VOC biomarker scores differentiated metabolic subgroups of cardiorespiratory exacerbation. Louvain clustering of VOCs coupled with metabolite enrichment and similarity assessment revealed highly specific enrichment patterns in all acute disease subgroups, for example, selective enrichment of correlated C5-7 hydrocarbons and C3-5 carbonyls in heart failure and selective depletion of correlated aldehydes in acute asthma. This study identified breath VOCs that differentiate acute cardiorespiratory exacerbations and associated subtypes and metabolic clusters of disease-associated VOCs.

Pediatr Pulmonol

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The association between pre-existing asthma and reduced risk of death among children and adolescents hospitalized with COVID-19 in Brazil

Maria Christina L Oliveira[1], Enrico A Colosimo[2], Mariana A Vasconcelos[1], Hercílio Martelli-Júnior[3], Robert H Mak[4], Ludmila R Silva[5], Clara C Pinhati[1], Ana Cristina Simões E Silva[1], Eduardo A Oliveira[1]

Affiliations expand

- PMID: 36382503

- DOI: 10.1002/ppul.26245

Abstract

Objective: There have been conflicting reports on the relationship between asthma and COVID-19 severity. This study aimed to compare the risk of death among children with asthma and healthy peers hospitalized due to COVID-19.

Methods: We carried out an analysis of all pediatric patients 2-19 years of age with asthma and COVID-19 registered in SIVEP-Gripe, a Brazilian nationwide surveillance database, between February 2020 and March 2022. The primary outcome was time to death, which was evaluated considering discharge as a competitive risk using the cumulative incidence function.

Results: Among 30,405 hospitalized children with COVID-19, 21,340 (70.2%) had no comorbidities, 6,444 (21.2%) had comorbidities other than asthma, 2,165 (7.1%) had asthma, and 465 (1.5%) had asthma with other comorbidities. The estimated probability of a fatal outcome for each group was 4.1%, 14.9%, 2.1%, and 10.7%, respectively. After adjustment, children with asthma had a 60% reduction in the hazard of death than healthy peers (Hazard ratio [HR], = 0.39, 95% CI, 0.29 - 0.53, P < 0.0001). Among children with asthma and no other comorbidities, two covariates were independently associated with in-hospital mortality, age > 12 years, HR 4.0, 95% CI 2.5 - 6.4), and low oxygen saturation at admission (HR 2.3, 95% CI 1.4 - 3.2).

Conclusion: Children with asthma and no comorbidities had a lower risk of death compared with healthy peers after controlling for clinical and demographic confounding factors.

Keywords: COVID-19; SARS-CoV-2; asthma; children; outcome; risk factors.

Editorial

ERJ Open Res

. 2022 Nov 14;8(4):00322-2022.

doi: 10.1183/23120541.00322-2022. eCollection 2022 Oct.

Complex pathways leading to future paediatric asthma exacerbations

Amrita Dosanjh[1]

Affiliations expand

- PMID: 36382235
- PMCID: PMC9661246
- DOI: 10.1183/23120541.00322-2022

Free PMC article

Abstract

Childhood asthma studies to identify additional risk factors, triggers and biomarkers may reveal novel pathways leading to exacerbation https://bit.ly/3BOhSWy.

Conflict of interest statement

Conflict of interest: A. Dosanjh has nothing to disclose

- 12 references

SUPPLEMENTARY INFO

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ERJ Open Res

-
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. 2022 Nov 14;8(4):00174-2022.

doi: 10.1183/23120541.00174-2022. eCollection 2022 Oct.

Past asthma exacerbation in children predicting future exacerbation: a systematic review

Rachel Lowden[1], Steve Turner[1,2]

Affiliations expand

- PMID: 36382233

- PMCID: PMC9661269

- DOI: 10.1183/23120541.00174-2022

Free PMC article

Abstract

Acute exacerbations are common in children and potentially preventable. Currently, a past exacerbation is the best predictor of a future exacerbation. We undertook a systematic review of the literature describing the relationship between past and future exacerbations. Our analysis considered whether the odds ratios for one exacerbation to predict a recurrence were different across different categories of exacerbation. Four databases were searched systematically (MEDLINE, Embase, the Cumulative Index to Nursing and Allied Health and PsycInfo). Exacerbations were categorised by severity as: presentation to emergency department (ED); hospital admission; paediatric intensive care unit (PICU) admission; and "unspecified severity" (*i.e.* no distinction between severity categories was made). Meta-analysis was performed for studies where sufficient data were provided for inclusion. There were 26 eligible articles from 9185 identified. There was significant heterogeneity in duration of follow-up, healthcare system and exacerbation definition between studies. For the unspecified severity definition, the odds ratio for an exacerbation after a previous exacerbation was 9.87 (95% CI 5.02-19.39; six studies, 162 583 individuals). PICU admission was also associated with increased risk of future admission (OR 5.87, 95% CI 2.96-11.64; two studies, 730 individuals). Meta-analysis was not possible for ED visits or hospitalisation. The median odds ratio (range) for past ED visit predicting future ED visit was 6.27 (3.3-8.26) and for past hospitalisation predicting future hospitalisation was 3.37 (1.89-5.36). The odds for a second asthma exacerbation do not necessarily increase with increasing severity of an initial exacerbation.

Conflict of interest statement

Conflict of interest: The authors declare that there are no conflicts of interest to disclose.

- 41 references
- 5 figures

Respiration

. 2022 Nov 14;1-13.

doi: 10.1159/000527268. Online ahead of print.

Audit of Asthma Exacerbation Management in a Swiss General Hospital

Dominik Schnyder[1,2], Giorgia Lüthi-Corridori[3,4], Anne Barbara Leuppi-Taegtmeyer[1,2,5], Maria Boesing[1,2], Nicolas Geigy[6], Joerg Daniel Leuppi[1,2]

Affiliations expand

- PMID: 36380628

- DOI: 10.1159/000527268

Free article

Abstract

Background: Adequate management is crucial to reduce symptoms, hospitalization, and relapses in patients with asthma. Hospitals often struggle to meet treatment guidelines, and no recent data for Switzerland are available.

Objectives: The aim of the study was to audit the asthma exacerbation management in the Cantonal Hospital of Baselland in order to evaluate the level of compliance with guidelines in a narrative discussion.

Method: The study design is a retrospective observational cohort study. We evaluated all adult patients presenting to the hospital with a physician-diagnosed asthma exacerbation in 2018 and 2019. The asthma management patients received was compared to the Swiss guidelines and the international GINA guidelines.

Results: 160 patients were included (mean age: 50 years old, 57.5% female). SpO2 and heart rate were assessed at presentation in nearly all patients. Peak expiratory flow (PEF) was measured in only 14%. Adequate management of asthma exacerbation with inhaled bronchodilator medication in a combination of short-acting beta-agonists and short-acting anticholinergics was administered to 96% of the patients. Patients with severe symptoms received systemic glucocorticosteroids within 6 h in 55%. At discharge, a reliever medication was prescribed for 64% of the patients and 55% received a new or increased controller therapy with inhaled glucocorticosteroid (ICS). 49% of the patients had no follow-up organized.

Conclusion: To increase the guideline conformity and quality of asthma exacerbation management, the severity should be better assessed, especially by routinely performing PEF measurements. Treatment needs to be intensified; in particular, the ICS dose should be increased significantly and systemic glucocorticosteroids should be given with a lower threshold.

Keywords: Asthma; Audit; Exacerbation; Management; Switzerland.

Curr Stem Cell Res Ther

. 2022 Nov 15.

doi: 10.2174/1574888X18666221115141022. Online ahead of print.

First Report in a Human of Successful Treatment of Asthma with Mesenchymal Stem Cells: A Case Report with Review of Literature

Joshua Sharan[1], Amir Barmada[2], Nicolas Band[1], Eliana Liebman[3], Chadwick Prodromos[1]

Affiliations expand

- PMID: 36380439

- DOI: 10.2174/1574888X18666221115141022

Abstract

Introduction: Asthma is a heterogeneous disorder characterized by chronic airway inflammation resulting in obstructive pulmonary symptoms. In preclinical studies, mesenchymal stem cells (MSCs) have demonstrated the ability to ameliorate the symptoms and immunologic pathways seen in asthma. Due to the known relationship between asthma and the hyper-responsive immune cascade, we hypothesized that MSCs could be an effective treatment option for patients with asthma due to their significant immunomodulatory properties.

Objective: We present the initial results for the first patient enrolled in a phase 1 clinical trial (Safety of Cultured Allogeneic Adult Umbilical Cord Derived Mesenchymal Stem Cell Intravenous Infusion for the Treatment of Pulmonary Diseases) Case Report: A 68-year-old male with a longstanding history of asthma presented requesting mesenchymal stem cell treatment for his persistent asthma symptoms. Cultured umbilical cord-derived mesenchymal stem cells were infused intravenously at a dose of 100 million cells over a period of 40 minutes. Post-treatment follow-up was performed after two and six months. The patient had no adverse events or complications related to treatment. In the two months post treatment, his usage of a rescue inhaler decreased to 1 time per month, over 90% reduction. In addition, he had a 70% reduction in nebulizer usage. Improvement was sustained in the 6 months follow-up.

Conclusion: We report the first case of mesenchymal stem cell treatment significantly and safely improving asthma clinical symptoms in a human. Additionally, an extensive literature

review provided several plausible mechanisms by which stem cells can ameliorate immune hyper-stimulation associated with asthma.

Keywords: Mesenchymal stem cells; allergy.; asthma; case report; pulmonary disease; stem cell.

Curr Opin Allergy Clin Immunol

. 2022 Nov 16.

doi: 10.1097/ACI.0000000000000873. Online ahead of print.

An update on patient reported outcomes in type 2 inflammation airway disease

Christian Korsgaard Pedersen[1], Christiane Haase, Kasper Aanaes, Christian von Buchwald, Vibeke Backer

Affiliations expand

- PMID: 36378110

- DOI: 10.1097/ACI.0000000000000873

Abstract

Purpose of review: Patient reported outcome measures (PROMs) play an important role in assessing so-called global airway disease caused by type-2 inflammation, not only in terms of patients' perspective on symptoms and treatment/side-effect, but they can also serve as a measure of disease control, and not least as an indicator of possible coexisting comorbidity otherwise unrecognized. The objective of this review was to investigate any newly developed PROMs for global airway disease and to give an overview of the most commonly used PROMs in the management of global airway disease.

Recent findings: The Standard Tests for Asthma, Allergic Rhinitis and Rhinosinusitis (STARR-15) is a recently developed PROM aimed to raise clinicians' awareness of coexisting type-2 inflammation disease. Strengths of the STARR-15 is that is quick and symptom-centered, i.e. items are not specifically aimed at a disease the patients might not be aware they have. The STARR-15 has, however, not yet been validated, so details of responsiveness and reproducibility are yet to be determined.

Summary: PROMs are a quick and cheap way to assess patient perspectives in global airway disease, and can play an important role in unveiling otherwise overlooked co-existing double disease.

- 41 references

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BMC Pulm Med

. 2022 Nov 14;22(1):418.

doi: 10.1186/s12890-022-02230-5.

Patients with allergic asthma have lower risk of severe COVID-19 outcomes than patients with nonallergic asthma

Thomas R Murphy[1], William Busse[2], Cecile T J Holweg[3], Yamina Rajput[3], Karina Raimundo[3], Craig S Meyer[3], Arpamas Seetasith[4], Sachin Gupta[3], Ahmar Iqbal[3], Robert J Kaner[5]

Affiliations expand

- PMID: 36376851

- PMCID: PMC9660106

- DOI: 10.1186/s12890-022-02230-5

Free PMC article

Abstract

Background: Although asthma does not appear to be a risk factor for severe coronavirus disease 2019 (COVID-19), outcomes could vary for patients with different asthma subtypes. The objective of this analysis was to compare COVID-19 outcomes in real-world cohorts in the United States among patients with asthma, with or without evidence of allergy.

Methods: In a retrospective analysis of the COVID-19 Optum electronic health record dataset (February 20, 2020-January 28, 2021), patients diagnosed with COVID-19 with a history of moderate-to-severe asthma were divided into 2 cohorts: those with evidence of allergic asthma and those without (nonallergic asthma). After 1:1 propensity score matching, in which covariates were balanced and potential bias was removed, COVID-19 outcomes were compared between cohorts.

Results: From a COVID-19 population of 591,198 patients, 1595 patients with allergic asthma and 8204 patients with nonallergic asthma were identified. After propensity score matching (n = 1578 per cohort), risk of death from any cause after COVID-19 diagnosis

was significantly lower for patients with allergic vs nonallergic asthma (hazard ratio, 0.48; 95% CI 0.28-0.83; P = 0.0087), and a smaller proportion of patients with allergic vs nonallergic asthma was hospitalized within - 7 to + 30 days of COVID-19 diagnosis (13.8% [n = 217] vs 18.3% [n = 289]; P = 0.0005). Among hospitalized patients, there were no significant differences between patients with allergic or nonallergic asthma in need for intensive care unit admission, respiratory support, or COVID-19 treatment.

Conclusions: Asthma subtype may influence outcomes after COVID-19; patients with allergic asthma are at lower risk for hospitalization/death than those with nonallergic asthma.

Keywords: Allergic asthma; Allergy; Asthma; Atopic; COVID-19; Coronavirus; Nonallergic asthma; Pandemic; Respiratory; SARS-CoV-2.

Conflict of interest statement

TRM has been part of speaker bureaus for ALK, AstraZeneca, Boehringer Ingelheim, Genentech, Inc., and Optinose, and an advisory board member for Stallergenes Greer. WB has received grant support from the National Institutes of Health (NIH)-National Institute of Allergy and Infectious Diseases, and consultant fees from AstraZeneca, Genentech, Inc., GlaxoSmithKline, Novartis, and Sanofi/Regeneron. CTJH, YR, and CSM are former employees of Genentech, Inc. AS holds stock in F. Hoffmann-La Roche Ltd. KR, AS, SG, and AI are employees of Genentech, Inc. RJK has consulted for Boehringer Ingelheim, Genentech, Inc., and United Therapeutics; has received research support from Boehringer Ingelheim and the NIH; was a clinical investigator for Bellerophon, the NIH, Respivant, and Toray; and was on the data and safety monitoring board for Pliant and PureTech.

- 38 references
- 1 figure

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J Asthma

. 2022 Nov 14;1-15.

doi: 10.1080/02770903.2022.2144350. Online ahead of print.

Epidemiology, Treatment and Health Care Resource Use of Patients with severe Asthma in Germany – a retrospective Claims Data Analysis

Fraence Hardtstock[1], Julia Krieger[1], Thomas Wilke[1], Marco Lukas[2], Bernhard Ultsch[2], Robert Welte[2], Renate Quinzler[3], Ulf Maywald[4], Hartmut Timmermann[5]

Affiliations expand

- PMID: 36373984

- DOI: 10.1080/02770903.2022.2144350

Abstract

Background: Asthma causes various clinical symptoms, including unpredictable severe exacerbations, and even though most patients can achieve a reasonable disease control due to adequate treatment, some patients do not. This study seeks to describe healthcare resource utilization (HCRU) and treatment of asthma and severe asthma patients in Germany.

Method: A retrospective claims data analysis has been conducted on adult asthma patients and a subset of patients with severe asthma, identified during July 2017 - June 2018. A proxy was used to identify severe asthma patients based on therapy options recommended within the German treatment guideline for treating these patients. These include (i) biologics, (ii) medium/high-dose inhaled corticosteroids (ICS) in conjunction with LABA/montelukast and antibiotics/oral corticosteroids (OCS), and (iii) long-term OCS

therapy. HCRU and treatment of patients were observed during a 1-year follow-up period (July 2018 - June 2019).

Results: The study included 388 932 adult asthma patients (prevalence: 7.90%), with 2.51%-12.88% affected by severe asthma (depending on the definition). 22.60% of all asthma patients experienced hospitalizations (severe asthma: 36.11%). Furthermore, 13.59% received OCS (severe asthma: 39.91%), but only 0.18% (severe asthma: 1.25%) received biologics. Only 23.95% (severe asthma: 41.17%) visited a pulmonologist.

Conclusions: A considerable proportion of severe asthma patients receive long-term OCS therapy. However, less than 50% have seen a pulmonologist who would typically seek a change in treatment to avoid the long-term consequences of OCS. To optimize the treatment of severe asthma in Germany, better referral of these patients to specialists is needed and considering potential treatment alternatives.

Keywords: Disease burden; Germany; Oral corticosteroids; Real-world evidence; Treatment pattern.

J Asthma

. 2022 Nov 15;1-9.

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

Objective: 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)).**Conclusions:** 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; Jordan; asthma control test; inhaler technique.

. 2022 Nov 15;1-9.

doi: 10.1080/02770903.2022.2144348. Online ahead of print.

Association between air pollution levels and drug sales for asthma and allergy in 63 million people in metropolitan France

Marwan El Homsi[1], Stéphane Sclison[2], Domitille Huguet[2], Boris Dessimond[1], Luciana Kase Tanno[1], Julie Prud'homme[1], Augustin Collette[3], Isabella Annesi-Maesano[1]

Affiliations expand

- PMID: 36332169

- DOI: 10.1080/02770903.2022.2144348

Abstract

Introduction: Air pollution is known to have an impact on respiratory health. However, the assessment of this relationship is far from complete and is rarely extended to the country level. We used drug sales data, both Over-The-Counter (OTC) and prescription drugs, to assess exhaustively the impact of air pollution on asthma and allergy at the national level in France.

Methods: The WHO Anatomical Therapeutic Chemical (ATC) classification system was used to describe the distribution of sales of drugs of class R03 (Drugs for obstructive airways diseases, overall for asthma) and R06 (Antihistamines for systemic use). We performed a Quasi-Poisson regression model with a generalized additive model (GAM) to estimate the relationship (Relative Risks and 95% Confidence Interval) between drug sales and air pollutants, that is Particulate Matter with a diameter less than 2.5 micrometers ($PM_{2.5}$) and less than 10 micrometers (PM_{10}) and Nitrogen dioxide (NO_2), as assessed using the high-resolution CHIMERE dispersion model. We designed unadjusted and adjusted single-pollutant models as well as two-pollutant models.

Results: $PM_{2.5}$, PM_{10}, and NO_2 were significantly and positively associated with sales of R03 and R06 class drugs, after adjustment for potential confounders. Results were confirmed in the two-pollutant model for PM_{10} and NO_2 but not for $PM_{2.5}$.

Conclusions: Our study confirms the presence of an association between major air pollutants and the sales of drugs against asthma and allergies. Further studies on larger databases and over several years are necessary to confirm and better understand these results.

Keywords: Air pollution; asthma; drug; epidemiology.

J Asthma

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Cost-effectiveness of benralizumab versus mepolizumab and dupilumab in patients with severe uncontrolled eosinophilic asthma in Spain

M Mareque[1], M Climente[2], E Martinez-Moragon[2], A Padilla[3], I Oyagüez[1], C Touron[4], C Torres[4], A Martinez[4]

Affiliations expand

- PMID: 36322679

- DOI: 10.1080/02770903.2022.2139718

Abstract

Objective: To assess the cost-effectiveness of benralizumab (benra) vs. mepolizumab (mepo) and dupilumab (dupi) for the treatment of patients with severe uncontrolled asthma from the Spanish Health System perspective.

Methods: Exacerbations avoided, quality-adjusted life years (QALYs) gained and costs in a 5-year period were estimated with a Markov model for a cohort of 1,000 patients in which, based on published evidence, 31% of the patients received biologics + oral corticosteroids (OCS) and 69% received only biologics. Efficacy data (exacerbation reduction and OCS elimination) were derived from a matching-adjusted indirect comparison. Published EQ-5D utilities per health state (biologic alone, biologic + OCS, standard of care + OCS, exacerbations, and post-exacerbations) were used for QALY estimation. Utility decrements associated with exacerbation management [-0.1 (OCS or emergency visits), -0.2 (hospitalization)] derived from the literature were applied. Costs (€, 2022) included drug acquisition (ex-factory price), administration and disease management. An expert panel (2 pneumologists and 1 pharmacist) validated all inputs.

Results: Benra was more effective (52.21 QALYs) than mepo (51.39 QALYs) and dupi (51.30 QALYs). Benra avoided more exacerbations (2.87 exacerbations) compared to mepo (4.70 exacerbations) and dupi (5.11 exacerbations) for the 5-year horizon. Total costs/patient were €56,093.77 (benra), €59,280.45 (mepo) and €62,991.76 (dupi), resulting in benra dominating (more QALYs with lower costs) vs. mepo and dupi.

Conclusions: Benralizumab can be considered as a dominant treatment alternative vs. other biologic drugs for the treatment of uncontrolled severe eosinophilic asthma patients in Spain.

Keywords: Economics; treatment.

J Asthma

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Factors associated with frequent physical activity among United States adults with asthma

Ziyad Almatruk[1,2], David R Axon[2,3]

Affiliations expand

- PMID: 36316286

- DOI: 10.1080/02770903.2022.2142134

Abstract

Objective: This study investigated factors associated with frequent moderate-to-vigorous intensity physical activity among United States (US) adults with asthma.**Methods:** This retrospective cross-sectional study included US adults (≥18 years) with asthma in the 2019 Medical Expenditure Panel Survey data. Logistic regression models that added sequential groups of variables were used to assess associations between predisposing (age, gender, race), enabling (marital status, poverty level, education level, insurance coverage, employment status), and need (smoking status, co-morbidities, mental health, physical health, functional limitations) factors and doing ≥30 min moderate-to-vigorous intensity physical activity ≥ five times per week. The alpha level was 0.05.**Results:** The study included 2,410 individuals, of which 46.9% (95% confidence interval [CI] = 44.2-49.6) reported doing frequent moderate-to-vigorous intensity physical activity. In fully adjusted analyses, the following variables were associated with a greater odds of reporting frequent moderate-to-vigorous intensity physical activity: men vs. women (adjusted odds ratio [AOR] = 1.4, 95% CI = 1.1-1.7), white vs. other races (AOR = 1.3, 95% CI = 1.0-1.6), excellent/very good/good vs. fair/poor physical health (AOR = 2.3, 95% CI = 1.7-3.0), and functional limitations no vs. yes (AOR = 1.7, 95% CI = 1.3-2.2).**Conclusions:** The factors identified in this study (gender, race, health status, and limitation status) may be helpful to target interventions to raise awareness and increase physical activity among US adults with

asthma. Studies that can demonstrate a temporal relationship are needed to further our understanding of this topic.

Keywords: Respiratory; exercise; medical expenditure panel survey.

J Asthma

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Use of FeNO to predict anti-IL-5 and IL-5R biologics efficacy in a real-world cohort of adults with severe eosinophilic asthma

C Menigoz[1], S Dirou[1], A Chambellan[2], D Hassoun[3], A Moui[1], A Magnan[4], F X Blanc[1]

Affiliations expand

- PMID: 36301080

- DOI: 10.1080/02770903.2022.2136526

Abstract

Introduction: Severe eosinophilic asthma (SEA) is associated with multiple exacerbations. Fractional exhaled nitric oxide (FeNO), a biomarker of airway T2 inflammation, is known to be correlated with the risk of exacerbations. While the use of FeNO is well established to predict the therapeutic response to dupilumab (anti-IL-4/IL-13), it remains uncertain for biologics targeting the IL-5 pathway.

Methods: We conducted an observational, retrospective, monocentric analysis of adults with SEA who started mepolizumab (anti-IL-5) or benralizumab (anti-IL-5R) between January 1, 2016 and December 31, 2020.

Results: Data were collected for 109 patients. All participants reported uncontrolled asthma with a median of 3 annual exacerbations and a median *Asthma Control Test* score of 12. They all had an initial blood eosinophilia >300/mm^3, with a median at 610/mm^3 (IQR 420-856). Patients with a baseline FeNO ≥50 ppb reported more exacerbations in the previous year than those with a FeNO <50 ppb (p = 0.02). After initiation of treatment, change in FeNO was not associated with therapeutic response. However, decrease in the annual number of exacerbations was significantly greater in patients with a baseline FeNO ≥50 ppb than in those with a baseline FeNO <50 ppb (-3.3 ± 2.7 vs -0.9 ± 2.4, respectively; p = 0.01). There was no association between baseline FeNO values and subsequent lung function, asthma control or reduction of oral corticosteroids use.

Conclusion: In this real-world cohort, adults with SEA who had a baseline FeNO ≥50 ppb experienced a greater decrease in exacerbations after 12 months of anti-IL-5 or IL-5R biologics than those with a FeNO <50 ppb.

Keywords: Exhaled nitric oxide; benralizumab; exacerbation; interleukin-5; mepolizumab; severe asthma.

J Asthma

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doi: 10.1080/02770903.2022.2140435. Online ahead of print.

Primary antibody deficiencies represent an underestimated comorbidity in asthma patients: efficacy of immunoglobulin replacement therapy in asthma control

Emanuele Vivarelli[1], Andrea Matucci[1], Paola Parronchi[2], Francesco Liotta[2], Lorenzo Cosmi[2], Oliviero Rossi[1], Edoardo Cavigli[3], Alessandra Vultaggio[1]

Affiliations expand

- PMID: 36282045

- DOI: 10.1080/02770903.2022.2140435

Abstract

Objective: Primary antibody deficiencies (PAD) are an underestimated comorbidity in asthma and its treatment could improve disease control.

Methods: a retrospective cohort of asthmatics, affected by IgG subclass deficiency or unclassified antibody deficiency and treated with low-dose intravenous immunoglobulin replacement therapy (IRT) was recruited. Demographic and clinical data, chest CT scan, blood eosinophils, atopy, chronic oral corticosteroid (OCS) therapy were evaluated at baseline. Asthma exacerbations, lower respiratory tract infections (LRTI), upper respiratory tract infections (URTI) and asthma-related hospitalizations were assessed after one and two years of IRT.

Results: 57 moderate-to-severe asthmatics were enrolled, mostly affected by T2 low asthma (39/57, 68.4%). After one year, IRT was effective in improving, irrespective of bronchiectasis, atopy, eosinophils and PAD type: 1) trough IgG (826.9 ± 221.3 vs 942.2 ± 195.1 mg/dl; $p < 0.0001$) and IgG subclasses (IgG1 355.4 ± 88.4 vs 466.7 ± 122.3, $p < 0.0001$; IgG2 300.1 ± 130.1 vs 347.6 ± 117.3, $p < 0.0005$) serum levels. 2) asthma exacerbations (6.4 ± 4.1 vs 2.4 ± 1.9, $p < 0.0001$), LRTI (4.3 ± 3.9 vs 1.3 ± 1.5, $p < 0.0001$) and hospitalization rate (0.26 ± 0.7 vs 0.05 ± 0.2, $p < 0.01$). These results persisted after 2 years of therapy. Estimated mean cumulative OCS exposure was reduced by 4500 mg over the 2-year period.

Conclusions: low-dose IRT is effective in improving asthma control and lessening OCS burden in asthmatics affected by PAD.

Keywords: Asthma; OCS sparing; bronchiectasis; immunoglobulin replacement therapy; primary antibody deficiencies.

J Asthma

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Bronchodilator reversibility testing in long-term cough and dyspnea after Covid-19 viral infection: a trigger for asthma?

Aysegul Gencer[1], Buket Caliskaner Ozturk[2], Sermin Borekci[2], Bilun Gemicioglu[2]

Affiliations expand

- PMID: 36279253

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Abstract

Objective: This study aims to investigate the presence of underlying chronic airway disease in individuals with chronic cough and dyspnea lasting longer than eight weeks and who had previously Coronavirus disease 2019 (COVID-19) and had no known lung disease.**Methods:** A total of 151 patients admitted to the respiratory diseases outpatient room with the complaint of cough and/or dyspnea that persisted for at least eight weeks following COVID-19 infection were accrued to the study. Demographic characteristics, smoking history, the severity of lung involvement on chest computed tomography in the acute phase of Covid-19 infection, and bronchodilator reversibility test results were recorded. Smoking history and forced expiratory volume in the first second (FEV1) were compared.**Results:** FEV1 increase ≥ 200 ml was observed in 40 (26.5%) patients. In 24 (15.9%) patients, an increase in FEV1 was found to be 200 ml and above, and the percentage of FEV1 was 12% or more. While 14 (9.3%) patients were diagnosed with asthma, 13 (8.6%) patients were diagnosed with nonreversible airflow obstruction (NRAO), and 1 (0.7%) patient was diagnosed with chronic obstructive pulmonary disease (COPD).**Conclusions:** COVID-19 infection may play a vital role in initiating asthma pathogenesis. It should be kept in mind that viral infection-related asthma may be the underlying cause of prolonged cough and dyspnea after COVID-19 infection.

Keywords: Post-COVID-19; airway reversibility; bronchial hyperresponsiveness; post-COVID cough; viral infection related-asthma.

J Asthma

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Factors associated with medication adherence among adults with asthma

Kudret C Özdemir[1,2], Ramune Jacobsen[1], Morten Dahl[2,3], Eskild Landt[2]

Affiliations expand

- PMID: 36278848

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Abstract

Objective: Asthma medication adherence is of crucial importance for successful disease management. The aim of this study was to identify and rank factors associated with medication adherence among adults with asthma in the general population.

Methods: We used data on physician-diagnosed asthma, medication adherence, and factors associated with asthma medication adherence from the Danish General Suburban Population Study using a cross-sectional study design. We ranked factors associated with asthma medication adherence based on the magnitude of odds ratios, and the population attributable fractions.

Results: Among 20,032 individuals from the general population, 1,128 (6%) suffered from asthma and 822 (73%) of these were adherent to asthma medications. Based on odds ratios, the three top-ranked factors associated with asthma medication adherence were asthma attacks within the past year (4.0; 95% CI: 2.9-5.5), allergy medication use (3.8; 2.6-5.6), and age above median (3.4; 2.4-4.7), followed by asthma severity markers like airway obstruction, and coughing with mucus. Based on population attributable fractions, the three top-ranked factors associated with adherence to asthma medications were asthma attacks within the past year (70%), age above median (57%), and use of allergy medication (49%).

Conclusions: The study showed that in the general population recent asthma attacks, higher age, and taking allergy medication were the three most important factors associated with asthma medication adherence. The importance of maintaining adherence to asthma medications even in the absence of severe disease or expressed asthma symptoms should be better communicated to the general population.

Keywords: Disease management; asthma symptoms; bronchodilator; epidemiology; inhalation.

J Immunol

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Mechanisms of Corticosteroid Resistance in Type 17 Asthma

Lingzi Hong[1,2], Tomasz Herjan[1], Katarzyna Bulek[1], Jianxin Xiao[1], Suzy A A Comhair[1], Serpil C Erzurum[1], Xiaoxia Li[3], Caini Liu[3]

Affiliations expand

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Free PMC article

Abstract

IL-17A plays an important role in the pathogenesis of asthma, particularly the neutrophilic corticosteroid (CS)-resistant subtype of asthma. Clinical studies suggest that a subset of asthma patients, i.e., Th17/IL-17A-mediated (type 17) CS-resistant neutrophilic asthma, may improve with Th17/IL-17A pathway blockade. However, little is known about the mechanisms underlying type 17 asthma and CS response. In this article, we show that blood levels of lipocalin-2 (LCN2) and serum amyloid A (SAA) levels are positively correlated with IL-17A levels and are not inhibited by high-dose CS usage in asthma patients. In airway cell culture systems, IL-17A induces these two secreted proteins, and

their induction is enhanced by CS. Furthermore, plasma LCN2 and SAA levels are increased in mice on a preclinical type 17 asthma model, correlated to IL-17A levels, and are not reduced by glucocorticoid (GC). In the mechanistic studies, we identify CEBPB as the critical transcription factor responsible for the synergistic induction of LCN2 and SAA by IL-17A and GC. IL-17A and GC collaboratively regulate CEBPB at both transcriptional and posttranscriptional levels. The posttranscriptional regulation of CEBPB is mediated in part by Act1, the adaptor and RNA binding protein in IL-17A signaling, which directly binds CEBPB mRNA and inhibits its degradation. Overall, our findings suggest that blood LCN2 and SAA levels may be associated with a type 17 asthma subtype and provide insight into the molecular mechanism of the IL-17A-Act1/CEBPB axis on these CS-resistant genes.

Conflict of interest statement

The authors have no financial conflicts of interest.

- 6 figures

Am J Respir Crit Care Med

. 2022 Nov 15;206(10):1208-1219.

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Exposome Profiles and Asthma among French Adults

Alicia Guillien[1], Annabelle Bédard[2], Orianne Dumas[2], Julien Allegre[3], Nathalie Arnault[3], Audrey Bochaton[4], Nathalie Druesne-Pecollo[3], Dorothée Dumay[5], Léopold K Fezeu[3], Serge Hercberg[3], Nicole Le Moual[2], Hugo Pilkington[5], Stéphane Rican[4], Guillaume Sit[2], Fabien Szabo de Edelenyi[3], Mathilde Touvier[3], Pilar Galan[3], Thierry Feuillet[3,5], Raphaëlle Varraso[2], Valérie Siroux[1]

Affiliations expand

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- DOI: 10.1164/rccm.202205-0865OC

Abstract

Rationale: Although previous studies in environmental epidemiology focused on single or a few exposures, a holistic approach combining multiple preventable risk factors is needed to tackle the etiology of multifactorial diseases such as asthma. **Objectives:** To investigate the association between combined socioeconomic, external environment, early-life environment, and lifestyle-anthropometric factors and asthma phenotypes. **Methods:** A total of 20,833 adults from the French NutriNet-Santé cohort were included (mean age, 56.2 yr; SD, 13.2; 72% women). The validated asthma symptom score (continuous) and asthma control (never asthma, controlled asthma, and uncontrolled asthma) were considered. The exposome (n = 87 factors) covered four domains: socioeconomic, external environment, early-life environment, and lifestyle-anthropometric. Cluster-based analyses were performed within each exposome domain, and the identified profiles were studied in association to asthma outcomes in negative binomial (asthma symptom score) or multinomial logistic (asthma control) regression models. **Measurements and Main Results:** In total, 5,546 (27%) individuals had an asthma symptom score $\geqslant$1, and 1,206 (6%) and 194 (1%) had controlled and uncontrolled asthma, respectively. Three early-life exposure profiles ("high passive smoking-own dogs," "poor birth parameters-daycare attendance-city center," or "$\geqslant$2 siblings-breastfed" compared with "farm-pet owner-molds-low passive smoking") and one lifestyle-anthropometric profile ("unhealthy diet-high smoking-overweight" compared with "healthy diet-nonsmoker-thin") were associated with more asthma symptoms and uncontrolled asthma. **Conclusions:** This large-scale exposome-based study revealed early-life and lifestyle exposure profiles that were at risk for asthma in adults. Our findings support the importance of multiinterventional programs for the primary and secondary prevention of asthma, including control of specific early-life risk factors and promotion of a healthy lifestyle in adulthood.

Keywords: asthma; cluster; exposome.

Comment in

- The Exposome Applied: A Step toward Defining the Totality of Environmental Exposures in Asthma.
  Sillé FCM, McCormack M, Hartung T.Am J Respir Crit Care Med. 2022 Nov 15;206(10):1187-1188. doi: 10.1164/rccm.202207-1430ED.PMID: 35925019 No abstract available.

SUPPLEMENTARY INFO

MeSH terms, Substances, Grant supportexpand

FULL TEXT LINKS

AJRCCM Final Version

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Eur Respir J

. 2022 Nov 17;60(5):2200298.

doi: 10.1183/13993003.00298-2022. Print 2022 Nov.

Effect of asthma management with exhaled nitric oxide *versus* usual care on perinatal outcomes

Vanessa E Murphy[1,2], Megan E Jensen[3,2], Elizabeth G Holliday[2], Warwick B Giles[4], Helen L Barrett[5,6], Leonie K Callaway[7,8], Andrew Bisits[9], Michael J Peek[10,11], Sean K Seeho[4], Alistair Abbott[12], Annelies L Robijn[3], Paul B Colditz[13], Andrew Searles[14], John Attia[2], Kirsten McCaffery[15], Michael J Hensley[16], Joerg Mattes[3,17], Peter G Gibson[16,18]

Affiliations expand

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- PMCID: PMC9669403

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Free PMC article

Abstract

Introduction: Asthma exacerbations in pregnancy are associated with adverse perinatal outcomes. We aimed to determine whether fractional exhaled nitric oxide (F_{ENO})-based asthma management improves perinatal outcomes compared to usual care.

Methods: The Breathing for Life Trial was a multicentre, parallel-group, randomised controlled trial conducted in six hospital antenatal clinics, which compared asthma management guided by F_{ENO} (adjustment of asthma treatment according to exhaled nitric oxide and symptoms each 6-12 weeks) to usual care (no treatment adjustment as part of the trial). The primary outcome was a composite of adverse perinatal events (preterm birth, small for gestational age (SGA), perinatal mortality or neonatal hospitalisation) assessed using hospital records. Secondary outcomes included maternal asthma exacerbations. Concealed random allocation, stratified by study site and self-reported smoking status was used, with blinded outcome assessment and statistical analysis (intention to treat).

Results: Pregnant women with current asthma were recruited; 599 to the control group (608 infants) and 601 to the intervention (615 infants). There were no significant group differences for the primary composite perinatal outcome (152 (25.6%) out of 594 control, 177 (29.4%) out of 603 intervention; OR 1.21, 95% CI 0.94-1.56; p=0.15), preterm birth (OR 1.14, 95% CI 0.78-1.68), SGA (OR 1.06, 95% CI 0.78-1.68), perinatal mortality (OR 3.62, 95% CI 0.80-16.5), neonatal hospitalisation (OR 1.24, 95% CI 0.89-1.72) or maternal asthma exacerbations requiring hospital admission or emergency department presentation (OR 1.19, 95% CI 0.69-2.05).

Conclusion: F_{ENO}-guided asthma pharmacotherapy delivered by a nurse or midwife in the antenatal clinic setting did not improve perinatal outcomes.

Conflict of interest statement

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

Comment in

- Randomised controlled trials utilising F_{ENO} to manage asthma: is it time to acknowledge that "one size does not fit all"?
  Petsky H.Eur Respir J. 2022 Nov 17;60(5):2201639. doi: 10.1183/13993003.01639-2022. Print 2022 Nov.PMID: 36396158 No abstract available.

- 26 references
- 4 figures

Eur Respir J

. 2022 Nov 17;60(5):2200446.

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Allergen immunotherapy effectively reduces the risk of exacerbations and lower respiratory tract infections in both seasonal and perennial allergic asthma: a nationwide epidemiological study

Christian Woehlk[1], Anna Von Bülow[2], Muzhda Ghanizada[2], Marianne Baastrup Søndergaard[2], Susanne Hansen[2], Celeste Porsbjerg[2]

Affiliations expand

- PMID: 35618279

- DOI: 10.1183/13993003.00446-2022

Abstract

Background: Allergic asthma is associated with increased risk of respiratory tract infections and exacerbations. It remains unclear whether this susceptibility is conditioned by seasonal or by perennial allergy.

Aim: To investigate perennial allergy compared with seasonal allergy as a risk factor for lower respiratory tract infections and exacerbations in asthma and whether this risk can be reduced by allergen immunotherapy (AIT).

Methodology: This is a prospective register-based nationwide study of 18-44-year-olds treated with AIT during 1995-2014. Based on the type of AIT and use of anti-asthmatic drugs, patients were subdivided into two groups: perennial allergic asthma (PAA) *versus* seasonal allergic asthma (SAA). Data on antibiotics against lower respiratory tract infections (LRTI) and oral corticosteroids for exacerbations were analysed before starting AIT (baseline) and 3 years after completing AIT (follow-up).

Results: We identified 2688 patients with asthma treated with AIT, of whom 1249 had PAA and 1439 had SAA. At baseline, patients with SAA had more exacerbations (23.8% *versus* 16.5%, p≤0.001), but there were no differences in LRTI. During the 3-year follow-up, we observed a highly significant reduction of exacerbations with an average decrease of 57% in PAA and 74% in SAA. In addition, we observed a significant reduction of LRTI in both PAA and SAA: 17% and 20% decrease, respectively.

Conclusion: AIT effectively reduced the risk of exacerbations and lower respiratory tract infections in both seasonal and perennial allergic asthma. Perennial allergy is seemingly not a stronger risk factor for respiratory infections and exacerbations than seasonal allergy.

Conflict of interest statement

Conflict of interest: C. Woehlk has received speaker fees from ALK Abelló Nordic A/s. M.B. Søndergaard reports speaker fees from GlaxoSmithKline. A. Von Bülow has received speaker fees from AstraZeneca, GlaxoSmithKline and Novartis, and has attended advisory boards for Novartis and AstraZeneca. C. Porsbjerg reports grants or contracts from AstraZeneca, GlaxoSmithKline, Novartis, TEVA, Sanofi, Chesi and ALK Abelló A/s paid to

institution; consulting fees from AstraZeneca, GlaxoSmithKline, Novartis, TEVA, Sanofi, Chesi and ALK Abelló A/s; speaker fees from AstraZeneca, GlaxoSmithKline, Novartis, TEVA, Sanofi, Chesi and ALK Abelló A/s; advisory board honoraria from AstraZeneca, Novartis, TEVA, Sanofi, and ALK Abelló A/s. M. Ghanizada and S. Hansen report no conflicts of interest.

Comment in

- Is it time to consider allergen immunotherapy earlier in the management of allergic asthma?
  Roberts G.Eur Respir J. 2022 Nov 17;60(5):2201686. doi: 10.1183/13993003.01686-2022. Print 2022 Nov.PMID: 36396157 No abstract available.

Ann Behav Med

. 2022 Nov 18;56(12):1201-1217.

doi: 10.1093/abm/kaab080.

A Scoping Review of Methods Used to Assess Medication Adherence in Patients with Chronic Conditions

Pinelopi Konstantinou[1], Orestis Kasinopoulos[1], Christiana Karashiali[1], Georgios Georgiou[2], Andreas Panayides[3,4], Alexia Papageorgiou[5], Greta Wozniak[1], Angelos P Kassianos[1,6], Maria Karekla[1]

Affiliations expand

- PMID: 34570875

- DOI: 10.1093/abm/kaab080

Abstract

Background: Medication nonadherence of patients with chronic conditions is a complex phenomenon contributing to increased economic burden and decreased quality of life. Intervention development relies on accurately assessing adherence but no "gold standard" method currently exists.

Purpose: The present scoping review aimed to: (a) review and describe current methods of assessing medication adherence (MA) in patients with chronic conditions with the highest nonadherence rates (asthma, cancer, diabetes, epilepsy, HIV/AIDS, hypertension), (b) outline and compare the evidence on the quality indicators between assessment methods (e.g., sensitivity), and (c) provide evidence-based recommendations.

Methods: PubMed, PsycINFO and Scopus databases were screened, resulting in 62,592 studies of which 71 met criteria and were included.

Results: Twenty-seven self-report and 10 nonself-report measures were identified. The Medication Adherence Report Scale (MARS-5) was found to be the most accurate self-report, whereas electronic monitoring devices such as Medication Event Monitoring System (MEMS) corresponded to the most accurate nonself-report. Higher MA rates were reported when assessed using self-reports compared to nonself-reports, except from pill counts.

Conclusions: Professionals are advised to use a combination of self-report (like MARS-5) and nonself-report measures (like MEMS) as these were found to be the most accurate and reliable measures. This is the first review examining self and nonself-report methods for MA, across chronic conditions with the highest nonadherence rates and provides evidence-based recommendations. It highlights that MA assessment methods are understudied in certain conditions, like epilepsy. Before selecting a MA measure, professionals are advised to inspect its quality indicators. Feasibility of measures should be explored in future studies as there is presently a lack of evidence.

Keywords: Assessment; Chronic conditions; Medication adherence; Scoping review; Self-reports.

SUPPLEMENTARY INFO

Grant supportexpand

BRONCHIECTASIS

1
Respir Res

.
. 2022 Nov 19;23(1):317.

doi: 10.1186/s12931-022-02229-w.

Altered fecal microbiome and metabolome in adult patients with non-cystic fibrosis bronchiectasis

Wen-Wen Wang[#1], Bei Mao[#1], Yang Liu[#1], Shu-Yi Gu[1], Hai-Wen Lu[1], Jiu-Wu Bai[1], Shuo Liang[1], Jia-Wei Yang[1], Jian-Xiong Li[1], Xiao Su[2], Hai-Yang Hu[3], Chen Wang[3], Jin-Fu Xu[4]

Affiliations expand

- PMID: 36403022

- DOI: 10.1186/s12931-022-02229-w

Abstract

Background: Emerging experimental and epidemiological evidence highlights a crucial cross-talk between the intestinal flora and the lungs, termed the "gut-lung axis". However, the function of the gut microbiota in bronchiectasis remains undefined. In this study, we aimed to perform a multi-omics-based approach to identify the gut microbiome and metabolic profiles in patients with bronchiectasis.

Methods: Fecal samples collected from non-CF bronchiectasis patients (BE group, n = 61) and healthy volunteers (HC group, n = 37) were analyzed by 16 S ribosomal RNA (rRNA)

sequencing. The BE group was divided into two groups based on their clinical status: acute exacerbation (AE group, n = 31) and stable phase (SP group, n = 30). Further, metabolome (lipid chromatography-mass spectrometry, LC-MS) analyses were conducted in randomly selected patients (n = 29) and healthy volunteers (n = 31).

Results: Decreased fecal microbial diversity and differential microbial and metabolic compositions were observed in bronchiectasis patients. Correlation analyses indicated associations between the differential genera and clinical parameters such as bronchiectasis severity index (BSI). Disease-associated gut microbiota was screened out, with eight genera exhibited high accuracy in distinguishing SP patients from HCs in the discovery cohort and validation cohort using a random forest model. Further correlation networks were applied to illustrate the relations connecting disease-associated genera and metabolites.

Conclusion: The study uncovered the relationships among the decreased fecal microbial diversity, differential microbial and metabolic compositions in bronchiectasis patients by performing a multi-omics-based approach. It is the first study to characterize the gut microbiome and metabolome in bronchiectasis, and to uncover the gut microbiota's potentiality as biomarkers for bronchiectasis.

Trial registration: This study is registered with ClinicalTrials.gov, number NCT04490447.

Keywords: Biomarkers; Bronchiectasis; Gut microbiome; Metabolomics.

- 55 references

SUPPLEMENTARY INFO

Associated data, Grant supportexpand

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Radiology

-
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. 2022 Nov 15;212611.

doi: 10.1148/radiol.212611. Online ahead of print.

Chest CT Findings in Marijuana Smokers

Luke Murtha[1], Paul Sathiadoss[1], Jean-Paul Salameh[1], Matthew D F Mcinnes[1], Giselle Revah[1]

Affiliations expand

- PMID: 36378033

- DOI: 10.1148/radiol.212611

Abstract

Background Global consumption of marijuana is increasing, but there is a paucity of evidence concerning associated lung imaging findings. Purpose To use chest CT to investigate the effects of marijuana smoking in the lung. Materials and Methods This retrospective case-control study evaluated results of chest CT examinations (from October 2005 to July 2020) in marijuana smokers, nonsmoker control patients, and tobacco-only smokers. We compared rates of emphysema, airway changes, gynecomastia, and coronary artery calcification. Age- and sex-matched subgroups were created for comparison with tobacco-only smokers older than 50 years. Results were analyzed using χ^2 tests. Results A total of 56 marijuana smokers (34 male; mean age, 49 years ± 14 [SD]), 57 nonsmoker control patients (32 male; mean age, 49 years ± 14), and 33 tobacco-only smokers (18 male; mean age, 60 years ± 6) were evaluated. Higher rates of emphysema were seen among marijuana smokers (42 of 56 [75%]) than nonsmokers (three of 57 [5%]) ($P < .001$) but not tobacco-only smokers (22 of 33 [67%]) ($P = .40$). Rates of bronchial thickening, bronchiectasis, and mucoid impaction were higher among marijuana smokers compared with the other groups ($P < .001$ to $P = .04$). Gynecomastia was more common in marijuana smokers (13 of 34 [38%]) than in control patients (five of 32 [16%]) ($P = .039$) and tobacco-only smokers (two of 18 [11%]) ($P = .040$). In age-matched subgroup analysis of 30 marijuana smokers (23 male), 29 nonsmoker control patients (17 male), and 33 tobacco-only smokers (18 male), rates of bronchial thickening, bronchiectasis, and mucoid impaction were again higher in the marijuana smokers than in the tobacco-only smokers ($P < .001$ to $P = .006$). Emphysema rates were higher in age-matched marijuana smokers (28 of 30 [93%]) than in tobacco-only smokers (22 of 33 [67%]) ($P = .009$). There was no difference in rate of coronary artery calcification between age-matched marijuana smokers (21 of 30 [70%]) and tobacco-only smokers (28 of 33 [85%]) ($P = .16$). Conclusion Airway inflammation and emphysema were more common in marijuana smokers than in nonsmokers and tobacco-only smokers, although variable interobserver agreement and concomitant cigarette smoking among the marijuana-smoking cohort limits our ability to draw strong conclusions. © RSNA, 2022 See also the editorial by Galvin and Franks in this issue.

Comment in

- Marijuana and the Vulnerable Lung: The Role of Imaging and the Need to Move Quickly.
  Galvin J, Franks T.Radiology. 2022 Nov 15:222745. doi: 10.1148/radiol.222745. Online ahead of print.PMID: 36378035 No abstract available.

Eur Respir J

. 2022 Nov 17;60(5):2200176.

doi: 10.1183/13993003.00176-2022. Print 2022 Nov.

Genome sequencing reveals underdiagnosis of primary ciliary dyskinesia in bronchiectasis

Amelia Shoemark[1 2 3], Helen Griffin[4 3], Gabrielle Wheway[5], Claire Hogg[2], Jane S Lucas[6 7], Genomics England Research Consortium; Carme Camps[8 9], Jenny Taylor[8 9], Mary Carroll[6], Michael R Loebinger[2], James D Chalmers[10], Deborah Morris-Rosendahl[11], Hannah M Mitchison[12 13], Anthony De Soyza[3 13], Genomics England Research Consortium:; D Brown, J C Ambrose, P Arumugam, R Bevers, M Bleda, F Boardman-Pretty, C R Boustred, H Brittain, M J Caulfield, G C Chan, T Fowler, A Giess, A Hamblin, S Henderson, T J P Hubbard, R Jackson, L J Jones, D Kasperaviciute, M Kayikci, A Kousathanas, L Lahnstein, S E A Leigh, I U S Leong, F J Lopez, F Maleady-Crowe, M McEntagart, F Minneci, L Moutsianas, M Mueller, N Murugaesu, A C Need, P O'Donovan, C A Odhams, C Patch, D Perez-Gil, M B Pereira, J Pullinger, T Rahim, A Rendon, T Rogers, K Savage, K Sawant, R H Scott, A Siddiq, A Sieghart, S C Smith, A Sosinsky, A Stuckey, M Tanguy, A L Taylor Tavares, E R A Thomas, S R Thompson, A Tucci, M J Welland, E Williams, K Witkowska, S M Wood

Affiliations expand

- PMID: 35728977

- DOI: 10.1183/13993003.00176-2022

Abstract

Background: Bronchiectasis can result from infectious, genetic, immunological and allergic causes. 60-80% of cases are idiopathic, but a well-recognised genetic cause is the motile ciliopathy, primary ciliary dyskinesia (PCD). Diagnosis of PCD has management implications including addressing comorbidities, implementing genetic and fertility counselling and future access to PCD-specific treatments. Diagnostic testing can be complex; however, PCD genetic testing is moving rapidly from research into clinical diagnostics and would confirm the cause of bronchiectasis.

Methods: This observational study used genetic data from severe bronchiectasis patients recruited to the UK 100,000 Genomes Project and patients referred for gene panel testing within a tertiary respiratory hospital. Patients referred for genetic testing due to clinical suspicion of PCD were excluded from both analyses. Data were accessed from the British Thoracic Society audit, to investigate whether motile ciliopathies are underdiagnosed in people with bronchiectasis in the UK.

Results: Pathogenic or likely pathogenic variants were identified in motile ciliopathy genes in 17 (12%) out of 142 individuals by whole-genome sequencing. Similarly, in a single centre with access to pathological diagnostic facilities, 5-10% of patients received a PCD diagnosis by gene panel, often linked to normal/inconclusive nasal nitric oxide and cilia functional test results. In 4898 audited patients with bronchiectasis, <2% were tested for PCD and <1% received genetic testing.

Conclusions: PCD is underdiagnosed as a cause of bronchiectasis. Increased uptake of genetic testing may help to identify bronchiectasis due to motile ciliopathies and ensure appropriate management.

Conflict of interest statement

Conflict of interest: A. Shoemark has received grants from AstraZeneca. G. Wheway is currently employed by Illumina Inc. M.R. Loebinger has received consultancy or speaker fees from Insmed, AstraZeneca, Parion, Grifols and Armata. J.D. Chalmers has received grants or contracts from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Gilead Sciences, Novartis and Insmed; and received consultancy or speaker fees from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Insmed, Janssen, Novartis and

Zambon. J.S. Lucas reports grants from NHS England, NIHR and AIR Charity. H.M. Mitchison is a Trustee of Ciliopathy Alliance. A. De Soyza reports grants from AstraZeneca, GlaxoSmithKline and Pfizer; consulting fees and lecture honoraria from Gilead, GlaxoSmithKline, AstraZeneca, LifeArc and 30T; participation on advisory board at Bayer; receipt of equipment from GlaxoSmithKline. All other authors have nothing to disclose.

CHRONIC COUGH

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Medicine (Baltimore)

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. 2022 Nov 18;101(46):e31636.

doi: 10.1097/MD.0000000000031636.

A randomized, double-blind, placebo-controlled multicenter clinical trial of Xiehuang Jiejing granule in the treatment of cough variant asthma in children

Yi-Na Qiao[1], Shuang-Zhu Lin[2], Xiao-Zheng Duan[2], Ming-Hang Yang[1], Xiao-Fang Zhang[1], Jing-Jing Li[1], Sai-Nan Kang[1], Yu-Ting Wang[1], Ying Zhang[3], Xiao-Chun Feng[2]

Affiliations expand

- PMID: 36401471

- DOI: 10.1097/MD.0000000000031636

Abstract

Background: Cough variant asthma (CVA), also called concealed asthma or allergic asthma, is the most common cause of chronic cough in children. The disorder is mainly characterized by a nonproductive dry cough associated with a high recurrence rate that is conventionally treated with antibiotics, anti-inflammatory medications, cough suppressants, or expectorants. For millennia, Chinese herbal medicine (CHM) has been used widely in China to treat pediatric CVA cases, although high-quality evidence of CHM efficacy is lacking. In this study, the effectiveness and safety of Xiehuangjiejing (XHJJ) granule will be evaluated when used alone to treat children with CVA.

Methods and analysis: A randomized, double-blind, parallel, placebo-controlled multicenter trial will be conducted over the course of 2 weeks. A total of 180 CVA patients of ages between 4 and 7 years old will be randomly assigned to the experimental group (XHJJ granules, 4.5 g administered 3 times daily) or control group (matched placebo, 4.5 g administered 3 times daily) in a 2:1 ratio based on subject number per group, respectively. The trial will consist of a 7-day medical interventional stage and a 7-day follow-up stage. On day 7 of the follow-up stage, an evaluation of all subjects will be carried out to assess cough symptom score as the primary outcome and several secondary outcomes, including TCM (traditional Chinese medicine) syndrome score, lung function, and dosage of salbutamol aerosol inhaler therapy. Safety assessments will also be evaluated during the trial.

Discussion: The aim of this study was to examine the effectiveness and safety of Xiehuangjiejing (XHJJ) granule using a trial protocol designed to yield high-quality, statistically robust results for use in evaluating CHM as a treatment for CVA in children.

Conflict of interest statement

The authors have no conflicts of interest to disclose.

- 29 references

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BMC Pulm Med

. 2022 Nov 19;22(1):426.

doi: 10.1186/s12890-022-02228-z.

A register-based study: cough - a frequent phenomenon in the adult population

Vibeke Backer[1,2], Andreas Porsborg[3], Victor Hansen[3], Tina Skjold[3], Johannes Martin Schmid[3], Mette Kehlet[4], Christian Torp-Pedersen[5,6,7], Kristian Aasbjerg[7]

Affiliations expand

- PMID: 36401236

- DOI: 10.1186/s12890-022-02228-z

Free article

Abstract

Background: Chronic cough, more than 8 weeks, can either be without co-morbidity called unexplained chronic cough (UCC) or with co-morbidity called refractory chronic cough (RCC). Using datasets from the Danish National Prescription Registry (Prescription Registry) and Danish National Patient Registry (Patient Registry) we wanted to investigate the prevalence and factors of importance of cough in a Nationwide registry.

Material and methods: Inclusion criteria were patients 18-90 years with at least one final cough diagnosis (ICD-10 DR05/DR059) in Patient registry or patients who have redeemed ≥2 prescriptions for relevant cough-medication within a 90-day harvest in the Prescription registry from 2008 to 2017. To validate this study's chosen proxy on chronic cough an analysis of the Patient registry sub-population with a contact of ≥8 weeks and then final diagnosis code DR05/DR059 was also performed. The population was divided into UCC and RCC.

Results: Of the 104,216 patients from the Prescription registry, 52,727 were classified as having UCC and 51,489 were classified with RCC. From the Patient registry 34,260 were included, of whom 12,278 had UCC and 21,982 had RCC. Cough were frequently found among females ($p < 0.0001$). Both genders were around 2 years older in RCC than UCC (p

< 0.0001) Spirometry was performed in 69 and 57%, X-ray in 73 and 58% and asthma challenge test performed in 13 and 5% (UCC and RCC, respectively, p < 0.0001). The frequency of co-morbidities such as heart failure, rheumatologic disease, pulmonary embolism, and diabetes was < 10%.

Conclusion: Many patients suffer from chronic cough or cough requiring medications, with or without co-morbidity; frequently found among menopausal women. Most patients had a substantial work-up performed. The high frequency and the resources consuming work-up program call for systematic coding of disease, systematic patient evaluation and more specific treatment options. The study was approved (ID: no. P-2019-191).

Keywords: Cough; Nationwide cohort; Refractory chronic cough; Register-based study; Unexplained chronic cough.

- 24 references

BMC Pulm Med

. 2022 Nov 17;22(1):423.

doi: 10.1186/s12890-022-02225-2.

Tracheobronchopathia osteochondroplastica: clinical, bronchoscopic, and comorbid features in a case series

Antoine Dumazet[1], Claire Launois[2], Francois Lebargy[2], Romain Kessler[3], Hervé Vallerand[2], Pierre Schmitt[4], Christophe Hermant[5], Sandra Dury[2], Maxime Dewolf[2], Julien Dutilh[6], Maher Abouda[7], Marion Ferreira[8], Ihab Atallah[9], Samy Lachkar[10], Jérémy Charriot[11], Stéphane Jouneau[12], Yurdagul Uzunhan[13], Stéphane Chouabe[14], Benjamin Coiffard[15], Hervé Dutau[15], Jean Hagenburg[2], Amandine Briault[16], Valérian Dormoy[17], Marion Lirsac[18], Jean-Michel Vergnon[19], Gaetan Deslee[2 17], Jeanne-Marie Perotin[2 17]

Affiliations expand

- PMID: 36397041

- PMCID: PMC9670617

- DOI: 10.1186/s12890-022-02225-2

Free PMC article

Abstract

Background: Tracheobronchopathia osteochondroplastica (TO) is a rare condition of unknown etiology. TO is characterized by submucosal nodules, with or without calcifications, protruding in the anterolateral walls of the trachea and proximal bronchi. The objective of this study was to describe TO features and associated comorbidities in a series of patients.

Methods: Patients suffering from TO were retrospectively included by investigators from the Groupe d'Endoscopie Thoracique et Interventionnelle Francophone (GETIF). Demographic, clinical, comorbidities, bronchoscopic, functional, and radiological characteristics, and outcomes were recorded and analyzed.

Results: Thirty-six patients were included (69% male with a mean of 65 ± 12 years). Chronic symptoms were described by 81% of patients including cough (74%) and dyspnea on exertion (74%). TO was associated with COPD in 19% of the cases and gastroesophageal reflux disease in 6%. A mild to severe airflow obstruction was present in 55% of the cases. CT scan showed tracheal submucosal nodules in 93% of patients and tracheal stenosis in 17%. Bronchoscopy identified TO lesions in the trachea in 65% of the cases, and 66% of them were scattered. A bronchoscopic reevaluation was performed in 7 cases, 9 ± 14 months [1-56] after initial diagnosis, and showed the stability of lesions in all cases. Three patients underwent interventional bronchoscopic treatment.

Conclusion: The diagnosis of TO relies on typical bronchoscopic findings and can be evoked on a CT scan. Histologic diagnosis can be useful in atypical cases for differential

diagnosis. Given its low consequences in terms of symptoms, lung functions, and evolution, no treatment is usually required.

Keywords: Bronchoscopy; Case report; Tracheal stenosis; Tracheobronchopathia osteochondroplastica.

Conflict of interest statement

The authors declare that they have no competing interests" in this section.

- 42 references
- 2 figures

Bioorg Med Chem Lett

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. 2022 Nov 14;129067.

doi: 10.1016/j.bmcl.2022.129067. Online ahead of print.

Novel α7 Nicotinic Acetylcholine Receptor Modulators as Potential Antitussive Agents

Anatoly Mazurov[1], Jenny Ho[1], Tiffany Low[1], Julia Hoeng[2]

Affiliations expand

- PMID: 36395996

- DOI: 10.1016/j.bmcl.2022.129067

Abstract

A novel series of α7 nicotinic acetylcholine receptor (nAChR) modulators was designed and evaluated for antitussive activity in an in vivo guinea pig model of chemically induced cough. Compound 16 significantly ($p<0.01$) reduced the cumulative number of coughs and showed similar results to a positive control (30 mg/kg codeine) at concentration 3-fold, when compared to negative control (saline or air). Among three different administration routes (intraperitoneal, oral and inhalation), compound 16 exerted a significant antitussive effect in guinea pigs at an inhaled dose as low as 0.4 mg/kg ($p<0.05$). α7 nAChR modulators may provide a novel, non-narcotic approach to therapy in patients with acute and chronic cough.

Keywords: antitussive effect; in vivo guinea pig model; α7 nicotinic acetylcholine receptor modulator.

Conflict of interest statement

Declaration of Competing Interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

. 2022 Nov 16;22(1):420.

doi: 10.1186/s12890-022-02136-2.

Aspergillus tracheobronchitis with Birt–Hogg–Dubè syndrome as a rare cause of chronic cough

Lianrong Huang[#1], Fang Yi[#1], Chen Zhan[1], Kefang Lai[2]

Affiliations expand

- PMID: 36384555

- PMCID: PMC9670559

- DOI: 10.1186/s12890-022-02136-2

Free PMC article

Abstract

Background: Aspergillus tracheobronchitis (ATB) is confined as a condition of chronic superficial infection of tracheobronchial tree. Its diagnosis is difficult due to atypical manifestations and low detective rate of Aspergillus thus far.

Case presentation: Herein, we presented a 45-year-old male patient with a sole chronic productive cough for five years referred to our cough specialist clinic. Chest high-resolution computed tomography showed multiple lung cysts predominantly located in the subpleural lesions and near the mediastinum. Neither bacteria nor fungi were identified by sputum culture. However, metagenomic next-generation sequencing in sputum detected Aspergillus fumigatus DNA. The genetic testing of whole blood suggested the germline mutation of the tumor suppressor gene folliculin, supporting a diagnosis of Birt-Hogg-Dubé (BHD) syndrome. His productive cough symptom significantly improved after receiving itraconazole treatment for 2 months. After discontinuation of antifungal treatment, there was no relapse for four months follow-up. A diagnosis of ATB with BHD syndrome was eventually established in this patient.

Conclusion: ATB should be considered in any patient with prolonged unexplained productive cough. Next-generation sequencing technologies may be useful to identify ATB which is uncommon and easily ignored in clinical practice.

Keywords: Aspergillus tracheobronchitis; Birt-Hogg-Dubé syndrome; Case report; Chronic cough; Multiple lung cysts.

Conflict of interest statement

The authors declare that they have no competinxg interests.

- 14 references
- 2 figures

BMC Pulm Med

. 2022 Nov 16;22(1):419.

doi: 10.1186/s12890-022-02222-5.

Impact of high-risk of obstructive sleep apnea on chronic cough: data from the Korea National Health and Nutrition Examination Survey

Tae Hoon Kim[1], I Re Heo[1], Ho Cheol Kim[2]

Affiliations expand

- PMID: 36384528
- PMCID: PMC9666978
- DOI: 10.1186/s12890-022-02222-5

Free PMC article

Abstract

Background: Chronic cough is an extremely common clinical symptom of various diseases. However, the relationship between obstructive sleep apnea (OSA) and chronic cough in the general population has not been sufficiently studied.

Methods: Using the 2019 Korean National Health and Nutrition Examination Survey data, we identified a group at high-risk of OSA via the STOP-Bang questionnaire and determined the association between OSA and chronic cough by a regression model.

Results: Of the eligible 4,217 participants, 97.1% and 2.9% were classified into the non-chronic cough and chronic cough groups, respectively. The chronic cough group had higher STOP-Bang scores than those of the group without chronic cough (2.32 ± 1.38 vs. 2.80 ± 1.39; P < 0.001). In the group at high-risk of OSA, 40.4% and 52.0% of participants scored ≥ 3 in STOP-Bang, depending on the absence or presence of chronic cough (P = 0.012), respectively. Chronic cough independently correlated with impaired lung function (forced expiratory volume in one second ≥ 50-<80% predicted value, P = 0.001; <50, P < 0.001), low household income (P = 0.015), and a group at high-risk of OSA (STOP-Bang score 3-4, P = 0.004; 5-8, P < 0.001). Obesity I had a protective role against the occurrence of chronic cough (P = 0.023).

Conclusion: A high-risk for OSA is a significant risk factor for chronic cough. OSA should be considered when evaluating chronic cough patients.

Keywords: Chronic cough; Obesity; Obstructive sleep apnea; Respiratory function tests; Risk factors.

Conflict of interest statement

The authors declare that they have no conflict of interests.

- 44 references
- 2 figures

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Review

Cochrane Database Syst Rev

. 2022 Nov 17;11(11):CD010216.

doi: 10.1002/14651858.CD010216.pub7.

Electronic cigarettes for smoking cessation

Jamie Hartmann-Boyce[1], Nicola Lindson[1], Ailsa R Butler[1], Hayden McRobbie[2], Chris Bullen[3], Rachna Begh[1], Annika Theodoulou[1], Caitlin Notley[4], Nancy A Rigotti[5], Tari Turner[6], Thomas R Fanshawe[1], Peter Hajek[7]

Affiliations expand

- PMID: 36384212

- PMCID: PMC9668543 (available on 2023-11-17)

- DOI: 10.1002/14651858.CD010216.pub7

Abstract

Background: Electronic cigarettes (ECs) are handheld electronic vaping devices which produce an aerosol by heating an e-liquid. Some people who smoke use ECs to stop or reduce smoking, although some organizations, advocacy groups and policymakers have discouraged this, citing lack of evidence of efficacy and safety. People who smoke, healthcare providers and regulators want to know if ECs can help people quit smoking, and if they are safe to use for this purpose. This is a review update conducted as part of a living systematic review.

Objectives: To examine the effectiveness, tolerability, and safety of using electronic cigarettes (ECs) to help people who smoke tobacco achieve long-term smoking abstinence.

Search methods: We searched the Cochrane Tobacco Addiction Group's Specialized Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, and PsycINFO to 1 July 2022, and reference-checked and contacted study authors. SELECTION CRITERIA: We included randomized controlled trials (RCTs) and randomized cross-over trials, in which people who smoke were randomized to an EC or control condition. We also included uncontrolled intervention studies in which all participants received an EC intervention. Studies had to report abstinence from cigarettes at six months or longer or data on safety markers at one week or longer, or both.

Data collection and analysis: We followed standard Cochrane methods for screening and data extraction. Our primary outcome measures were abstinence from smoking after at least six months follow-up, adverse events (AEs), and serious adverse events (SAEs). Secondary outcomes included the proportion of people still using study product (EC or pharmacotherapy) at six or more months after randomization or starting EC use, changes in carbon monoxide (CO), blood pressure (BP), heart rate, arterial oxygen saturation, lung function, and levels of carcinogens or toxicants, or both. We used a fixed-effect Mantel-Haenszel model to calculate risk ratios (RRs) with a 95% confidence interval (CI) for dichotomous outcomes. For continuous outcomes, we calculated mean differences. Where appropriate, we pooled data in meta-analyses.

Main results: We included 78 completed studies, representing 22,052 participants, of which 40 were RCTs. Seventeen of the 78 included studies were new to this review update. Of the included studies, we rated ten (all but one contributing to our main comparisons) at low risk of bias overall, 50 at high risk overall (including all non-randomized studies), and the remainder at unclear risk. There was high certainty that quit rates were higher in people randomized to nicotine EC than in those randomized to nicotine replacement therapy (NRT) (RR 1.63, 95% CI 1.30 to 2.04; I^2 = 10%; 6 studies, 2378 participants). In absolute terms, this might translate to an additional four quitters per 100 (95% CI 2 to 6). There was moderate-certainty evidence (limited by imprecision) that the rate of occurrence of AEs was similar between groups (RR 1.02, 95% CI 0.88 to 1.19; I^2 = 0%; 4 studies, 1702 participants). SAEs were rare, but there was insufficient evidence to determine whether

rates differed between groups due to very serious imprecision (RR 1.12, 95% CI 0.82 to 1.52; I^2 = 34%; 5 studies, 2411 participants). There was moderate-certainty evidence, limited by imprecision, that quit rates were higher in people randomized to nicotine EC than to non-nicotine EC (RR 1.94, 95% CI 1.21 to 3.13; I^2 = 0%; 5 studies, 1447 participants). In absolute terms, this might lead to an additional seven quitters per 100 (95% CI 2 to 16). There was moderate-certainty evidence of no difference in the rate of AEs between these groups (RR 1.01, 95% CI 0.91 to 1.11; I^2 = 0%; 5 studies, 1840 participants). There was insufficient evidence to determine whether rates of SAEs differed between groups, due to very serious imprecision (RR 1.00, 95% CI 0.56 to 1.79; I^2 = 0%; 8 studies, 1272 participants). Compared to behavioural support only/no support, quit rates were higher for participants randomized to nicotine EC (RR 2.66, 95% CI 1.52 to 4.65; I^2 = 0%; 7 studies, 3126 participants). In absolute terms, this represents an additional two quitters per 100 (95% CI 1 to 3). However, this finding was of very low certainty, due to issues with imprecision and risk of bias. There was some evidence that (non-serious) AEs were more common in people randomized to nicotine EC (RR 1.22, 95% CI 1.12 to 1.32; I^2 = 41%, low certainty; 4 studies, 765 participants) and, again, insufficient evidence to determine whether rates of SAEs differed between groups (RR 1.03, 95% CI 0.54 to 1.97; I^2 = 38%; 9 studies, 1993 participants). Data from non-randomized studies were consistent with RCT data. The most commonly reported AEs were throat/mouth irritation, headache, cough, and nausea, which tended to dissipate with continued EC use. Very few studies reported data on other outcomes or comparisons, hence evidence for these is limited, with CIs often encompassing clinically significant harm and benefit.

Authors' conclusions: There is high-certainty evidence that ECs with nicotine increase quit rates compared to NRT and moderate-certainty evidence that they increase quit rates compared to ECs without nicotine. Evidence comparing nicotine EC with usual care/no treatment also suggests benefit, but is less certain. More studies are needed to confirm the effect size. Confidence intervals were for the most part wide for data on AEs, SAEs and other safety markers, with no difference in AEs between nicotine and non-nicotine ECs nor between nicotine ECs and NRT. Overall incidence of SAEs was low across all study arms. We did not detect evidence of serious harm from nicotine EC, but longest follow-up was two years and the number of studies was small. The main limitation of the evidence base remains imprecision due to the small number of RCTs, often with low event rates, but further RCTs are underway. To ensure the review continues to provide up-to-date information to decision-makers, this review is a living systematic review. We run searches monthly, with the review updated when relevant new evidence becomes available. Please refer to the Cochrane Database of Systematic Reviews for the review's current status.

Conflict of interest statement

RB holds an NIHR grant, but this did not directly fund this current work. She is principal investigator of an ongoing study listed in this review.

CB was principal investigator on the ASCEND e-cigarette trial reported in the Cochrane Review and a co-investigator on the ASCEND II trial and several other studies included in the review. CB has provided consultancy for J&J KK (Japan) on NRT products. CB reports research grants from the Health Research Council of NZ, the Heart Foundation of NZ and the NZ Ministry of Health. He has recently led a project funded by Pfizer (NZ) on chronic disease management.
ARB's work on this review has been supported by Cancer Research UK Project Award funding. This is not deemed a conflict of interest.
TF has no known conflicts of interest.
PH provided consultancy for and received research funding from Pfizer, a manufacturer of stop-smoking medications. He was principal investigator on one of the trials included in this review and co-investigator on other relevant studies.
JHB has received support for this work from the Cochrane Review Support Programme and the University of Oxford's Returning Carer's Fund. Neither of these are deemed conflicts of interest.
NL has received payment for lectures on systematic review methodology, and has been an applicant on project funding to carry out priority setting and systematic reviews in the area of tobacco control (NIHR funded). None of this is deemed a conflict of interest.
HM has no known conflicts of interest.
CN has no known conflicts of interest.
NAR has received royalties from UpToDate, Inc., for chapters on electronic cigarettes and occasional fees from academic hospitals or professional medical societies for lectures on smoking cessation that include discussion of electronic cigarettes. NAR was a member of the committee that produced the 2018 National Academies of Science, Engineering, and Medicine's Consensus Study Report on the Public Health Benefits of E-cigarettes. She was unpaid for this work. Outside the topic of e-cigarettes, NAR is a consultant for Achieve LifeSciences, which is developing an investigational smoking cessation medication for FDA approval (cytisine) and her institution (MGH) receives a grant from the company as a site for a clinical trial testing the safety and efficacy of cytisine. NAR holds grants from NIH for research work.
AT's work on this review has been supported by the Cochrane Review Support Programme and the University of Oxford's Returning Carer's Fund. Neither of these are deemed conflicts of interest.
TT has no known conflicts of interest.

Update of

- doi: 10.1002/14651858.CD010216.pub6

SUPPLEMENTARY INFO

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FULL TEXT LINKS

J Asthma

. 2022 Nov 14;1-6.

doi: 10.1080/02770903.2022.2139719. Online ahead of print.

Bronchodilator reversibility testing in long-term cough and dyspnea after Covid-19 viral infection: a trigger for asthma?

Aysegul Gencer[1], Buket Caliskaner Ozturk[2], Sermin Borekci[2], Bilun Gemicioglu[2]

Affiliations expand

- PMID: 36279253

- DOI: 10.1080/02770903.2022.2139719

Abstract

Objective: This study aims to investigate the presence of underlying chronic airway disease in individuals with chronic cough and dyspnea lasting longer than eight weeks and who had previously Coronavirus disease 2019 (COVID-19) and had no known lung disease.**Methods:** A total of 151 patients admitted to the respiratory diseases outpatient room with the complaint of cough and/or dyspnea that persisted for at least eight weeks following COVID-19 infection were accrued to the study. Demographic characteristics, smoking history, the severity of lung involvement on chest computed tomography in the

acute phase of Covid-19 infection, and bronchodilator reversibility test results were recorded. Smoking history and forced expiratory volume in the first second (FEV1) were compared.**Results:** FEV1 increase ≥ 200 ml was observed in 40 (26.5%) patients. In 24 (15.9%) patients, an increase in FEV1 was found to be 200 ml and above, and the percentage of FEV1 was 12% or more. While 14 (9.3%) patients were diagnosed with asthma, 13 (8.6%) patients were diagnosed with nonreversible airflow obstruction (NRAO), and 1 (0.7%) patient was diagnosed with chronic obstructive pulmonary disease (COPD).**Conclusions:** COVID-19 infection may play a vital role in initiating asthma pathogenesis. It should be kept in mind that viral infection-related asthma may be the underlying cause of prolonged cough and dyspnea after COVID-19 infection.

Keywords: Post-COVID-19; airway reversibility; bronchial hyperresponsiveness; post-COVID cough; viral infection related-asthma.