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

1
Cancer Epidemiol

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. 2023 Aug 18;86:102439.
doi: 10.1016/j.canep.2023.102439. Online ahead of print.

Lung cancer in nonsmokers- A risk factor analysis

Denise Albano[1], Ankit Dhamija[2], Yunhan Liao[3], Allison Mclarty[2], Hannah Talavera[2], Esther K Kim[2], Mark Ashamalla[4]
Affiliations expand

- PMID: 37598649

- DOI: 10.1016/j.canep.2023.102439

Abstract

Institutions: STONY BROOK MEDICAL CENTERRATIONALE: Lung Cancer screening for the high-risk smoking population has been proven to save lives. However, in 2022, 20% of newly diagnosed lung cancers (47,300) were in nonsmokers. These patients were found to be diagnosed at later stages. This may be at least partly due to not meeting criteria for and

participating in current lung cancer screening. This study aims to describe characteristics of a never smoker patient population to help identify common risk factors which might merit inclusion in lung cancer screening and thus improve patient outcomes.

Methods: This retrospective single center study included never-smoker patients diagnosed with lung nodules and never-smoker patients diagnosed with lung cancer from 2016 to 2022. Data was obtained from the Stony Brook Medical Center electronic medical record. 16,056 patients were identified as never-smokers who were asked by the medical assistant if they ever smoked in their lifetime. Patients were eliminated if they had any smoking history up to first diagnosis date. Demographics, radiology, histology, diagnosis dates, comorbidities, smoking status, and exposures collected through ICD10 codes and not self-reported, were investigated.

Results: Of 16,056 never-smoking patients, 9315 (58.02%) were females diagnosed with lung nodules and 6741 (41.98%) were males diagnosed with lung nodules. The univariate analysis showed significant differences between gender, age at nodule diagnosis, and patients with and without comorbidities including chronic obstructive pulmonary disease (COPD), hypertension (HTN), and family history (FHX) of lung cancer. The percentage of lung cancer patients among females was significantly higher than among males. Patients having lung cancer were older. The percentages of lung cancer patients with these comorbidities were significantly higher than those without. However, there was no significant difference found between patients with and without diabetes mellitus (DM). The multivariable logistic regression suggested that age at nodule diagnosis and comorbidities including COPD (which included asthma, emphysema and chronic bronchitis) and family history of lung cancer were significantly associated with lung cancer. Older patients and patients with those comorbidities had a higher risk of developing cancer than those who were younger or without those comorbidities. The study excluded HTN and included age at nodule diagnosis in the logistic regression model as HTN was found to be protective against lung cancer due to age at lung nodule diagnosis. Please refer to the appendix for further details.

Conclusion: Never-smoker patients who were older and with COPD and Family History of lung cancer had higher risk of developing lung cancer than younger patients without these comorbidities. In this study, gender had no impact on outcome.

Keywords: Lung neoplasm (D008175); NLM class WF 658.

Conflict of interest statement

Declaration of Competing Interest All authors do not have any financial and or personal relationships with other people or organizations that could inappropriately influence their work. NONE.

Eur J Med Res
. 2023 Aug 18;28(1):291.
doi: 10.1186/s40001-023-01269-2.

Evaluation of the safety and efficacy of extracorporeal carbon dioxide removal in the critically ill using the PrismaLung+ device

Ravindranath Tiruvoipati[1,2,3], Jarryd Ludski[4], Sachin Gupta[4,5], Ashwin Subramaniam[4,5,6,7], Mallikarjuna Ponnapa Reddy[4,5,8], Eldho Paul[6,9], Kavi Haji[4,5,10]
Affiliations expand

- PMID: 37596670
- PMCID: PMC10436516
- DOI: 10.1186/s40001-023-01269-2

Abstract

Background: Several extracorporeal carbon dioxide removal ($ECCO_2R$) devices are currently in use with variable efficacy and safety profiles. PrismaLung+ is an $ECCO_2R$ device that was recently introduced into clinical practice. It is a minimally invasive, low flow device that provides partial respiratory support with or without renal replacement therapy. Our aim was to describe the clinical characteristics, efficacy, and safety of PrismaLung+ in patients with acute hypercapnic respiratory failure.

Methods: All adult patients who required $ECCO_2R$ with PrismaLung+ for hypercapnic respiratory failure in our intensive care unit (ICU) during a 6-month period between March and September 2022 were included.

Results: Ten patients were included. The median age was 55.5 (IQR 41-68) years, with 8 (80%) male patients. Six patients had acute respiratory distress syndrome (ARDS), and two patients each had exacerbations of asthma and chronic obstructive pulmonary disease (COPD). All patients were receiving invasive mechanical ventilation at the time of initiation of $ECCO_2R$. The median duration of $ECCO_2R$ was 71 h (IQR 57-219). A significant improvement in pH and $PaCO_2$ was noted within 30 min of initiation of $ECCO_2R$. Nine patients (90%) survived to weaning of $ECCO_2R$, eight (80%) survived to ICU discharge and seven (70%) survived to hospital discharge. The median duration of ICU and hospital stays were 14.5 (IQR 8-30) and 17 (IQR 11-38) days, respectively. There were no patient-related complications with the use of $ECCO_2R$. A total of 18 circuits were used in ten patients (median 2 per patient; IQR 1-2). Circuit thrombosis was noted in five circuits (28%) prior to reaching the expected circuit life with no adverse clinical consequences.

Conclusion(s): PrismaLung+ rapidly improved $PaCO_2$ and pH with a good clinical safety profile. Circuit thrombosis was the only complication. This data provides insight into the safety and efficacy of PrismaLung+ that could be useful for centres aspiring to introduce $ECCO_2R$ into their clinical practice.

Keywords: Extracorporeal therapies; Hypercapnia; PrismaLung+; Respiratory acidosis; Respiratory failure.

Conflict of interest statement

RT was an invited speaker at a Baxter sponsored meeting in March 2023. Rest of the authors declare that they have no competing interests.

- 28 references
- 3 figures

. 2023 Aug 18.
doi: 10.1007/s11356-023-29269-z. Online ahead of print.

Environmental and occupational risk factors for COPD and its prevalence among miners worldwide: a Mendelian randomization and meta-analysis study

Zikai Liu[#1], Haihong Pan[#1], Bin Liu[2], Lanlan Li[1], Hongxu Yang[1], Tong Shen[3]
Affiliations expand

- PMID: 37592069

- DOI: 10.1007/s11356-023-29269-z

Abstract

Chronic obstructive pulmonary disease (COPD) is the third leading cause of death after cardiovascular disease and stroke, and its incidence is associated with genetic, environmental, and occupational factors. Miner is high-risk population for COPD, but the global prevalence of COPD in this group is inaccurate. In this study, the environmental and occupational risk factors for COPD were explored comprehensively with a two-sample Mendelian randomization study by combining genome-wide association data from two large global sample sizes of publicly available databases, UK Biobank (n = 503,317) and FinnGen (n = 193,638), as well as the prevalence of COPD among miners was investigated with meta-analysis followed a random-effects model including seven studies (16,033 miners in total). This study found that asthma, smoking, shift work, and workplace dust exposure may increase an individual's risk of COPD. The pooled prevalence of COPD among miners globally was 12% (95% CI: 8%, 18%), with higher prevalence of COPD among ex-smokers and dust-exposed individuals, and was significantly influenced by the method of diagnosis. Our findings suggest that there is currently a lack of practical criteria for diagnosing COPD in the physical examination and screening of miners. The actual prevalence of COPD may be underestimated due to the healthy worker effect and the phenomenon of job switching, and appropriate policies should be favored in the future to reduce the risk of COPD in miner.

Keywords: Chronic obstructive pulmonary disease; Mendelian randomization; Meta-analysis; Miner; Prevalence; Risk factors.

- 63 references

SUPPLEMENTARY INFO

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Respirology

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. 2023 Aug 17.
doi: 10.1111/resp.14577. Online ahead of print.

Whole lung health for the whole of life

Christine Jenkins[1]
Affiliations expand

- PMID: 37592458

- DOI: 10.1111/resp.14577

No abstract available

Keywords: COPD; air pollution; lung physiology; newborn; paediatrics.

FULL TEXT LINKS

Respir Res
. 2023 Aug 17;24(1):201.
doi: 10.1186/s12931-023-02508-0.

Apoptosis inhibitor of macrophage (AIM)/CD5L is involved in the pathogenesis of COPD

Michiko Takimoto-Sato[1], Masaru Suzuki[2], Hiroki Kimura[1,3], Haiyan Ge[4], Munehiro Matsumoto[1], Hironi Makita[5], Satoko Arai[6,7], Toru Miyazaki[7,8], Masaharu Nishimura[1,5], Satoshi Konno[1]
Affiliations expand

- PMID: 37592330
- PMCID: PMC10433671
- DOI: 10.1186/s12931-023-02508-0

Free PMC article

Abstract

Background: Alveolar macrophages (AMs) and AM-produced matrix metalloprotease (MMP)-12 are known to play critical roles in the pathogenesis of chronic obstructive pulmonary disease (COPD). The apoptosis inhibitor of the macrophages (AIM)/CD5 molecule-like (CD5L) is a multifunctional protein secreted by the macrophages that mainly exists in the blood in a combined form with the immunoglobulin (Ig)M pentamer.

Although AIM has both facilitative and suppressive roles in various diseases, its role in COPD remains unclear.

Methods: We investigated the role of AIM in COPD pathogenesis using porcine pancreas elastase (PPE)-induced and cigarette smoke-induced emphysema mouse models and an in vitro model using AMs. We also analyzed the differences in the blood AIM/IgM ratio among nonsmokers, healthy smokers, and patients with COPD and investigated the association between the blood AIM/IgM ratio and COPD exacerbations and mortality in patients with COPD.

Results: Emphysema formation, inflammation, and cell death in the lungs were attenuated in AIM$^{-/-}$ mice compared with wild-type (WT) mice in both PPE- and cigarette smoke-induced emphysema models. The PPE-induced increase in MMP-12 was attenuated in AIM$^{-/-}$ mice at both the mRNA and protein levels. According to in vitro experiments using AMs stimulated with cigarette smoke extract, the MMP-12 level was decreased in AIM$^{-/-}$ mice compared with WT mice. This decrease was reversed by the addition of recombinant AIM. Furthermore, an analysis of clinical samples showed that patients with COPD had a higher blood AIM/IgM ratio than healthy smokers. Additionally, the blood AIM/IgM ratio was positively associated with disease severity in patients with COPD. A higher AIM/IgM ratio was also associated with a shorter time to the first COPD exacerbation and higher all-cause and respiratory mortality.

Conclusions: AIM facilitates the development of COPD by upregulating MMP-12. Additionally, a higher blood AIM/IgM ratio was associated with poor prognosis in patients with COPD.

Trial registration: This clinical study, which included nonsmokers, healthy smokers, and smokers with COPD, was approved by the Ethics Committee of the Hokkaido University Hospital (012-0075, date of registration: September 5, 2012). The Hokkaido COPD cohort study was approved by the Ethics Committee of the Hokkaido University School of Medicine (med02-001, date of registration: December 25, 2002).

Keywords: Alveolar macrophage; Apoptosis inhibitor of macrophage; Chronic obstructive lung disease; Matrix metalloprotease-12.

Conflict of interest statement

The authors declare no competing interests.

- 60 references
- 6 figures

SUPPLEMENTARY INFO

Grant supportexpand

FULL TEXT LINKS

BMC Pulm Med

. 2023 Aug 17;23(1):304.
doi: 10.1186/s12890-023-02602-5.

Effect of fracture risk in inhaled corticosteroids in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis

Shisheng Peng[1], Cong Tan[1], Lirong Du[1], Yanan Niu[1], Xiansheng Liu[1,2], Ruiying Wang[3]
Affiliations expand

- PMID: 37592316
- PMCID: PMC10436625
- DOI: 10.1186/s12890-023-02602-5

Free PMC article

Abstract

Background: The fracture risk of patients with chronic obstructive pulmonary disease (COPD) treated with inhaled corticosteroids is controversial. And some large-scale randomized controlled trials have not solved this problem. The purpose of our systematic review and meta-analysis including 44 RCTs is to reveal the effect of inhaled corticosteroids on the fracture risk of COPD patients.

Methods: Two reviewers independently retrieved randomized controlled trials of inhaled corticosteroids or combinations of inhaled corticosteroids in the treatment of COPD from PubMed, Embase, Medline, Cochrane Library, and Web of Science. The primary outcome was a fracture event. This study was registered at PROSPERO (CRD42022366778).

Results: Forty-four RCTs were performed in 87,594 patients. Inhaled therapy containing ICSs (RR, 1.19; 95%CI, 1.04-1.37; P = 0.010), especially ICS/LABA (RR, 1.30; 95%CI, 1.10-1.53; P = 0.002) and triple therapy (RR, 1.49; 95%CI, 1.03-2.17; P = 0.04) were significantly associated with the increased risk of fracture in COPD patients when compared with inhaled therapy without ICSs. Subgroup analyses showed that treatment duration ≥ 12 months (RR, 1.19; 95%CI, 1.04-1.38; P = 0.01), budesonide therapy (RR, 1.64; 95%CI., 1.07-2.51; P = 0.02), fluticasone furoate therapy (RR, 1.37; 95%CI, 1.05-1.78; P = 0.02), mean age of study participants ≥ 65 (RR, 1.27; 95%CI, 1.01-1.61; P = 0.04), and GOLD stage III(RR, 1.18; 95%CI, 1.00-1.38; P = 0.04) were significantly associated with an increased risk of fracture. In addition, budesonide ≥ 320 ug bid via MDI (RR, 1.75; 95%CI, 1.07-2.87; P = 0.03) was significantly associated with the increased risk of fracture.

Conclusion: Inhalation therapy with ICSs, especially ICS/LABA or triple therapy, increased the risk of fracture in patients with COPD compared with inhaled therapy without ICS. Treatment duration, mean age of participants, GOLD stage, drug dosage form, and drug dose participated in this association. Moreover, different inhalation devices of the same drug also had differences in risk of fracture.

Keywords: COPD; Fracture; Inhaled glucocorticoids; Triple therapy.

Conflict of interest statement

The authors declare no competing interests.

- 71 references
- 10 figures

BMC Pulm Med

. 2023 Aug 17;23(1):302.
doi: 10.1186/s12890-023-02566-6.

Identifying critical inhalation technique errors in Dry Powder Inhaler use in patients with COPD based on the association with health status and exacerbations: findings from the multi-country cross-sectional observational PIFotal study

Janwillem Kocks[1,2,3,4], Sinthia Bosnic-Anticevich[5,6], Joyce van Cooten[7], Jaime Correia de Sousa[8], Biljana Cvetkovski[5], Richard Dekhuijzen[9], Lars Dijk[7], Marina Garcia Pardo[10], Asparuh Gardev[11], Radosław Gawlik[12], Iris van der Ham[7], Ymke Janse[7], Federico Lavorini[13], Tiago Maricoto[14], Jiska Meijer[7], Boyd Metz[7], David Price[15,16], Miguel Roman Rodriguez[10], Kirsten Schuttel[7], Nilouq Stoker[7], Ioanna Tsiligianni[17], Omar Usmani[18], Jaco Voorham[19], Marika T Leving[7]
Affiliations expand

- PMID: 37592263

- PMCID: PMC10433653

- DOI: 10.1186/s12890-023-02566-6

Free PMC article

Abstract

Background: Correct inhaler use depends on a complex interplay of factors, including device preparation and generating sufficient inspiratory flow. It is currently unknown which inhalation technique errors can be considered critical in Chronic Obstructive Pulmonary Disease (COPD) patients on Dry Powder Inhaler (DPI) maintenance therapy.

Objective: To investigate the association between inhalation technique errors and health status or exacerbations in patients with COPD. Additionally, the association between the number of errors and COPD outcomes was determined.

Methods: The PIFotal study is a cross-sectional multi-country observational study in a primary care setting, including 1434 COPD patients aged ≥ 40 years (50.1% female; mean age 69.2 yrs) using a DPI for their maintenance therapy. Inhalation technique was video recorded and scored by two independent researchers using inhaler-specific checklists. Health status was assessed with two questionnaires; the Clinical COPD Questionnaire (CCQ) and the COPD Assessment Test (CAT). The number of moderate and severe exacerbations in the past 12 months was recorded. Critical errors were identified based on their association with health status or exacerbations through multi-level prediction models adjusted for identified confounding.

Results: Errors in inhalation technique steps 'Breathe in', 'Hold breath', and 'Breathe out calmly after inhalation' were significantly associated with poorer CCQ and CAT outcomes and thus deemed critical. None of the errors were significantly associated with moderate exacerbations. Patients with errors 'Preparation', 'Hold inhaler in correct position during inhalation', and 'Breathe in' had significantly more severe exacerbations, and therefore these errors were also deemed critical. 81.3% of patients with COPD made at least one critical error. Specific combinations of errors were associated with worse outcomes. The more inhalation technique errors identified, the poorer the health status and the higher the exacerbation rate.

Conclusion: In this study, we identified multiple critical inhalation technique errors in COPD patients using DPIs each associated with poorer outcomes. Explorative analysis revealed that specific combinations of errors may be of clinical relevance, especially those related to the inhalation manoeuvre. COPD outcomes worsened with increasing error count. These results warrant further prospective longitudinal studies to establish the effect of correcting these errors on COPD control.

Trial registration: https://clinicaltrials.gov/ct2/show/NCT04532853 (31/08/2020).

Keywords: COPD health status; Chronic Obstructive Pulmonary Disease; Exacerbation; Inhaler errors; Inhaler technique.

Conflict of interest statement

JK reports grants, personal fees, and non-financial support from AstraZeneca, GSK, and Boehringer Ingelheim; grants and personal fees from Chiesi Pharmaceuticals and TEVA; grants from Mundipharma; personal fees from MSD and COVIS Pharma; and also holds 72.5% of shares in the General Practitioners Research Institute and 4% of shares in Lothar MedTec GmbH.
SB-A has received grants from TEVA, and personal fees from TEVA, Boehringer Ingelheim, AstraZeneca, GSK, Sanofi and Mylan.
JCdS reports or personal fees from AstraZeneca, Bial, Boehringer Ingelheim, GSK, Medinfar, Mundipharma and Sanofi.
BC received an honorarium from GSK and Sanofi.
JvC, LD, IvdH, YJ, BM, KS, NS, TM, BM, ML were employed by General Practitioners Research Institute (GPRI) at the time of the study. In the past three years (2020–2023), GPRI conducted investigator- and sponsor-initiated research funded by non-commercial organizations, academic institutes, and pharmaceutical companies (including AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Mundipharma, Novartis, Teva, Valneva, Eli Lilly and G3P).
RD has received grants and personal fees from TEVA, Boehringer Ingelheim, AstraZeneca, GSK, Chiesi, Focus Care, and Glenmark.
RG has received personal fees from AstraZeneca, GSK, and Chiesi.
MGP receives grants from AstraZeneca, GSK and Boehringer Ingelheim.
AG is an employee of Boehringer Ingelheim.
FL received grants and personal fees from GSK, personal fees from AstraZeneca, Boehringer Ingelheim, Chiesi, Menarini International, Novartis, Orion, and Trudell International, outside the submitted work.
TM has no competing interests to declare.
JM received grants from Boehringer Ingelheim, during the conduct of the study; and grants from AstraZeneca, Chiesi, Novartis, and GSK, outside the submitted work.
DP reports grants and personal fees from AstraZeneca, Boehringer Ingelheim, Chiesi, Mylan, Novartis, Regeneron Pharmaceuticals, Sanofi Genzyme, Theravance and Zentiva (Sanofi Generics); grants from the British Lung Foundation, Respiratory Effectiveness Group, UK National Health Service, and AKL Research and Development Ltd; personal fees from Cipla, GlaxoSmithKline, Kyorin, Merck, Mundipharma, Airway Vista Secretariat, EPG Communication Holdings Ltd, FIECON Ltd, Fieldwork International, OM Pharma SA, PeerVoice, Phadia AB, Spirosure Inc, Strategic North Limited, Synapse Research Management Partners S.L., Talos Health Solutions, and WebMD Global LLC; non-financial support from Efficacy and Mechanism Evaluation programme and Health Technology Assessment; stock/stock options from AKL Research and Development Ltd, which produces phytopharmaceuticals; owns 74% of the social enterprise Optimum Patient Care Ltd (Australia and UK) and 92.61% of Observational and Pragmatic Research Institute Pte Ltd (Singapore); and 5% shareholding in Timestamp, which develops adherence monitoring technology.
MR-R receives grants and personal fees from AstraZeneca and GSK; and personal fees from Boehringer Ingelheim, Chiesi, Menarini, Mundipharma, Novartis, Pfizer, TEVA and BIAL.

IT reports grants and personal fees from GSK, AstraZeneca, Boehringer Ingelheim, Menarini, Novartis, Chiesi and Elpen.
OU reports grants and personal fees from AstraZeneca, Boehringer Ingelheim, Edmond Pharma, Chiesi and GSK; grants from Edmond Pharma; and personal fees from Napp, Mundipharma, Sandoz, Takeda, Cipla, COVIS, Novartis, Mereobiopharma, Orion, and Menarini.
JV has no competing interests to declare.

- 33 references
- 7 figures

SUPPLEMENTARY INFO

Associated dataexpand

Editorial

Thorax
. 2023 Aug 17;thorax-2023-220458.
doi: 10.1136/thorax-2023-220458. Online ahead of print.

Reimagining emphysema for a computational age

Joseph Jacob[1,2]
Affiliations expand

- PMID: 37591700
- DOI: 10.1136/thorax-2023-220458

No abstract available

Keywords: COPD Pathology; Emphysema; Imaging/CT MRI etc.

Conflict of interest statement

Competing interests: JJ declares fees from Boehringer Ingelheim, F. Hoffmann-La Roche, GlaxoSmithKline, NHSX and Takeda. Grant Funding from GlaxoSmithKline, Wellcome Trust and Microsoft Research. Patents: UK patent application numbers 2113765.8 and GB2211487.0.

Editorial

Eur Respir J

. 2023 Aug 17;62(2):2301076.

doi: 10.1183/13993003.01076-2023. Print 2023 Aug.

Palliative care in COPD and ILD: a call for action

Marlies Wijsenbeek[1], Claudia Valenzuela[2], Anne Holland[3]

Affiliations expand

- PMID: 37591552

- DOI: 10.1183/13993003.01076-2023

No abstract available

Conflict of interest statement

Conflict of interest: M. Wijsenbeek reports grants from The Netherlands Organisation for Health Research and Development, The Dutch Lung Foundation, The Dutch Pulmonary Fibrosis Organization, Sarcoidosis.nl, Boehringer Ingelheim, Hoffman la Roche and AstraZeneca-Daiichi, consulting fees from Bristol Myers Squibb, Boehringer Ingelheim, Galapagos, Galecto, Hoffman la Roche, Horizon Therapeutics, Kinevant Sciences, Molecure, Nerre Therapeutics, Novartis, PureTech Health, Thyron, Trevi and Vicore, lecture honoraria from Boehringer Ingelheim, CSL Behring, Hoffman la Roche and Novartis, travel support from Boehringer Ingelheim, Hoffman la Roche and Galapagos, advisory board participation with Savara and Galapagos, leadership roles as Chair of the Idiopathic Interstitial Pneumonia group of the European Respiratory Society, member of the board of the Netherlands Respiratory Society, member of the scientific advisory board of the European Idiopathic Pulmonary Fibrosis and related disorders federation, and chair of the educational committee of the European Reference Network for rare Lung Diseases, and is a member of the advisory board of the Dutch Lung Fibrosis and Sarcoidosis patient associations, outside the submitted work. C. Valenzuela reports consulting fees from Boehringer Ingelheim, Hoffmann-La Roche Ltd and BMS, and lecture honoraria and travel support from Boehringer Ingelheim, outside the submitted work. A. Holland reports grants from Medical Research Future Fund, Australia, National Health and Medical Research Council, Australia, and iCare NSW, Australia, and a leadership role as President, Thoracic Society of Australia and New Zealand, outside the submitted work.

Comment on

- European Respiratory Society clinical practice guideline: palliative care for people with COPD or interstitial lung disease.
  Janssen DJA, Bajwah S, Boon MH, Coleman C, Currow DC, Devillers A, Vandendungen C, Ekström M, Flewett R, Greenley S, Guldin MB, Jácome C, Johnson MJ, Kurita GP, Maddocks M, Marques A, Pinnock H, Simon ST, Tonia T, Marsaa K.Eur Respir J. 2023 Aug 17;62(2):2202014. doi: 10.1183/13993003.02014-2022. Print 2023 Aug.PMID: 37290789

Review

Eur Respir J

. 2023 Aug 17;62(2):2300115.
doi: 10.1183/13993003.00115-2023. Print 2023 Aug.

Simplifying pharmacotherapy for patients with COPD: a viewpoint

Bartolome Celli[1], Jørgen Vestbo[2]
Affiliations expand

- PMID: 37591551

- DOI: 10.1183/13993003.00115-2023

No abstract available

Conflict of interest statement

Conflict of interest: J. Vestbo has received consulting fees from AstraZeneca for serving on a trial steering committee, and has received payment or honoraria for presenting at meetings from ALK-Abello, AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, and Teva. B. Celli reports receiving personal fees from GlaxoSmithKline without time limit for support for the present manuscript, and personal fees from GlaxoSmithKline, AstraZeneca, Boehringer Ingelheim, Novartis, Sanofi Aventis and Menarini for consulting services rendered in the past 36 months.

Ann Am Thorac Soc
.
. 2023 Aug 17.
doi: 10.1513/AnnalsATS.202304-391CME. Online ahead of print.

Supplemental Oxygen Therapy in Interstitial Lung Disease: A Narrative Review

Kristopher P Clark[1], Howard B Degenholtz[2], Kathleen O Lindell[3], Daniel J Kass[4]
Affiliations expand

- PMID: 37590496

- DOI: 10.1513/AnnalsATS.202304-391CME

Abstract

Patients with interstitial lung diseases (ILD) often have hypoxemia at rest and/or with exertion for which supplemental oxygen is commonly prescribed. The number of patients with ILD who require supplemental oxygen is unknown though estimates suggest it could be as much as 40%, many of whom may require high flow support (>4 L/min). Despite its frequent use, there is limited evidence for supplemental oxygen's impact on clinical outcomes in ILD with recommendations for its use primarily based on older studies in patients with chronic obstructive pulmonary disease (COPD). Oxygen use in ILD is rarely included as an outcome in clinical trials. Available evidence suggests that supplemental oxygen in ILD may improve quality of life and some exercise parameters in patients whose hypoxemia is a limiting factor; however, oxygen therapy also places new burdens and barriers on some patients that may counter its beneficial effects. The cost of supplemental oxygen in ILD is also unknown but likely represents a significant portion of overall healthcare costs in these patients. Current Centers for Medicare and Medicaid (CMS) reimbursement policies provides only modest increase in payment for high oxygen flows which may negatively impact access to oxygen services and equipment for some ILD

patients. Future studies should examine clinical and quality of life outcomes for oxygen use in ILD. In the meantime, given the current limited evidence for supplemental oxygen and considering cost factors and other barriers, providers should take a patient-focused approach when considering supplemental oxygen prescriptions in patients with ILD.

Eur Respir J

. 2023 Aug 17;62(2):2300442.

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European Respiratory Society statement on frailty in adults with chronic lung disease

Christian R Osadnik[1,2], Lisa J Brighton[3,4], Chris Burtin[5], Matteo Cesari[6], Lies Lahousse[7], Will D C Man[8,9,10], Alessandra Marengoni[11,12], Andreja Sajnic[13], Jonathan P Singer[14], Lies Ter Beek[15], Ioanna Tsiligianni[16], Janos T Varga[17,18], Stefano Pavanello[19], Matthew Maddocks[3]

Affiliations expand

- PMID: 37414420

- DOI: 10.1183/13993003.00442-2023

Abstract

Frailty is a complex, multidimensional syndrome characterised by a loss of physiological reserves that increases a person's susceptibility to adverse health outcomes. Most knowledge regarding frailty originates from geriatric medicine; however, awareness of its importance as a treatable trait for people with chronic respiratory disease (including asthma, COPD and interstitial lung disease) is emerging. A clearer understanding of frailty

and its impact in chronic respiratory disease is a prerequisite to optimise clinical management in the future. This unmet need underpins the rationale for undertaking the present work. This European Respiratory Society statement synthesises current evidence and clinical insights from international experts and people affected by chronic respiratory conditions regarding frailty in adults with chronic respiratory disease. The scope includes coverage of frailty within international respiratory guidelines, prevalence and risk factors, review of clinical management options (including comprehensive geriatric care, rehabilitation, nutrition, pharmacological and psychological therapies) and identification of evidence gaps to inform future priority areas of research. Frailty is underrepresented in international respiratory guidelines, despite being common and related to increased hospitalisation and mortality. Validated screening instruments can detect frailty to prompt comprehensive assessment and personalised clinical management. Clinical trials targeting people with chronic respiratory disease and frailty are needed.

Conflict of interest statement

Conflict of interest: The task force members report no conflicts of interest for the present work, but acknowledge the following roles and funding sources during the conduct of this work. C.R. Osadnik received a Rebecca L. Cooper Medical Research Foundation project grant (2020–21) and an education grant from GSK Australia, paid to his institution, and delivered an educational lecture for Novartis Australia, all outside of the present work. L.J. Brighton is supported by the NIHR Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust, and is funded by an Economic and Social Research Council Post-Doctoral Fellowship (ES/X005259/1). L. Lahousse reports external expert consultation for AstraZeneca and lectures for Chiesi and IPSA vzw, a non-profit organisation facilitating lifelong learning for healthcare providers, (to be) paid to her institution, outside this manuscript. W.D.C. Man is supported by National Institute for Health and Care Research (NIHR) Research for Patient Benefit awards (PB-PG-0816-20022 and PB-PG-0317-20032) and a NIHR Artificial Intelligence Award (AI_AWARD02204). A. Marengoni received fees for lectures provided to Vyvamed and Oliba. A. Sajnic reports advisory board membership for AstraZeneca and delivery of a lecture for Roche. J.P. Singer reports funding (NHLBI U01HL163242, U01HL145435, R01HL134851) and scientific advisory board membership for Altavant Sciences and Mallinckrodt Pharmaceuticals. I. Tsiligianni reports grants/advisory boards all unrelated to the current work from Novartis, GSK, Boehringer Ingelheim, AstraZeneca and Chiesi. J.T. Varga reports unrelated grants/advisory boards from Chiesi and Boehringer Ingelheim. S. Pavanello is president of Unione Trapiantati Polmone, Padua, Italy. M. Maddocks is supported by a National Institute for Health and Care Research (NIHR) Career Development Fellowship (CDF-2017–10-009) and the NIHR Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust. The remaining authors have no potential conflicts of interest to disclose.

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European Respiratory Society clinical practice guideline: palliative care for people with COPD or interstitial lung disease

Daisy J A Janssen[1,2], Sabrina Bajwah[3], Michele Hilton Boon[4], Courtney Coleman[5], David C Currow[6], Albert Devillers[7], Chantal Vandendungen[7], Magnus Ekström[8], Ron Flewett[9], Sarah Greenley[10], Mai-Britt Guldin[11], Cristina Jácome[12], Miriam J Johnson[13], Geana Paula Kurita[14,15], Matthew Maddocks[3], Alda Marques[16], Hilary Pinnock[17], Steffen T Simon[18], Thomy Tonia[19], Kristoffer Marsaa[20]

Affiliations expand

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Abstract

There is increased awareness of palliative care needs in people with COPD or interstitial lung disease (ILD). This European Respiratory Society (ERS) task force aimed to provide

recommendations for initiation and integration of palliative care into the respiratory care of adult people with COPD or ILD. The ERS task force consisted of 20 members, including representatives of people with COPD or ILD and informal caregivers. Eight questions were formulated, four in the Population, Intervention, Comparison, Outcome format. These were addressed with full systematic reviews and application of Grading of Recommendations Assessment, Development and Evaluation for assessing the evidence. Four additional questions were addressed narratively. An "evidence-to-decision" framework was used to formulate recommendations. The following definition of palliative care for people with COPD or ILD was agreed. A holistic and multidisciplinary person-centred approach aiming to control symptoms and improve quality of life of people with serious health-related suffering because of COPD or ILD, and to support their informal caregivers. Recommendations were made regarding people with COPD or ILD and their informal caregivers: to consider palliative care when physical, psychological, social or existential needs are identified through holistic needs assessment; to offer palliative care interventions, including support for informal caregivers, in accordance with such needs; to offer advance care planning in accordance with preferences; and to integrate palliative care into routine COPD and ILD care. Recommendations should be reconsidered as new evidence becomes available.

Conflict of interest statement

Conflict of interest: D.J.A. Janssen reports lecture fees from Boehringer Ingelheim (personal), Chiesi (non-personal), AstraZeneca (non-personal) and Abbott (non-personal) within the previous three years outside the submitted work. Conflict of interest: C. Coleman is an employee of the European Lung Foundation. Conflict of interest: D.C. Currow has received intellectual property payments and consultancy fees from Mayne Pharma International Pty Ltd, manufacturers of Kapanol and is a paid adviser to Helsinn Pharmaceuticals. Conflict of interest: G.P. Kurita has received grants from Novo Nordisk Foundation, the Danish Cancer Society and European Commission outside the submitted work. Conflict of interest: M. Maddocks is supported by the National Institute for Health and Care Research (NIHR) Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust; the views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care. Conflict of interest: H. Pinnock has received speaker fees from Boehringer Ingelheim, Teva, and Sandoz for non-promotional talks on digital respiratory health and asthma supported selfmanagement. Conflict of interest: T. Tonia is a methodologist for the European Respiratory Society. Conflict of interest: K. Marsaa reports lecture fees from Astellas Pharma, GlaxoSmithKline, AstraZeneca, Novartis, Boehringer Ingelheim, Kyowa Kirin, Norgine, Roche, Bristol-Myers Squibb, Chiesi Pharma outside the submitted work. Conflict of interest: All other panellists have no conflicts of interest to report.

Comment in

- Palliative care in COPD and ILD: a call for action.
  Wijsenbeek M, Valenzuela C, Holland A.Eur Respir J. 2023 Aug 17;62(2):2301076. doi: 10.1183/13993003.01076-2023. Print 2023 Aug.PMID: 37591552 No abstract available.

J Allergy Clin Immunol

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Polygenic risk scores identify heterogeneity in asthma and chronic obstructive pulmonary disease

Matthew Moll[1], Joanne E Sordillo[2], Auyon J Ghosh[3], Lystra P Hayden[4], Gregory McDermott[5], Michael J McGeachie[6], Amber Dahlin[6], Anshul Tiwari[6], Monica G Manmadkar[6], Eric D Abston[7], Chandan Pavuluri[1], Aabida Saferali[6], Sofina Begum[6], John P Ziniti[6], Amund Gulsvik[8], Per S Bakke[8], Hugues Aschard[9], Carlos Iribarren[10], Craig P Hersh[1], Jeffrey A Sparks[5], Brian D Hobbs[1], Jessica A Lasky-Su[6], Edwin K Silverman[6], Scott T Weiss[6], Ann Chen Wu[2], Michael H Cho[1]
Affiliations expand

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Abstract

Rationale: Asthma and chronic obstructive pulmonary disease (COPD) have distinct and overlapping genetic and clinical features.

Objectives: We hypothesized that polygenic risk scores (PRSs) for asthma (PRS_{Asthma}) and spirometry (FEV_1 and FEV_1/FVC; PRS_{spiro}) would demonstrate differential associations with asthma, COPD, and asthma-COPD overlap (ACO).

Methods: We developed and tested two asthma PRSs and applied the higher performing PRS_{Asthma} and a previously-published PRS_{spiro} to research (COPDGene and CAMP, with spirometry) and electronic-health record (EHR)-based (MGB Biobank and GERA) studies. We assessed the association of PRSs with COPD and asthma using modified random and binary effects meta-analyses, and ACO and asthma exacerbations in specific cohorts. Models were adjusted for confounders and genetic ancestry.

Measurements and main results: In meta-analyses of 102,477 participants, the PRS_{Asthma} (OR per SD 1.16 [95% CI: 1.14-1.19]) and PRS_{spiro} (OR per SD 1.19 [95% CI: 1.17-1.22]) both predicted asthma, while the PRS_{spiro} predicted COPD (OR per SD 1.25 [95% CI: 1.21-1.30]). However, results differed by cohort. The PRS_{spiro} was not associated with COPD in GERA and MGB. In COPDGene, the PRS_{Asthma} (OR per SD: Whites: 1.3; African Americans (AA): 1.2) and PRS_{spiro} (OR per SD: Whites: 2.2; AA: 1.6) were both associated with ACO. In GERA, the PRS_{Asthma} was associated with asthma exacerbations (OR 1.18) in whites; the PRS_{spiro} was associated with asthma exacerbations in white, LatinX, and East Asian participants.

Conclusions: Polygenic risk scores for asthma and spirometry are both associated with asthma-COPD overlap and asthma exacerbations. Genetic prediction performance differs in research versus EHR-based cohorts.

Keywords: asthma; asthma-COPD overlap; chronic obstructive pulmonary disease; heterogeneity; polygenic risk scores.

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Short-term exposure to ultrafine particles and mortality and hospital admissions due to respiratory and cardiovascular diseases in Copenhagen, Denmark

Marie L Bergmann[1], Zorana J Andersen[1], Andreas Massling[2], Paula A Kindler[3], Steffen Loft[1], Heresh Amini[4], Thomas Cole-Hunter[1], Yuming Guo[5], Matija Maric[1], Claus Nordstrøm[2], Mahmood Taghavi[1], Stéphane Tuffier[1], Rina So[1], Jiawei Zhang[1], Youn-Hee Lim[6]
Affiliations expand

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Abstract

Ultrafine particles (UFP; particulate matter <0.1 µm in diameter) may be more harmful to human health than larger particles, but epidemiological evidence on their health effects is still limited. In this study, we examined the association between short-term exposure to UFP and mortality and hospital admissions in Copenhagen, Denmark. Daily concentrations of UFP (measured as particle number concentration in a size range 11-700 nm) and meteorological variables were monitored at an urban background station in central Copenhagen during 2002-2018. Daily counts of deaths from all non-accidental causes, as well as deaths and hospital admissions from cardiovascular and respiratory diseases were obtained from Danish registers. Mortality and hospital admissions associated with an interquartile range (IQR) increase in UFP exposure on a concurrent day and up to six preceding days prior to the death or admission were examined in a case-crossover study design. Odds ratios (OR) with 95% confidence intervals (CI) per one IQR increase in UFP were estimated after adjusting for temperature and relative humidity. We observed 140,079 deaths in total, 236,003 respiratory and 342,074 cardiovascular hospital admissions between 2002 and 2018. Hospital admissions due to respiratory and cardiovascular diseases were significantly positively associated with one IQR increase in UFP (OR: 1.04 [95% CI: 1.01, 1.07], lag 0-4, and 1.02 [1.00, 1.04], lag 0-1, respectively). Among the specific

causes, the strongest associations were found for chronic obstructive pulmonary disease (COPD) mortality and asthma hospital admissions and two-day means (lag 0-1) of UFP (OR: 1.13 [1.01, 1.26] and 1.08 [1.00, 1.16], respectively, per one IQR increase in UFP). Based on 17 years of UFP monitoring data, we present novel findings showing that short-term exposure to UFP can trigger respiratory and cardiovascular diseases mortality and morbidity in Copenhagen, Denmark. The strongest associations with UFP were observed with COPD mortality and asthma hospital admissions.

Keywords: Air pollution; Cardiovascular diseases; Mortality; Particle number concentration; Respiratory tract diseases; Ultrafine particles.

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.

Immune treatment tackles chronic obstructive pulmonary disease

John V Fahy, Richard M Locksley

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- DOI: 10.1038/d41586-023-02517-5

No abstract available

Keywords: Immunology; Medical research.

- 11 references

SUPPLEMENTARY INFO

Publication typesexpand

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17

Meta-Analysis

Sci Rep

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doi: 10.1038/s41598-023-40489-8.

Efficacy and safety of inhaled heparin in asthmatic and chronic obstructive pulmonary disease patients: a systematic review and a meta-analysis

Rasha Ashmawy[1], Adel Zaki[2], Ayman Baess[3], Iman El Sayed[4]

Affiliations expand

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Free PMC article

Abstract

Asthma and chronic obstructive pulmonary disease (COPD) are prevalent chronic respiratory disorders that cause significant morbidity and mortality. Some studies evaluated the use of inhaled unfractionated heparin (UFH) in the treatment of asthma and COPD. We aimed to synthesize the available evidence for the efficacy and safety of inhaled heparin in improving lung functions among asthmatic and COPD patients. A comprehensive search was performed using Pubmed, Embase, EBSCO, Scopus, Web of Science, Cochrane CENTRAL, WHO Clinical trials, clinicaltrials.gov, Iranian Clinical trials, Google Scholar, Research Gate, ProQuest Thesis, OVID, and medRxiv databases. Two independent reviewers included all pertinent articles according to PRISMA guidelines, and extract data independently. The two reviewers checked the quality of studies using the ROB2 tool. To determine the pooled effect estimate of the efficacy and safety of inhaled heparin, a meta-analysis was carried out using the R programming language. Publication bias was evaluated using Egger's regression test. The heterogeneity was explained using a meta-regression, and the quality of evidence was assessed by the GRADE approach. Twenty-six studies with a total of 581 patients were included in the qualitative analysis and 16 in the meta-analysis. The primary outcome was treatment success (improvement of lung function) that was measured by standardized mean differences (SMD) of the forced expiratory volume per second (FEV1) either per ml or percentage. Heparin has a large effect on both FEV1% and FEV1 ml when compared to the control group (SMD 2.7, 95% CI 1.00; 4.39; GRADE high, SMD 2.12, 95% CI - 1.49; 5.72: GRADE moderate, respectively). Secondary outcomes are other lung functions improving parameters such as PC20 (SMD 0.91, 95% CI - 0.15; 1.96). Meta-regression and subgroup analysis show that heparin type, dose, year of publication, study design, and quality of studies had a substantial effect. Regarding safety, inhaled heparin showed a good coagulation profile and mild tolerable side effects. Inhaled heparin showed improvement in lung functions either alone or when added to standard care. More large parallel RCTs are needed including COPD patients, children, and other types, and stages of asthmatic patients.

Conflict of interest statement

The authors declare no competing interests.

- 69 references
- 5 figures

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Does COPD Originate from Different Cell Types?

Yohannes Tesfaigzi[1], Jeffrey L Curtis[2], Irina Petrache[3], Francesca Polverino[4,5], Farrah Kheradmand[6], Ian M Adcock[7], Stephen I Rennard[8]
Affiliations expand

- PMID: 37584669

- DOI: 10.1165/rcmb.2023-0175PS

Abstract

The onset of chronic obstructive pulmonary disease (COPD) is heterogeneous, and current approaches to define distinct disease phenotypes are lacking. In addition to clinical methodologies, subtyping COPD has also been challenged by the reliance on human lung samples from late-stage diseases. Different COPD phenotypes may be initiated from the susceptibility of different cell types to cigarette smoke, environmental pollution, and infections at early stages that ultimately converge at later stages in airway remodeling and destruction of the alveoli when the disease is diagnosed. This perspective provides discussion points on how studies to date define different cell types of the lung that can initiate COPD pathogenesis, focusing on the susceptibility of macrophages, T and B cells,

mast cells, dendritic cells, endothelial and airway epithelial cells. Additional cell types, including fibroblasts, smooth muscle, neuronal, or other rare cell types, not covered here, may also play a role in orchestrating COPD. Here we discuss current knowledge gaps, such as, which cell types drive distinct disease phenotypes and/or stages of the disease, and which cells are primarily affected by the genetic variants identified by whole genome-wide association studies. Applying new technologies that interrogate the functional role of a specific cell type or a combination of cell types as well as single-cell transcriptomics and proteomic approaches are creating new opportunities to understand and clarify the pathophysiology and thereby the clinical heterogeneity of COPD.

Keywords: gene-and-environment interaction; lung cell types , single nucleotide polymorphysims , single-cell transcriptomics , lineage tracing.

19

Curr Med Res Opin

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Mortality risk reduction with budesonide/glycopyrrolate/formoterol fumarate versus fluticasone furoate/umeclidinium/vilanterol in COPD: a matching-adjusted indirect comparison based on ETHOS and IMPACT

Daiana Stolz[1], Erik Hermansson[2], Mario Ouwens[2], Barinder Singh[3], Akanksha Sharma[3], Dan Jackson[4], Patrick Darken[5], Jonathan Marshall[4], Karin Bowen[5], Hana Müllerová[4], Bernardino Alcázar Navarrete[6,7], Richard Russell[8], MeiLan K Han[9], Deniz Tansey-Dwyer[4]

Affiliations expand

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- DOI: 10.1080/03007995.2023.2247969

Abstract

Objective: Chronic obstructive pulmonary disease (COPD) is a leading cause of death worldwide. While two approved fixed-dose inhaled corticosteroid/long-acting muscarinic antagonist (LAMA)/long-acting β_2-agonist (LABA) triple therapies reduce all-cause mortality (ACM) versus dual LAMA/LABA therapy in patients with COPD, head-to-head studies have not compared the effects of these therapies on ACM. We compared ACM in adults with moderate-to-very severe COPD receiving budesonide/glycopyrrolate/formoterol fumarate (BGF) in ETHOS versus fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) in IMPACT using a matching-adjusted indirect comparison (MAIC).

Methods: A systematic literature review identified two studies (ETHOS [NCT02465567]; IMPACT [NCT02164513]) of ≥52 weeks reporting ACM as an efficacy endpoint in patients receiving triple therapy. As ETHOS and IMPACT lack a common comparator, an unanchored MAIC compared ACM between licensed doses of BGF (320/18/9.6 µg) from ETHOS and FF/UMEC/VI (100/62.5/25 µg) from IMPACT in patients with moderate-to-very severe COPD. Using on- and off-treatment data from the final retrieved datasets of the intention-to-treat populations, BGF data were adjusted according to aggregate FF/UMEC/VI data using 11 baseline covariates; a supplementary unadjusted indirect treatment comparison was also conducted. *P*-values for these post-hoc analyses are not adjusted for Type I error.

Results: ACM over 52 weeks was statistically significantly reduced by 39% for BGF versus FF/UMEC/VI in the MAIC (hazard ratio [HR] [95% CI]: 0.61 [0.38, 0.95], $P = 0.030$) and unadjusted analysis (HR [95% CI]: 0.61 [0.41, 0.92], $P = 0.019$).

Conclusion: In this MAIC, which adjusted for population heterogeneity between ETHOS and IMPACT, ACM was significantly reduced with BGF versus FF/UMEC/VI in patients with moderate-to-very severe COPD.

Keywords: All-cause mortality; Budesonide/glycopyrrolate/formoterol fumarate; Chronic obstructive pulmonary disease; Fixed-dose; Fluticasone furoate/umeclidinium/vilanterol; Inhaled corticosteroid/long-acting muscarinic antagonist/long-acting β2-agonist; Matching-adjusted indirect comparison; single-inhaler triple therapy.

Plain language summary

Chronic obstructive pulmonary disease (known as COPD) is a leading cause of death worldwide, being responsible for over 3 million deaths in 2019. People living with COPD are more likely to die. Importantly, a sudden worsening of COPD symptoms (known as an exacerbation) is associated with a higher chance of death from heart-related and breathing-related problems. Therefore, reducing risk of death is an important treatment goal for COPD. Of the three medications approved for treating COPD that combine three drugs in a single-inhaler device, there are two—referred to generically as budesonide/glycopyrrolate/formoterol fumarate (BGF) and fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI)—that can reduce the risk of death in people living with COPD compared with treatments that combine two drugs. However, no studies have directly compared the risk of death in people living with COPD treated with these medicines. We compared the risk of death in people living with moderate-to-very severe COPD who received either BGF during a clinical trial called ETHOS or FF/UMEC/VI during a clinical trial called IMPACT. To make this comparison, we used a method called "matching-adjusted indirect comparison", which used specific features (such as sex, breathing difficulty, and whether they were current smokers) to match patients from the two studies to ensure similar groups were examined. Our analysis showed a 39% decrease in the chance of death in patients who received BGF compared with patients who received FF/UMEC/VI. This finding may be important for doctors to improve patient health and reduce the risk of death in people living with COPD.

Observational Study

BMC Psychiatry

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Validation of the Generalized Anxiety Disorder-7 in patients with COPD: a cross-sectional study

Meishan Liu[1], Dong Wang[2], Jiexin Fang[2], Yuhan Chang[1], Yongdong Hu[3], Kewu Huang[4]
Affiliations expand

- PMID: 37582707

- PMCID: PMC10428582

- DOI: 10.1186/s12888-023-05072-5

Free PMC article

Abstract

Background: Patients with chronic obstructive pulmonary disease (COPD) often have comorbid generalized anxiety disorder (GAD), which requires early screening in respiratory clinics. The Generalized Anxiety Disorder-7 (GAD-7) questionnaire is a brief and commonly used screening tool for GAD but has not been validated among patients with COPD in China.

Methods: Stable patients with COPD from a cross-sectional observational study were assessed using the GAD-7 questionnaire and then assessed by a senior psychiatrist to confirm a diagnosis of GAD according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Demographic characteristics, spirometry, and patient-reported outcomes were collected. Cronbach's α coefficient was calculated, and receiver operating curve (ROC) analysis was performed to validate the GAD-7.

Results: A total of 226 patients with COPD were enrolled, and 50 (22.1%) of these patients were diagnosed with GAD. The Cronbach's α coefficient for the GAD-7 was 0.869, which indicated good internal consistency. ROC curve analysis showed that the GAD-7 had an area under the curve (AUC) value of 0.829 (95% CI: 0.774-0.876) for identifying GAD. The optimal cut-off score was ≥ 4, with a sensitivity of 66.0% and a specificity of 89.2%. Higher GAD-7 scores were significantly associated with health-related quality of life and the symptom burden of COPD. The discriminatory power of GAD-7 did not differ statistically when stratified by COPD severity.

Conclusions: The GAD-7 was shown to be a reliable and valid screening tool for patients with COPD in China, and its screening performance for GAD was not influenced by disease severity.

Keywords: Chronic obstructive pulmonary disease; GAD-7; Generalized anxiety disorder; Screening; Validation.

Conflict of interest statement

The authors declare no competing interests.

- 45 references
- 2 figures

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Observational Study

PLoS One
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Follow-up evaluation of pulmonary function and computed tomography findings in chronic kidney disease patients after COVID-19 infection

Solos Jaturapisanukul[1], Nadwipa Yuangtrakul[1], Dearada Wangcharoenrung[1], Krongkan Kanchanarat[1], Kan Radeesri[1], Jakravoot Maneerit[1], Anan Manomaipiboon[1], Khemika Rojtangkom[2], Chompoonuth Ananthanalapa[2], Siwaporn Rungrojthanakit[1], Peerawit Thinpangnga[1], Joshua Alvior[3], Thananda Trakarnvanich[1]
Affiliations expand

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- PMCID: PMC10427007

- DOI: 10.1371/journal.pone.0286832

Free PMC article

Abstract

Pulmonary complications are common after SARS-CoV2- infection. However, data on pulmonary sequelae of COVID-19 after recovery in dialysis patients are limited. We determined the prevalence of abnormal lung function tests and CT findings and investigate the association factors impacting pulmonary dysfunction. This prospective observational cohort study enrolled 100 patients with stage 5 chronic kidney disease (CKD) undergoing dialysis who had recovered from COVID-19 for ≥3 months. Pulmonary function test (PFT) and chest computed tomography (CT) were performed. Demographic data and laboratory results were recorded. The mean patient age was 55.15 ± 12.84 years. Twenty-one patients (21%) had severe COVID-19, requiring mechanical ventilation or oxygen supplementation. Pulmonary function tests revealed a restrictive pattern in 41% (95% confidence interval [CI], 31.73-50.78;) and an obstructive pattern in 7.29% (95% CI, 3.19-13.25) patients. The severe group showed PFT test results similar to the non-severe group, with three patients showing severe obstructive lung disease. The CT scan findings included reticulation (64%), multifocal parenchymal band (43%), ground glass opacities (32%), and bronchiectasis (28%). The median total CT score was 3 (interquartile range, 1-8.5). The CT score and PFT findings showed no association with pulmonary dysfunction extent, except in bronchiectasis. Lung function indices were associated with abnormal CT findings. Abnormal CT findings (bronchiectasis, reticulation, and ground-glass opacities) was associated with higher oxygen requirements than normal CT findings ($p = 0.008$, bronchiectasis; $p = 0.041$, reticulation; $p = 0.032$, ground-glass appearance). Aside from CT findings and CRP levels, no significant lung abnormalities were observed in severe and non-severe patients. Some patients had residual symptoms at follow-up. The findings indicate persistence of both radiological and physiological abnormalities in dialysis patients after COVID-19. However, the prevalence of these abnormalities was comparable to that in the normal population; few patients experienced ongoing symptoms. Follow-up observations and evaluations are warranted. Trial registration. Clinicaltrials.gov Identifier: NCT05348759.

Conflict of interest statement

The authors declare no competing interests.

- 32 references
- 3 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated data, Grant supportexpand

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22
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doi: 10.5152/ThoracResPract.2023.23040. Online ahead of print.

Adding Non-Invasive Positive Pressure Ventilation to Supplemental Oxygen During Exercise Training in Severe Chronic Obstructive Pulmonary Disease: A Randomized Controlled Study

Sami Deniz[1], Şenay Tuncel[2], Alev Gürgün[3], Funda Elmas[3]
Affiliations expand

- PMID: 37581377

- DOI: 10.5152/ThoracResPract.2023.23040

Abstract

Objective: Chronic obstructive pulmonary disease is currently the fourth leading cause of death in the world. Pulmonary rehabilitation is recommended for chronic obstructive pulmonary disease.

Material and methods: This study aimed to evaluate the effects of non-invasive ventilation, supplemental oxygen, and exercise training and supplemental oxygen during exercise training during pulmonary rehabilitation practice in comparison with only exercise training on lung functions, blood gases, lactate levels, respiratory muscle pressures, dyspnea, walking distances, quality of life, and depression in patients with severe chronic obstructive pulmonary disease. The main outcome measure is exercise capacity (6-minute walk test), and the secondary end-point included quality of life.

Results: Thirty-five patients (mean ± SD age, 65.4 ± 6.5 years) with a mean bronchodilator forced expiratory volume in the first second of expiration of 39.4 ± 7%, undergoing an 8-week outpatient pulmonary rehabilitation, were randomized to either non-invasive ventilation, supplemental oxygen, and exercise training, supplemental oxygen during exercise training, or exercise training groups. The improvements in respiratory muscle strength were higher in non-invasive ventilation, supplemental oxygen, and exercise training patients than the moderate improvements in the exercise training group. Both non-invasive ventilation, supplemental oxygen, and exercise training and supplemental oxygen during exercise training groups showed significant increases in the 6-minute walk test and incremental shuttle walk test. However, the increase in walking distance was better in non-invasive ventilation, supplemental oxygen, and exercise training group (69.8 ± 53.2 m in 6-minute walk test and 66.6 ± 65.2 m in incremental shuttle walk test, P = .001 and P = .005, respectively) compared to supplemental oxygen during exercise training group (42.5+55.5 m in 6-minute walk test and 53.5+70.2 m in incremental shuttle walk test, P = .01 each, respectively). The total St. George's Respiratory Questionnaire score was similar in all study groups after the intervention. Symptoms of depression significantly improved only in non-invasive ventilation, supplemental oxygen, and exercise training group (-2.8+2.8, P = .006).

Conclusion: Non-invasive positive-pressure ventilation (NIPPV) added to supplemental oxygen during exercise training was associated with better physiological adaptations than other modalities.

Review

J Clin Invest

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The vascular perspective on acute and chronic lung disease

Izabela Borek[1], Anna Birnhuber[1,2], Norbert F Voelkel[3,4], Leigh M Marsh[1,2], Grazyna Kwapiszewska[1,2,5]
Affiliations expand

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- PMCID: PMC10425217
- DOI: 10.1172/JCI170502

Free PMC article

Abstract

The pulmonary vasculature has been frequently overlooked in acute and chronic lung diseases, such as acute respiratory distress syndrome (ARDS), pulmonary fibrosis (PF), and chronic obstructive pulmonary disease (COPD). The primary emphasis in the management of these parenchymal disorders has largely revolved around the injury and aberrant repair of epithelial cells. However, there is increasing evidence that the vascular endothelium plays an active role in the development of acute and chronic lung diseases. The endothelial cell network in the capillary bed and the arterial and venous vessels provides a metabolically highly active barrier that controls the migration of immune cells, regulates vascular tone and permeability, and participates in the remodeling processes. Phenotypically and functionally altered endothelial cells, and remodeled vessels, can be found in acute and chronic lung diseases, although to different degrees, likely because of

disease-specific mechanisms. Since vascular remodeling is associated with pulmonary hypertension, which worsens patient outcomes and survival, it is crucial to understand the underlying vascular alterations. In this Review, we describe the current knowledge regarding the role of the pulmonary vasculature in the development and progression of ARDS, PF, and COPD; we also outline future research directions with the hope of facilitating the development of mechanism-based therapies.

- 190 references
- 3 figures

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

. 2023 Aug 15;24(1):532.
doi: 10.1186/s13063-023-07558-9.

Effects of multimodal exercise program on postural balance in patients with chronic obstructive pulmonary disease: study protocol for a randomized controlled trial

Tamires Daros Dos Santos[1], Adriane Schmidt Pasqualoto[1], Dannuey Machado Cardoso[2,3], Ivana Beatrice Mânica Da Cruz[4], Rafael Noal Moresco[5], Aron Ferreira da Silveira[1], Isabella Martins de Albuquerque[6]
Affiliations expand

- PMID: 37580800

- PMCID: PMC10426202

- DOI: 10.1186/s13063-023-07558-9

Free PMC article

Abstract

Background: Evidence has shown that patients with chronic obstructive pulmonary disease present significant deficits in the control of postural balance when compared to healthy subjects. In view of this, it is pertinent to investigate the effects of different therapeutic strategies used alone or in association with pulmonary rehabilitation with the potential to improve postural balance and other outcomes with clinical significance in patients with chronic obstructive pulmonary disease. This study will investigate the effects of an 8-week (short-term) multimodal exercise program [inspiratory muscle training (IMT) plus neuromuscular electrical stimulation (NMES)] on postural balance in patients with chronic obstructive pulmonary disease enrolled in a pulmonary rehabilitation program compared to individualized addition of IMT or NMES to pulmonary rehabilitation or standard pulmonary rehabilitation.

Methods: This is a randomized, single-blind, 4-parallel-group trial. Forty patients with chronic obstructive pulmonary disease will be included prospectively to this study during a pulmonary rehabilitation program. Patients will be randomly assigned to one of four groups: multimodal exercise program (IMT + NMES + pulmonary rehabilitation group) or (IMT + pulmonary rehabilitation group) or (NMES + pulmonary rehabilitation group) or standard pulmonary rehabilitation group. Patients will receive two sessions per week for 8 weeks. The primary outcome will be static postural balance and secondary outcomes will include as follows: static and dynamic postural balance, fear of falling, muscle strength and endurance (peripheral and respiratory), functional capacity, health-related quality of life, muscle architecture (quadriceps femoris and diaphragm), and laboratory biomarkers.

Discussion: This randomized clinical trial will investigate the effects of adding of short-term multimodal exercise program, in addition to pulmonary rehabilitation program, in postural balance in patients with chronic obstructive pulmonary disease enrolled in a pulmonary rehabilitation. Furthermore, this randomized control trial will enable important directions regarding the effectiveness of short-term intervention as part of the need to expand the focus of pulmonary rehabilitation to include balance management in chronic obstructive pulmonary disease patients which will be generated.

Trial registration: ClinicalTrials.gov NCT04387318. Registered on May 13, 2020.

Keywords: Breathing exercises; Electric stimulation; Postural balance; Randomized controlled trial; Rehabilitation.

Conflict of interest statement

The authors declare that they have no competing interests.

- 40 references
- 2 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Associated dataexpand

FULL TEXT LINKS

Editorial

Am J Respir Crit Care Med

. 2023 Aug 15;208(4):349-351.
doi: 10.1164/rccm.202306-1114ED.

Addressing the Use of the CAPTURE (a Chronic Obstructive Pulmonary Disease Screening Tool) in Chronic Obstructive Pulmonary Disease Treatment Decisions

Barbara P Yawn[1], Susan Murray[2]
Affiliations expand

- PMID: 37478328

- DOI: 10.1164/rccm.202306-1114ED

No abstract available

Comment on

- Use of CAPTURE to Identify Individuals Who May or May Not Require Treatment for Chronic Obstructive Pulmonary Disease.
  Li Y, Wen F, Ma Q, Chen R, Sun Y, Liu T, Gu C, Hu S, Song J, Compton C, Zheng J, Zhong N, Jones P.Am J Respir Crit Care Med. 2023 Aug 15;208(4):435-441. doi: 10.1164/rccm.202303-0504OC.PMID: 37315325

Editorial

Am J Respir Crit Care Med

. 2023 Aug 15;208(4):339-340.
doi: 10.1164/rccm.202307-1194ED.

From Conundrum to Cures, Pioneering Breakthroughs in Chronic Obstructive Pulmonary Disease

Research: Introduction to an *AJRCCM* Special Issue

MeiLan K Han[1]
Affiliations expand

- PMID: 37478015

- DOI: 10.1164/rccm.202307-1194ED

No abstract available

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

Editorial

Am J Respir Crit Care Med
. 2023 Aug 15;208(4):352-354.
doi: 10.1164/rccm.202307-1167ED.

Meeting Unmet Needs in Chronic Obstructive Pulmonary Disease Diagnosis and Treatment in Low- and Middle-Income Countries

Obianuju B Ozoh[1,2], Tochukwu Ayo-Olagunju[2], Kevin Mortimer[3,4]
Affiliations expand

- PMID: 37459643

- DOI: 10.1164/rccm.202307-1167ED

No abstract available

Comment on

- Unmet Diagnostic and Therapeutic Opportunities for Chronic Obstructive Pulmonary Disease in Low- and Middle-Income Countries.
  Florman KEH, Siddharthan T, Pollard SL, Alupo P, Barber JA, Chandyo RK, Flores-Flores O, Kirenga B, Mendes RG, Miranda JJ, Mohan S, Ricciardi F, Rykiel NA, Sharma AK, Wosu AC, Checkley W, Hurst JR; Additional GECo Study Investigators.Am J Respir Crit Care Med. 2023 Aug 15;208(4):442-450. doi: 10.1164/rccm.202302-0289OC.PMID: 37369142

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

Editorial

Am J Respir Crit Care Med
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-
. 2023 Aug 15;208(4):357-358.
doi: 10.1164/rccm.202307-1198ED.

Unraveling the Distal Lung Destruction in Emphysema

Irina Petrache[1]
Affiliations expand

- PMID: 37450936

- DOI: 10.1164/rccm.202307-1198ED

No abstract available

Comment on

- A Single-Cell Atlas of Small Airway Disease in Chronic Obstructive Pulmonary Disease: A Cross-Sectional Study.
  Booth S, Hsieh A, Mostaco-Guidolin L, Koo HK, Wu K, Aminazadeh F, Yang CX, Quail D, Wei Y, Cooper JD, Paré PD, Hogg JC, Vasilescu DM, Hackett TL.Am J Respir Crit Care Med. 2023 Aug 15;208(4):472-486. doi: 10.1164/rccm.202303-0534OC.PMID: 37406359

Editorial

Am J Respir Crit Care Med

. 2023 Aug 15;208(4):346-348.
doi: 10.1164/rccm.202307-1175ED.

Icenticaftor, Novel Therapy for COPD: This Glass Is Half Full

Stephen I Rennard[1]
Affiliations expand

- PMID: 37437299

- DOI: 10.1164/rccm.202307-1175ED

No abstract available

Comment on

- Icenticaftor, a CFTR Potentiator, in COPD: A Multicenter, Parallel-Group, Double-Blind Clinical Trial.
  Martinez FJ, Criner GJ, Gessner C, Jandl M, Scherbovsky F, Shinkai M, Siler TM, Vogelmeier CF, Voves R, Wedzicha JA, Bartels C, Bottoli I, Byiers S, Cardenas P, Eckert JH, Gutzwiller FS, Knorr B, Kothari M, Parlikar R, Tanase AM, Franssen FME.Am J Respir Crit Care Med. 2023 Aug 15;208(4):417-427. doi: 10.1164/rccm.202303-0458OC.PMID: 37411039 Clinical Trial.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

Editorial

Am J Respir Crit Care Med
. 2023 Aug 15;208(4):344-346.

doi: 10.1164/rccm.202307-1164ED.

A New Treatment for Chronic Obstructive Pulmonary Disease: Ensifentrine Moves Closer

Dave Singh[1]
Affiliations expand

- PMID: 37433204

- DOI: 10.1164/rccm.202307-1164ED

No abstract available

Comment on

- Ensifentrine, a Novel Phosphodiesterase 3 and 4 Inhibitor for the Treatment of Chronic Obstructive Pulmonary Disease: Randomized, Double-Blind, Placebo-controlled, Multicenter Phase III Trials (the ENHANCE Trials).
  Anzueto A, Barjaktarevic IZ, Siler TM, Rheault T, Bengtsson T, Rickard K, Sciurba F.Am J Respir Crit Care Med. 2023 Aug 15;208(4):406-416. doi: 10.1164/rccm.202306-0944OC.PMID: 37364283 Clinical Trial.

Editorial

. 2023 Aug 15;208(4):354-356.
doi: 10.1164/rccm.202306-1065ED.

Causes of Death in Smokers: Implications for Chronic Obstructive Pulmonary Disease Management across Disease Severity

Jadwiga A Wedzicha[1]
Affiliations expand

- PMID: 37429287

- DOI: 10.1164/rccm.202306-1065ED

No abstract available

Comment on

- Causes of and Clinical Features Associated with Death in Tobacco Cigarette Users by Lung Function Impairment.
  Labaki WW, Gu T, Murray S, Curtis JL, Wells JM, Bhatt SP, Bon J, Diaz AA, Hersh CP, Wan ES, Kim V, Beaty TH, Hokanson JE, Bowler RP, Arenberg DA, Kazerooni EA, Martinez FJ, Silverman EK, Crapo JD, Make BJ, Regan EA, Han MK; COPDGene Investigators – Core Units; COPDGene Investigators – Clinical Centers.Am J Respir Crit Care Med. 2023 Aug 15;208(4):451-460. doi: 10.1164/rccm.202210-1887OC.PMID: 37159910

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

Editorial

Am J Respir Crit Care Med

. 2023 Aug 15;208(4):348-349.
doi: 10.1164/rccm.202307-1146ED.

Age of Initiating Smoking: An Independent Predictor of Chronic Obstructive Pulmonary Disease in Later Life

Donald P Tashkin[1]
Affiliations expand

- PMID: 37429033

- DOI: 10.1164/rccm.202307-1146ED

No abstract available

Comment on

- Childhood Cigarette Smoking and Risk of Chronic Obstructive Pulmonary Disease in Older U.S. Adults.
  Sargent JD, Halenar M, Steinberg AW, Ozga J, Tang Z, Stanton CA, Paulin LM.Am J Respir Crit Care Med. 2023 Aug 15;208(4):428-434. doi: 10.1164/rccm.202303-0476OC.PMID: 37348105

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

Randomized Controlled Trial

Am J Respir Crit Care Med
.
. 2023 Aug 15;208(4):417-427.
doi: 10.1164/rccm.202303-0458OC.

Icenticaftor, a CFTR Potentiator, in COPD: A Multicenter, Parallel-Group, Double-Blind Clinical Trial

Fernando J Martinez[1], Gerard J Criner[2], Christian Gessner[3], Margret Jandl[4], Fernando Scherbovsky[5], Masaharu Shinkai[6], Thomas M Siler[7], Claus F Vogelmeier[8], Robert Voves[9], Jadwiga A Wedzicha[10], Christian Bartels[11], Ivan Bottoli[11], Stuart Byiers[11], Pamela Cardenas[12], Joerg H Eckert[11], Florian S Gutzwiller[11], Barbara Knorr[12], Mahavir Kothari[13], Rutvick Parlikar[13], Ana-Maria Tanase[11], Frits M E Franssen[14]
Affiliations expand

- PMID: 37411039

- DOI: 10.1164/rccm.202303-0458OC

Abstract

Rationale: CFTR (cystic fibrosis transmembrane conductance regulator) dysfunction is associated with mucus accumulation and worsening chronic obstructive pulmonary disease (COPD) symptoms. **Objectives:** The aim of this phase IIb dose-finding study was to compare a CFTR potentiator, icenticaftor (QBW251), with placebo in patients with COPD and chronic bronchitis. **Methods:** Patients with COPD on triple therapy for at least three months were randomized to six treatment arms (icenticaftor 450, 300, 150, 75, or 25 mg or placebo twice daily [b.i.d.]) in a 24-week, multicenter, parallel-group, double-blind study. The primary endpoint was change from baseline in trough FEV_1 after 12 weeks. Secondary endpoints included change from baseline in trough FEV_1 and Evaluating Respiratory

Symptoms in COPD (E-RS) total and cough and sputum scores after 24 weeks. Multiple comparison procedure-modeling was conducted to characterize dose-response relationship. Rescue medication use, exacerbations, and change in serum fibrinogen concentration after 24 weeks were assessed in exploratory and *post hoc* analyses, respectively. **Measurements and Main Results:** Nine hundred seventy-four patients were randomized. After 12 weeks of icenticaftor treatment, no dose-response relationship for change from baseline in trough FEV_1 was observed; however, it was observed for E-RS cough and sputum score. A dose-response relationship was observed after 24 weeks for trough FEV_1, E-RS cough and sputum and total scores, rescue medication use, and fibrinogen. A dose of 300 mg b.i.d. was consistently the most effective. Improvements for 300 mg b.i.d. versus placebo were also seen in pairwise comparisons of these endpoints. All treatments were well tolerated. **Conclusions:** The primary endpoint was negative, as icenticaftor did not improve trough FEV_1 over 12 weeks. Although the findings must be interpreted with caution, icenticaftor improved trough FEV_1; reduced cough, sputum, and rescue medication use; and lowered fibrinogen concentrations at 24 weeks. Clinical trial registered with www.clinicaltrials.gov (NCT04072887).

Keywords: CFTR dysfunction; CFTR potentiator; COPD; chronic bronchitis; icenticaftor.

Comment in

- Icenticaftor, Novel Therapy for COPD: This Glass Is Half Full.
  Rennard SI.Am J Respir Crit Care Med. 2023 Aug 15;208(4):346-348. doi: 10.1164/rccm.202307-1175ED.PMID: 37437299 No abstract available.

Am J Respir Crit Care Med

. 2023 Aug 15;208(4):472-486.
doi: 10.1164/rccm.202303-0534OC.

A Single-Cell Atlas of Small Airway Disease in Chronic Obstructive Pulmonary Disease: A Cross-Sectional Study

Steven Booth[1,2], Aileen Hsieh[1,2], Leila Mostaco-Guidolin[3], Hyun-Kyoung Koo[1,2], Keith Wu[1,2], Fatemeh Aminazadeh[1,2], Chen Xi Yang[1], Daniela Quail[4], Yuhong Wei[4], Joel D Cooper[5], Peter D Paré[1], James C Hogg[1,6], Dragoş M Vasilescu[1,6], Tillie-Louise Hackett[1,2]
Affiliations expand

- PMID: 37406359

- DOI: 10.1164/rccm.202303-0534OC

Abstract

Rationale: Emerging data demonstrate that the smallest conducting airways, terminal bronchioles, are the early site of tissue destruction in chronic obstructive pulmonary disease (COPD) and are reduced by as much as 41% by the time someone is diagnosed with mild (Global Initiative for Chronic Obstructive Lung Disease [GOLD] stage 1) COPD. **Objectives:** To develop a single-cell atlas that describes the structural, cellular, and extracellular matrix alterations underlying terminal bronchiole loss in COPD. **Methods:** This cross-sectional study of 262 lung samples derived from 34 ex-smokers with normal lung function (n = 10) or GOLD stage 1 (n = 10), stage 2 (n = 8), or stage 4 (n = 6) COPD was performed to assess the morphology, extracellular matrix, single-cell atlas, and genes associated with terminal bronchiole reduction using stereology, micro-computed tomography, nonlinear optical microscopy, imaging mass spectrometry, and transcriptomics. **Measurements and Main Results:** The lumen area of terminal bronchioles progressively narrows with COPD severity as a result of the loss of elastin fibers within alveolar attachments, which was observed before microscopic emphysematous tissue destruction in GOLD stage 1 and 2 COPD. The single-cell atlas of terminal bronchioles in COPD demonstrated M1-like macrophages and neutrophils located within alveolar attachments and associated with the pathobiology of elastin fiber loss, whereas adaptive immune cells (naive, CD4, and CD8 T cells, and B cells) are associated with terminal bronchiole wall remodeling. Terminal bronchiole pathology was associated with the upregulation of genes involved in innate and adaptive immune responses, the interferon response, and the degranulation of neutrophils. **Conclusions:** This comprehensive single-cell atlas highlights terminal bronchiole alveolar attachments as the initial site of tissue destruction in centrilobular emphysema and an attractive target for disease modification.

Keywords: COPD; elastin; micro–computed tomography; single-cell atlas; small airways disease.

Comment in

- Unraveling the Distal Lung Destruction in Emphysema.
  Petrache I.Am J Respir Crit Care Med. 2023 Aug 15;208(4):357-358. doi: 10.1164/rccm.202307-1198ED.PMID: 37450936 No abstract available.

Am J Respir Crit Care Med

. 2023 Aug 15;208(4):442-450.
doi: 10.1164/rccm.202302-0289OC.

Unmet Diagnostic and Therapeutic Opportunities for Chronic Obstructive Pulmonary Disease in Low- and Middle-Income Countries

Katia E H Florman[1], Trishul Siddharthan[2], Suzanne L Pollard[3,4], Patricia Alupo[5], Julie A Barber[6], Ram K Chandyo[7], Oscar Flores-Flores[8,9], Bruce Kirenga[5], Renata Gonçalves Mendes[10], J Jaime Miranda[11,12], Sakshi Mohan[13], Federico Ricciardi[6], Natalie A Rykiel[3,4], Arun K Sharma[14], Adaeze C Wosu[3,4], William Checkley[3,4], John R Hurst[15]; Additional GECo Study Investigators

Collaborators, Affiliations expand

- PMID: 37369142

- DOI: 10.1164/rccm.202302-0289OC

Abstract

Rationale: Chronic obstructive pulmonary disease (COPD) is a prevalent and burdensome condition in low- and middle-income countries (LMICs). Challenges to better care include more effective diagnosis and access to affordable interventions. There are no previous reports describing therapeutic needs of populations with COPD in LMICs who were identified through screening. **Objectives:** To describe unmet therapeutic need in screening-detected COPD in LMIC settings. **Methods:** We compared interventions recommended by the international Global Initiative for Chronic Obstructive Lung Disease COPD strategy document, with that received in 1,000 people with COPD identified by population screening at three LMIC sites in Nepal, Peru, and Uganda. We calculated costs using data on the availability and affordability of medicines. **Measurement and Main Results:** The greatest unmet need for nonpharmacological interventions was for education and vaccinations (applicable to all), pulmonary rehabilitation (49%), smoking cessation (30%), and advice on biomass smoke exposure (26%). Ninety-five percent of the cases were previously undiagnosed, and few were receiving therapy (4.5% had short-acting β-agonists). Only three of 47 people (6%) with a previous COPD diagnosis had access to drugs consistent with recommendations. None of those with more severe COPD were accessing appropriate maintenance inhalers. Even when available, maintenance treatments were unaffordable, with 30 days of treatment costing more than a low-skilled worker's daily average wage. **Conclusions:** We found a significant missed opportunity to reduce the burden of COPD in LMIC settings, with most cases undiagnosed. Although there is unmet need in developing novel therapies, in LMICs where the burden is greatest, better diagnosis combined with access to affordable interventions could translate to immediate benefit.

Keywords: COPD; LMIC; bronchodilator; guidelines; pulmonary rehabilitation.

Comment in

- Meeting Unmet Needs in Chronic Obstructive Pulmonary Disease Diagnosis and Treatment in Low- and Middle-Income Countries.
  Ozoh OB, Ayo-Olagunju T, Mortimer K.Am J Respir Crit Care Med. 2023 Aug 15;208(4):352-354. doi: 10.1164/rccm.202307-1167ED.PMID: 37459643 No abstract available.

Clinical Trial

Am J Respir Crit Care Med

. 2023 Aug 15;208(4):406-416.
doi: 10.1164/rccm.202306-0944OC.

Ensifentrine, a Novel Phosphodiesterase 3 and 4 Inhibitor for the Treatment of Chronic Obstructive Pulmonary Disease: Randomized, Double-Blind, Placebo-controlled, Multicenter Phase III Trials (the ENHANCE Trials)

Antonio Anzueto[1,2], Igor Z Barjaktarevic[3], Thomas M Siler[4], Tara Rheault[5], Thomas Bengtsson[6], Kathleen Rickard[5], Frank Sciurba[7]
Affiliations expand

- PMID: 37364283

- DOI: 10.1164/rccm.202306-0944OC

Abstract

Rationale: Ensifentrine is a novel, selective, dual phosphodiesterase (PDE)3 and PDE4 inhibitor with bronchodilator and antiinflammatory effects. Replicate phase III trials of nebulized ensifentrine were conducted (ENHANCE-1 and ENHANCE-2) to assess these effects in patients with chronic obstructive pulmonary disease (COPD). **Objectives:** To

evaluate the efficacy of ensifentrine compared with placebo for lung function, symptoms, quality of life, and exacerbations in patients with COPD. **Methods:** These phase III, multicenter, randomized, double-blind, parallel-group, placebo-controlled trials were conducted between September 2020 and December 2022 at 250 research centers and pulmonology practices in 17 countries. Patients aged 40-80 years with moderate to severe symptomatic COPD were enrolled. **Measurements and Main Results:** Totals of 760 (ENHANCE-1) and 789 (ENHANCE-2) patients were randomized and treated, with 69% and 55% receiving concomitant long-acting muscarinic antagonists or long-acting β_2-agonists, respectively. Post-bronchodilator FEV_1 percentage predicted values were 52% and 51% of predicted normal. Ensifentrine treatment significantly improved average FEV_1 area under the curve at 0-12 hours versus placebo (ENHANCE-1, 87 ml [95% confidence interval, 55, 119]; ENHANCE-2, 94 ml [65, 124]; both $P < 0.001$). Ensifentrine treatment significantly improved symptoms (Evaluating Respiratory Symptoms) and quality of life (St. George's Respiratory Questionnaire) versus placebo at Week 24 in ENHANCE-1 but not in ENHANCE-2. Ensifentrine treatment reduced the rate of moderate or severe exacerbations versus placebo over 24 weeks (ENHANCE-1, rate ratio, 0.64 [0.40, 1.00]; $P = 0.050$; ENHANCE-2, rate ratio, 0.57 [0.38, 0.87]; $P = 0.009$) and increased time to first exacerbation (ENHANCE-1, hazard ratio, 0.62 [0.39, 0.97]; $P = 0.038$; ENHANCE-2, hazard ratio, 0.58 [0.38, 0.87]; $P = 0.009$). Adverse event rates were similar to those for placebo. **Conclusions:** Ensifentrine significantly improved lung function in both trials, with results supporting exacerbation rate and risk reduction in a broad COPD population and in addition to other classes of maintenance therapies. Clinical trial registered with www.

Clinicaltrials: gov and EudraCT (ENHANCE-1, www.

Clinicaltrials: gov identifier NCT04535986, EudraCT identifier 2020-002086-34; ENHANCE-2, www.

Clinicaltrials: gov identifier NCT04542057, EudraCT identifier 2020-002069-32).

Keywords: COPD; dual PDE3 and PDE4 inhibitor; ensifentrine; nebulized therapy.

Comment in

- A New Treatment for Chronic Obstructive Pulmonary Disease: Ensifentrine Moves Closer.
  Singh D.Am J Respir Crit Care Med. 2023 Aug 15;208(4):344-346. doi: 10.1164/rccm.202307-1164ED.PMID: 37433204 No abstract available.

- Cited by 2 articles

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated data, Grant supportexpand

Review

Am J Respir Crit Care Med

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doi: 10.1164/rccm.202303-0455CI.

Targeting Type 2 Inflammation and Epithelial Alarmins in Chronic Obstructive Pulmonary Disease: A Biologics Outlook

Klaus F Rabe[1,2,3], Stephen Rennard[4], Fernando J Martinez[5], Bartolome R Celli[6,7], Dave Singh[8], Alberto Papi[9], Mona Bafadhel[10], Jigna Heble[11], Amr Radwan[12], Xavier Soler[12], Juby A Jacob Nara[11], Yamo Deniz[12], Paul J Rowe[11]

Affiliations expand

- PMID: 37348121

- DOI: 10.1164/rccm.202303-0455CI

Abstract

Chronic obstructive pulmonary disease (COPD) is a complex, heterogeneous, progressive inflammatory airway disease associated with a significant impact on patients' lives, including morbidity and mortality, and significant healthcare costs. Current pharmacologic strategies, including first- and second-line therapies such as long-acting β_2-agonists, long-acting muscarinic antagonists, inhaled corticosteroids, phosphodiesterase-4 inhibitors, and macrolides, provide relief to patients with COPD. However, many patients remain

symptomatic, with persistent symptoms and/or acute exacerbations and progressive lung function loss. Although neutrophilic inflammation is the most common type of inflammation in COPD, 20-40% of patients with COPD exhibit type 2 inflammation, with roles for $CD4^+$ (cluster of differentiation 4) T-helper cell type 1 cells, type 2 innate lymphoid cells, eosinophils, and alternatively activated macrophages. On the basis of the current limitations of available therapies, a significant unmet need exists in COPD management, including the need for targeted therapies to address the underlying pathophysiology leading to disease progression, such as type 2 inflammation, as well as biomarkers to help select the patients who would most benefit from the new therapies. Significant progress is being made, with evolving understanding of the pathobiology of COPD leading to novel therapeutic targets including epithelial alarmins. In this review, we describe the current therapeutic landscape in COPD, discuss unmet treatment needs, review the current knowledge of type 2 inflammation and epithelial alarmins in COPD, explore potential biomarkers of type 2 inflammation in COPD, and finally provide a rationale for incorporating therapies targeting type 2 inflammation and epithelial alarmins in COPD. **Video Abstract** available online at www.atsjournals.org.

Keywords: COPD; alarmins; biologics; eosinophils; type 2 inflammation.

Am J Respir Crit Care Med

. 2023 Aug 15;208(4):461-471.

doi: 10.1164/rccm.202212-2341OC.

Consequences of Using Post- or Prebronchodilator Reference Values in Interpreting Spirometry

Andrei Malinovschi[1], Xingwu Zhou[1,2,3], Anders Andersson[4,5], Helena Backman[6], Björn Bake[7], Anders Blomberg[8], Kenneth Caidahl[9,10,11,12], Maria J Eriksson[11,12], Jonas Eriksson Ström[8], Viktor Hamrefors[13,14], Ola Hjelmgren[9,10], Christer Janson[3], Reza Karimi[15], David Kylhammar[16], Anne Lindberg[8], Eva Lindberg[3], Per Liv[6], Anna-Carin Olin[17], Adel Shalabi[18], C Magnus Sköld[15,19], Johan Sundström[20,21], Hanan Tanash[22], Kjell Torén[17], Per Wollmer[23], Suneela Zaigham[1,13], Carl Johan Östgren[24,25], Jan E Engvall[16,24]
Affiliations expand

- PMID: 37339507

- DOI: 10.1164/rccm.202212-2341OC

Abstract

Rationale: Postbronchodilator spirometry is used for the diagnosis of chronic obstructive pulmonary disease. However, prebronchodilator reference values are used for spirometry interpretation. **Objectives:** To compare the resulting prevalence rates of abnormal spirometry and study the consequences of using pre- or postbronchodilator reference values generated within SCAPIS (Swedish CArdioPulmonary bioImage Study) when interpreting postbronchodilator spirometry in a general population. **Methods:** SCAPIS reference values for postbronchodilator and prebronchodilator spirometry were based on 10,156 and 1,498 never-smoking, healthy participants, respectively. We studied the associations of abnormal spirometry, defined by using pre- or postbronchodilator reference values, with respiratory burden in the SCAPIS general population (28,851 individuals). **Measurements and Main Results:** Bronchodilation resulted in higher predicted medians and lower limits of normal (LLNs) for FEV_1/FVC ratios. The prevalence of postbronchodilator FEV_1/FVC ratio lower than the prebronchodilator LLN was 4.8%, and that of postbronchodilator FEV_1/FVC lower than the postbronchodilator LLN was 9.9%, for the general population. An additional 5.1% were identified as having an abnormal postbronchodilator FEV_1/FVC ratio, and this group had more respiratory symptoms, emphysema (13.5% vs. 4.1%; $P < 0.001$), and self-reported physician-diagnosed chronic obstructive pulmonary disease (2.8% vs. 0.5%, $P < 0.001$) than subjects with a postbronchodilator FEV_1/FVC ratio greater than the LLN for both pre- and postbronchodilation. **Conclusions:** Pre- and postbronchodilator spirometry reference values differ with regard to FEV_1/FVC ratio. Use of postbronchodilator reference values doubled the population prevalence of airflow obstruction; this was related to a higher respiratory burden. Using postbronchodilator reference values when interpreting postbronchodilator spirometry might enable the identification of individuals with mild disease and be clinically relevant.

Keywords: post-bronchodilator; pre-bronchodilator; reference values; respiratory burden; spirometry.

Comment in

- Postbronchodilator Reference Values: Should They Be the Norm?
  Smith LJ.Am J Respir Crit Care Med. 2023 Aug 15;208(4):356-357. doi: 10.1164/rccm.202306-1082ED.PMID: 37478330 No abstract available.

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

FULL TEXT LINKS

Am J Respir Crit Care Med
. 2023 Aug 15;208(4):435-441.
doi: 10.1164/rccm.202303-0504OC.

Use of CAPTURE to Identify Individuals Who May or May Not Require Treatment for Chronic Obstructive Pulmonary Disease

Yun Li[1], Fuqiang Wen[2], Qianli Ma[3], Rongchang Chen[4], Yongchang Sun[5], Tiantian Liu[6], Chenjuan Gu[6], Shuling Hu[6], Jie Song[6], Chris Compton[7], Jinping Zheng[1], Nanshan Zhong[1], Paul Jones[7]
Affiliations expand

- PMID: 37315325

- DOI: 10.1164/rccm.202303-0504OC

Abstract

Rationale: The CAPTURE tool (Chronic Obstructive Pulmonary Disease [COPD] Assessment in Primary Care to Identify Undiagnosed Respiratory Disease and Exacerbation Risk) was developed to identify patients with undiagnosed COPD with an FEV_1 <60% predicted or risk of exacerbation as treatment criteria. **Objectives:** To test the ability of CAPTURE to identify patients requiring treatment because of symptoms or risk of exacerbation or hospitalization. **Methods:** Data were from COMPASS (Clinical, Radiological and Biological Factors Associated with Disease Progression, Phenotypes and Endotypes of COPD in China), a prospective study of COPD, chronic bronchitis without airflow limitation (postbronchodilator FEV_1/FVC ratio ≥0.70), and healthy never-smokers. CAPTURE was tested as questions alone and with peak expiratory flow measurement. Sensitivity, specificity, and positive and negative predicted values (PPV and NPV) were calculated for COPD Assessment Test (CAT) scores ⩾10 versus <10, modified Medical Research Council (mMRC) scores ⩾2 versus <2, and at least one moderate exacerbation or hospitalization in the previous year versus none. **Measurements and Main Results:** Patients with COPD (*n* = 1,696) had a mean age of 65 ± 7.5 years, and 90% were male, with a postbronchodilator FEV_1 of 66.5 ± 20.1% predicted. Control participants (*n* = 307) had a mean age of 60.2 ± 7.0 years, and 65% were male, with an FEV_1/FVC ratio of 0.78 ± 0.04. CAPTURE using peak expiratory flow showed the best combination of sensitivity and specificity. Sensitivity and specificity were 68.5% and 64.0%, respectively, to detect a CAT score ⩾10; 85.6% and 61.0% to detect an mMRC score ⩾2; 63.5% and 55.6% to detect at least one moderate exacerbation; and 70.2% and 59.4% to detect at least one hospitalization. PPVs ranged from 15.6% (moderate exacerbations) to 47.8% (CAT score). NPVs ranged from 80.8% (CAT score) to 95.6% (mMRC score). **Conclusions:** CAPTURE has good sensitivity to identify patients with COPD who may require treatment because of increased symptoms or risk of exacerbations or hospitalization, including those with an FEV_1 >60% predicted. High NPV values show that CAPTURE can also exclude those who may not require treatment. Clinical trial registered with www.clinicaltrials.gov (NCT04853225).

Keywords: COPD; case finding; peak expiratory flow; symptoms.

Comment in

- Addressing the Use of the CAPTURE (a Chronic Obstructive Pulmonary Disease Screening Tool) in Chronic Obstructive Pulmonary Disease Treatment Decisions. Yawn BP, Murray S.Am J Respir Crit Care Med. 2023 Aug 15;208(4):349-351. doi: 10.1164/rccm.202306-1114ED.PMID: 37478328 No abstract available.

Am J Respir Crit Care Med
. 2023 Aug 15;208(4):501-502.
doi: 10.1164/rccm.202303-0404LE.

Marijuana Use as a Risk Factor for Chronic Obstructive Pulmonary Disease: Not There Yet

Donald P Tashkin[1], Igor Barjaktarevic[1]
Affiliations expand

- PMID: 37311252
- DOI: 10.1164/rccm.202303-0404LE

No abstract available

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

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Am J Respir Crit Care Med

. 2023 Aug 15;208(4):502-504.
doi: 10.1164/rccm.202304-0691LE.

Cardiovascular Disease and Chronic Obstructive Pulmonary Disease: Adding a Third Dimension to the ABE Global Initiative for Chronic Obstructive Lung Disease 2023 Chronic Obstructive Pulmonary Disease Classification

Konstantinos Kostikas[1], Athena Gogali[1], Georgios Hillas[2]
Affiliations expand

- PMID: 37311251

- DOI: 10.1164/rccm.202304-0691LE

No abstract available

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

. 2023 Aug 15;208(4):505-506.
doi: 10.1164/rccm.202305-0833LE.

Sleep Apnea and Chronic Obstructive Pulmonary Disease Overlap: More Common Than You Think?

Janna R Raphelson[1], Ana Sanchez-Azofra[1], Atul Malhotra[1]
Affiliations expand

- PMID: 37311242

- DOI: 10.1164/rccm.202305-0833LE

No abstract available

Am J Respir Crit Care Med

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. 2023 Aug 15;208(4):504-505.
doi: 10.1164/rccm.202305-0795LE.

Sleep, the Forgotten, Yet Potentially Modifiable, Dimension in Chronic Obstructive Pulmonary Disease Care

Nancy H Stewart[1], Valerie G Press[2], Lucas Donovan[3,4]
Affiliations expand

- PMID: 37311239

- DOI: 10.1164/rccm.202305-0795LE

No abstract available

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

FULL TEXT LINKS

Am J Respir Crit Care Med

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-
-

. 2023 Aug 15;208(4):498-501.
doi: 10.1164/rccm.202302-0205LE.

Optimal Threshold of FEV_t/FVC Ratio for Detection of Airflow Limitation Associated with Structural Lung Disease

Surya P Bhatt[1,2,3], Arie Nakhmani[1,4], Carla G Wilson[5], Sandeep Bodduluri[1,2,3]
Affiliations expand

- PMID: 37285809

- DOI: 10.1164/rccm.202302-0205LE

No abstract available

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

FULL TEXT LINKS

Review

Am J Respir Crit Care Med

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. 2023 Aug 15;208(4):374-394.
doi: 10.1164/rccm.202303-0400SO.

An Update on Outcomes for COPD Pharmacological Trials: A COPD Investigators Report - Reassessment of the 2008 American Thoracic Society/European Respiratory Society Statement on Outcomes for COPD Pharmacological Trials

Mario Cazzola[1], Paola Rogliani[1], Peter J Barnes[2], Francesco Blasi[3,4], Bartolome Celli[5], Nicola A Hanania[6], Fernando J Martinez[7], Bruce E Miller[8], Marc Miravitlles[9], Clive P Page[10], Ruth Tal-Singer[11], Maria Gabriella Matera[12]

Affiliations expand

- PMID: 37236628

- DOI: 10.1164/rccm.202303-0400SO

Abstract

Background: In 2008, a dedicated American Thoracic Society/European Respiratory Society task force published a paper on the possible use and limitations of clinical outcomes and biomarkers to evaluate the impact of pharmacological therapy in patients with chronic obstructive pulmonary disease. Since then, our scientific understanding of chronic obstructive pulmonary disease has increased considerably; there has been a progressive shift from a one-size-fits-all diagnostic and therapeutic approach to a personalized approach; and many new treatments currently in development will require new endpoints to evaluate their efficacy adequately. **Objectives:** The emergence of several new relevant outcome measures motivated the authors to review advances in the field and highlight the need to update the content of the original report. **Methods:** The authors separately created search strategies for the literature, primarily based on their opinions and assessments supported by carefully chosen references. No centralized examination of the literature or uniform criteria for including or excluding evidence were used. **Measurements and Main Results:** Endpoints, outcomes, and biomarkers have been revisited. The limitations of some of those reported in the American Thoracic Society/European Respiratory Society task force document have been highlighted. In addition, new tools that may be useful, especially in evaluating personalized therapy, have been described. **Conclusions:** Because the "label-free" treatable traits approach is becoming an important step toward precision medicine, future clinical trials should focus on highly prevalent treatable traits, and this will influence the choice of outcomes and markers to be considered. The use of the new tools, particularly combination endpoints, could help better identify the right patients to be treated with the new drugs.

Keywords: chronic obstructive pulmonary disease; outcomes; personalized medicine; pharmacological trials.

Am J Respir Crit Care Med
. 2023 Aug 15;208(4):495-498.
doi: 10.1164/rccm.202303-0463LE.

High-Resolution Computed Tomography-approximated Perfusion Is Comparable to Nuclear Perfusion Imaging in Severe Chronic Obstructive Pulmonary Disease

T David Koster[1], Jean-Paul Charbonnier[2], Jan Pruim[3], Hester A Gietema[4,5], Rein Posthuma[6,7], Lowie E G W Vanfleteren[8,9], Marlies van Dijk[1], Karin Klooster[1], Dirk-Jan Slebos[1]
Affiliations expand

- PMID: 37192444
- DOI: 10.1164/rccm.202303-0463LE

No abstract available

- Cited by 1 article

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

Editorial

Am J Respir Crit Care Med
. 2023 Aug 15;208(4):342-344.
doi: 10.1164/rccm.202303-0550ED.

From Laënnec's Stethoscope to the Magic of Imaging, Big Data and Artificial Intelligence: A Timeline of Precision Medicine for Patients with Chronic Obstructive Pulmonary Disease

Bartolome Celli[1]
Affiliations expand

- PMID: 37167548
- DOI: 10.1164/rccm.202303-0550ED

No abstract available

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

Am J Respir Crit Care Med

. 2023 Aug 15;208(4):451-460.
doi: 10.1164/rccm.202210-1887OC.

Causes of and Clinical Features Associated with Death in Tobacco Cigarette Users by Lung Function Impairment

Wassim W Labaki[1], Tian Gu[2], Susan Murray[3], Jeffrey L Curtis[1,4], J Michael Wells[5], Surya P Bhatt[5], Jessica Bon[6,7], Alejandro A Diaz[8], Craig P Hersh[8,9], Emily S Wan[9,10], Victor Kim[11], Terri H Beaty[12], John E Hokanson[13], Russell P Bowler[14], Douglas A Arenberg[1], Ella A Kazerooni[1,15], Fernando J Martinez[16], Edwin K Silverman[8,9], James D Crapo[14], Barry J Make[14], Elizabeth A Regan[17], MeiLan K Han[1]; COPDGene Investigators – Core Units; COPDGene Investigators – Clinical Centers
Collaborators, Affiliations expand

- PMID: 37159910

- DOI: 10.1164/rccm.202210-1887OC

Abstract

Rationale: Cigarette smoking contributes to the risk of death through different mechanisms. **Objectives:** To determine how causes of and clinical features associated with death vary in tobacco cigarette users by lung function impairment. **Methods:** We stratified current and former tobacco cigarette users enrolled in Genetic Epidemiology of Chronic Obstructive Pulmonary Disease (COPDGene) into normal spirometry, PRISm (Preserved Ratio Impaired Spirometry), Global Initiative for Chronic Obstructive Lung Disease (GOLD) 1-2 COPD, and GOLD 3-4 COPD. Deaths were identified via longitudinal follow-up and Social Security Death Index search. Causes of death were adjudicated after a review of death certificates, medical records, and next-of-kin interviews. We tested associations between baseline clinical variables and all-cause mortality using multivariable Cox proportional hazards models. **Measurements and Main Results:** Over a 10.1-year median follow-up, 2,200 deaths occurred among 10,132 participants (age 59.5 ± 9.0 yr; 46.6% women). Death from cardiovascular disease was most frequent in PRISm (31% of deaths). Lung cancer deaths were most frequent in GOLD 1-2 (18% of deaths vs. 9-11% in other groups). Respiratory deaths outpaced competing causes of death in GOLD 3-4, particularly when BODE index ⩾7. St. George's Respiratory Questionnaire score ⩾25 was associated with higher mortality in all groups: Hazard ratio (HR), 1.48 (1.20-1.84) normal spirometry;

HR, 1.40 (1.05-1.87) PRISm; HR, 1.80 (1.49-2.17) GOLD 1-2; HR, 1.65 (1.26-2.17) GOLD 3-4. History of respiratory exacerbations was associated with higher mortality in GOLD 1-2 and GOLD 3-4, quantitative emphysema in GOLD 1-2, and airway wall thickness in PRISm and GOLD 3-4. **Conclusions:** Leading causes of death vary by lung function impairment in tobacco cigarette users. Worse respiratory-related quality of life is associated with all-cause mortality regardless of lung function.

Keywords: exacerbations; mortality; respiratory-related quality of life; smokers; spirometry.

Comment in

- Causes of Death in Smokers: Implications for Chronic Obstructive Pulmonary Disease Management across Disease Severity.
  Wedzicha JA.Am J Respir Crit Care Med. 2023 Aug 15;208(4):354-356. doi: 10.1164/rccm.202306-1065ED.PMID: 37429287 No abstract available.

Am J Respir Crit Care Med

. 2023 Aug 15;208(4):487-489.
doi: 10.1164/rccm.202303-0581RR.

Exacerbations in Chronic Obstructive Pulmonary Disease: Clinical, Genetic, and Mycobiome Risk Factors

Kenki Matsumoto[1], Nicola Read[1], Keir E J Philip[1,2], James P Allinson[1,2]
Affiliations expand

- PMID: 37104845

- DOI: 10.1164/rccm.202303-0581RR

No abstract available

- Cited by 1 article

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

Review

Lancet Respir Med
. 2023 Aug 14;S2213-2600(23)00259-X.
doi: 10.1016/S2213-2600(23)00259-X. Online ahead of print.

Pulmonary hypertension associated with lung disease: new insights into pathomechanisms, diagnosis, and management

Karen M Olsson[1], Tamera J Corte[2], Jan C Kamp[3], David Montani[4], Steven D Nathan[5], Lavinia Neubert[6], Laura C Price[7], David G Kiely[8]
Affiliations expand

- PMID: 37591300

- DOI: 10.1016/S2213-2600(23)00259-X

Abstract

Patients with chronic lung diseases, particularly interstitial lung disease and chronic obstructive pulmonary disease, frequently develop pulmonary hypertension, which results in clinical deterioration, worsening of oxygen uptake, and an increased mortality risk. Pulmonary hypertension can develop and progress independently from the underlying lung disease. The pulmonary vasculopathy is distinct from that of other forms of pulmonary hypertension, with vascular ablation due to loss of small pulmonary vessels being a key feature. Long-term tobacco exposure might contribute to this type of pulmonary vascular remodelling. The distinct pathomechanisms together with the underlying lung disease might explain why treatment options for this condition remain scarce. Most drugs approved for pulmonary arterial hypertension have shown no or sometimes harmful effects in pulmonary hypertension associated with lung disease. An exception is inhaled treprostinil, which improves exercise capacity in patients with interstitial lung disease and pulmonary hypertension. There is a pressing need for safe, effective treatment options and for reliable, non-invasive diagnostic tools to detect and characterise pulmonary hypertension in patients with chronic lung disease.

Conflict of interest statement

Declaration of interests KMO has received fees for lectures or consultancy from Acceleron, Actelion, Bayer, Ferrer, GlaxoSmithKline, Janssen, MSD, Pfizer, and United Therapeutics. TJC has received research grants and personal fees from Boehringer Ingelheim, Roche, and Bristol Myers Squibb; personal fees from Promedior, Vicore, and DevPro Therapeutics; and research grants from Actelion, Galapagos, and Biogen. JCK is supported by PRACTIS – Clinician Scientist Program at Hannover Medical School, funded by the German Research Foundation (DGF, ME 3696/3–1). DM has received grants from and is a consultant for Acceleron, Merck, Actelion, Bayer, Chiesi, GlaxoSmithKline, and Pfizer. SDN is a consultant and on the speakers bureau for United Therapeutics; on the speakers bureau for Bayer and Boehringer Ingelheim; and a consultant for Boehringer Ingelheim, Roche, Merck, Bellerophon, and Third Pole. LCP has received educational grants and payments for lectures and travel from Janssen, Ferrer, and Altavant. DGK has received honoraria for lectures or consultancy from Acceleron, Actelion, Altavant, Ferrer, GlaxoSmithKline, Janssen Pharmaceuticals, and MSD; research grants to his institution from Actelion, GlaxoSmithKline, and Janssen Pharmaceuticals; and funding from the National Institute of Health Research Biomedical Research Centre, Sheffield. LN declares no competing interests.

Randomized Controlled Trial

BMC Pulm Med

. 2023 Aug 14;23(1):298.
doi: 10.1186/s12890-023-02587-1.

Complexity in clinical diagnoses of acute exacerbation of chronic obstructive pulmonary disease

Alexandre J Pratt[1], Andrew Purssell[2], Tinghua Zhang[3], Vanessa P J Luks[3 4], Xavier Bauza[5], Sunita Mulpuru[3 4], Miranda Kirby[5], Shawn D Aaron[3 4], Juthaporn Cowan[6 7]
Affiliations expand

- PMID: 37580731

- PMCID: PMC10426055

- DOI: 10.1186/s12890-023-02587-1

Free PMC article

Abstract

Background: Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is a clinical syndrome with various causes. It is not uncommon that COPD patients presenting with dyspnea have multiple causes for their symptoms including AECOPD, pneumonia, or congestive heart failure occurring concurrently.

Methods: To identify clinical, radiographic, and laboratory characteristics that might help distinguish AECOPD from another dominant disease in patients with a history of COPD, we conducted a retrospective cohort study of hospitalized patients with admitting diagnosis of AECOPD who were screened for a prospective randomized controlled trial from Sep 2016 to Mar 2018. Clinical characteristics, course in hospital, and final diagnosis at discharge were reviewed and adjudicated by two authors. The final diagnosis of each patient was determined based on the synthesis of all presenting signs and symptoms, imaging, and laboratory results. We adhered to AECOPD diagnosis definitions based on the GOLD guidelines. Univariate and multivariate analyses were performed to identify any associated features of AECOPD with and without other acute processes contributing to dyspnea.

Results: Three hundred fifteen hospitalized patients with admitting diagnosis of AECOPD were included. Mean age was 72.5 (SD 10.6) years. Two thirds (65.4%) had spirometry defined COPD. The most common presenting symptom was dyspnea (96.5%), followed by cough (67.9%), and increased sputum (57.5%). One hundred and eighty (57.1%) had a final diagnosis of AECOPD alone whereas 87 (27.6%) had AECOPD with other conditions and 48 (15.2%) did not have AECOPD after adjudication. Increased sputum purulence (OR 3.35, 95%CI 1.68-6.69) and elevated venous pCO2 (OR 1.04, 95%CI 1.01 - 1.07) were associated with a diagnosis of AECOPD but these were not associated with AECOPD alone without concomitant conditions. Radiographic evidence of pleural effusion (OR 0.26, 95%CI 0.12 - 0.58) was negatively associated with AECOPD with or without other conditions while radiographic evidence of pulmonary edema (OR 0.31; 95%CI 0.11 - 0.91) and lobar pneumonia (OR 0.13, 95%CI 0.07 - 0.25) suggested against the diagnosis of AECOPD alone.

Conclusion: The study highlighted the complexity and difficulty of AECOPD diagnosis. A more specific clinical tool to diagnose AECOPD is needed.

Keywords: Acute exacerbation; Chronic obstructive pulmonary disease; Diagnosis.

Conflict of interest statement

JC received honoraria from GSK, Merck, Sanofi Genzyme, Takeda, CSL Behring, Biogen unrelated to this work. MK is a consultant for VIDA Diagnostics Inc. (Coralville, IA, USA). AJP, AP, TZ, VL, XB, SM, SDA do not have competing interests.

- 21 references
- 1 figure

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

Editorial

Respirology
. 2023 Aug 14.
doi: 10.1111/resp.14571. Online ahead of print.

Current evidence on supranormal lung function: A call for longitudinal research to optimize lung health

Shyamali C Dharmage[1], Dinh S Bui[1]
Affiliations expand

- PMID: 37580178
- DOI: 10.1111/resp.14571

Free article

No abstract available

Keywords: COPD; lung function trajectories; risk factors; supranormal lung function.

- 10 references

SUPPLEMENTARY INFO

Ann Am Thorac Soc

. 2023 Aug 14.

doi: 10.1513/AnnalsATS.202303-275OC. Online ahead of print.

Sleep Testing and Mortality in a Propensity-matched Cohort of Patients with Chronic Obstructive Pulmonary Disease

Lucas M Donovan[1,2], Travis Wai[3], Laura J Spece[4], Kevin I Duan[5], Matthew F Griffith[6], Aristotle Leonhard[1], Robert Plumley[7], Sophia A Hayes[8], Fernando Picazo[8], Kristina Crothers[9,10], Vishesh K Kapur[8], Brian N Palen[11,12], David H Au[12], Laura C Feemster[13,1]

Affiliations expand

- PMID: 37579136

- DOI: 10.1513/AnnalsATS.202303-275OC

Abstract

Rationale: Many advocate the application of propensity matching methods to 'real world' data to answer key questions around Obstructive Sleep Apnea (OSA) management. One such question is whether identifying undiagnosed OSA impacts mortality in high-risk populations like Chronic Obstructive Pulmonary Disease (COPD).

Objective: Assess the association of sleep testing with mortality among patients with COPD and high likelihood of undiagnosed OSA.

Methods: We identified patients with COPD and high likelihood of undiagnosed OSA. We then distinguished those receiving sleep testing within 90 days of index COPD encounters. We calculated propensity scores for testing based on 37 variables and compared long-term mortality in matched groups. In sensitivity analyses, we compared mortality using inverse propensity weighting and instrumental variable (IV) methods. We also compared incidence of non-fatal events including adverse outcomes (hospitalizations and COPD exacerbations) and routine services that are regularly indicated in COPD (influenza vaccination and pulmonary function testing). We compared the incidence of each non-fatal event as a composite outcome with death and separately compared the marginal probability of each non-fatal event independently with death as a competing risk.

Results: Among 135,958 patients, 1,957 (1.4%) received sleep testing. We propensity matched all patients with sleep testing to an equal number without testing, achieving excellent balance on observed confounders with standardized differences <0.10. We observed lower mortality risk among patients with sleep testing (IRR 0.88, 95%CI, 0.79-0.99) and similar results using inverse propensity weighting and IV methods. Contrary to mortality, we found that sleep testing was associated with similar or greater risks for non-fatal adverse events including inpatient COPD exacerbations (SHR 1.29, 95%CI 1.02-1.62) and routine services like influenza vaccination (SHR 1.26, 95% CI 1.17-1.36).

Conclusion: Our disparate findings can be interpreted in multiple ways. Sleep testing may indeed cause both reduced mortality and greater incidence of non-fatal adverse outcomes and routine services. However, it is also possible that our findings stem from residual confounding by patients' likelihood of accessing care. Given the limitations of propensity-based analyses, we cannot confidently distinguish these two possibilities. This uncertainty highlights the limitations of using propensity-based analyses to guide patient care and policy decisions.

Book

Six-Minute Walk Test

Harold A. Matos Casano[1], Fatima Anjum[2]

In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan.
2023 Aug 14.

Affiliations expand

- PMID: 35015445

- Bookshelf ID: NBK576420

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Excerpt

There are a number of field walking tests designed to measure the exercise capacity of patients with chronic respiratory disease. Among these, the 6-minute walk test (6MWT) is a key study providing a functional, therapeutic response, and prognostic data that is valuable in the care of patients with respiratory as well as cardiac diseases. It is used widely due to its simplicity and reproducibility, delivering a consolidated image of the cardiopulmonary and musculoskeletal response to exercise. It requires no special training on the part of the staff performing it, items and equipment available at any clinician's office or hospital may be used, and is safe and well-tolerated by most patients at any stage of disease, with the test being highly reflective of usual daily activity and exercise performance.

It is particularly useful in assessing and monitoring chronic obstructive pulmonary disease (COPD) and has a role in managing patients with other conditions, including those with diffuse parenchymal lung diseases and pulmonary arterial hypertension. Overall, it is an inexpensive test that can provide a wealth of data with potential impact on the treatment of several conditions. The test is self-paced, with standardized instructions and encouragement being given as patients walk as far as possible over 6 minutes through a flat corridor. The final distance is recorded in meters.

Conflict of interest statement

Disclosure: Harold Matos Casano declares no relevant financial relationships with ineligible companies.
Disclosure: Fatima Anjum declares no relevant financial relationships with ineligible companies.

- 30 references

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

Orphanet J Rare Dis
. 2023 Aug 12;18(1):243.
doi: 10.1186/s13023-023-02830-2.

The prevalence of bronchiectasis in patients with alpha-1 antitrypsin deficiency: initial report of EARCO

Robert A Stockley[1], Anita Pye[2], Joshua De Soyza[2], Alice M Turner[2], Marc Miravitlles[3]; EARCO study investigators
Collaborators, Affiliations expand

- PMID: 37573351
- PMCID: PMC10422747
- DOI: 10.1186/s13023-023-02830-2

Free PMC article

Abstract

Background: Although bronchiectasis has been recognised as a feature of some patients with Alpha1-Antitrypsin deficiency the prevalence and characteristics are not widely known. We wished to determine the prevalence of bronchiectasis and patient characteristics. The first cohort of patients recruited to the EARCO (European Alpha1

Research Collaboration) International Registry data base by the end of 2021 was analysed for radiological evidence of both emphysema and bronchiectasis as well as baseline demographic features.

Results: Of the first 505 patients with the PiZZ genotype entered into the data base 418 (82.8%) had a reported CT scan. There were 77 (18.4%) with a normal scan and 38 (9.1%) with bronchiectasis alone. These 2 groups were predominantly female never smokers and had lung function in the normal range. The remaining 303 (72.5%) ZZ patients all had emphysema on the scan and 113 (27%) had additional evidence of bronchiectasis.

Conclusions: The data indicates the bronchiectasis alone is a feature of 9.1% of patients with the PiZZ genotype of Alpha1-antitrypsin deficiency but although emphysema is the dominant lung pathology bronchiectasis is also present in 27% of emphysema cases and may require a different treatment strategy.

Keywords: Alpha-1 antitrypsin deficiency; Bronchiectasis; Emphysema; Prevalence.

Conflict of interest statement

Marc Miravitlles has received speaker fees from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, Menarini, Kamada, Takeda, Zambon, CSL Behring, Specialty Therapeutics, Janssen, Grifols and Novartis, consulting fees from AstraZeneca, Atriva Therapeutics, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, CSL Behring, Inhibrx, Ferrer, Menarini, Mereo Biopharma, Spin Therapeutics, ONO Pharma, Palobiofarma SL, Takeda, Novartis, Novo Nordisk, Sanofi, Zambon and Grifols and research grants from Grifols. Alice M Turner has received either grants or speaker fees from AstraZeneca, GlaxoSmithKline, Boehringer Ingelheim, Chiesi, CSL Behring, Takeda, Vertex and Grifols Biotherapeutics. Robert A Stockley has received research grants from Mereo BioPharma and CSL Behring, consulting fees from Mereo BioPharma, CSL Behring, Vertex, Inhibrx and chairs the DSMB for Takeda.

- 29 references
- 2 figures

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

1

Review

Dermatologie (Heidelb)

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. 2023 Aug 20.
doi: 10.1007/s00105-023-05207-5. Online ahead of print.

[Management of pruritus in the elderly]

[Article in German]

F Witte[1], C Zeidler[2], S Ständer[2]
Affiliations expand

- PMID: 37599291

- DOI: 10.1007/s00105-023-05207-5

Abstract

in English, German

Background: Chronic pruritus (CP), a frequent (20.3%) symptom in the elderly, increases with age. It has a significant impact on the quality of life, ranking among the 50 most burdensome diseases worldwide (Global Burden of Disease Study).

Objectives: The aim is to provide an overview of the symptom CP in the elderly and to improve differentiation of underlying conditions and management of this entity.

Materials and methods: A literature search in PubMed was performed, using the terms 'pruritus', 'elderly' and 'gerontodermatology'.

Results: The main causes of CP in the elderly are the physiologic aging process (xerosis cutis, immunosenescence, neuropathy), the increase in potentially pruritic diseases with increasing age (diabetes mellitus, chronic renal failure), and polypharmacy. Therapeutic options relate to causes, severity of pruritus, and individual patient factors (multimorbidity,

impaired organ function). The recently updated S2k guideline 'Diagnosis and therapy of chronic pruritus' is helpful.

Conclusion: CP in the elderly is challenging for both patients and physicians. Not only the difficulty of identifying the underlying cause, but the complexity of treatment and its tolerability and practicability determines these patients' further burden.

Keywords: Chronic prurigo; Etiology; Gerontodermatology; Quality of life; Therapy.

- 46 references

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

2
BMC Public Health
. 2023 Aug 18;23(1):1579.
doi: 10.1186/s12889-023-16485-y.

Organisation and integrated healthcare approaches for people living with HIV, multimorbidity, or both: a systematic review

Vanessa Nicolau[1], Daniela Brandão[2], Tiago Rua[3], Ana Escoval[2]
Affiliations expand

- PMID: 37596539

- PMCID: PMC10439547

- DOI: 10.1186/s12889-023-16485-y

Abstract

Background: Universal recommendation for antiretroviral drugs and their effectiveness has put forward the challenge of assuring a chronic and continued care approach to PLHIV (People Living with HIV), pressured by aging and multimorbidity. Integrated approaches are emerging which are more responsive to that reality. Studying those approaches, and their relation to the what of delivery arrangements and the how of implementation processes, may support future strategies to attain more effective organizational responses.

Methods: We reviewed empirical studies on either HIV, multimorbidity, or both. The studies were published between 2011 and 2020, describing integrated approaches, their design, implementation, and evaluation strategy. Quantitative, qualitative, or mixed methods were included. Electronic databases reviewed cover PubMed, SCOPUS, and Web of Science. A narrative analysis was conducted on each study, and data extraction was accomplished according to the Effective Practice and Organisation of Care taxonomy of health systems interventions.

Results: A total of 30 studies, reporting 22 different interventions, were analysed. In general, interventions were grounded and guided by models and frameworks, and focused on specific subpopulations, or priority groups at increased risk of poorer outcomes. Interventions mixed multiple integrated components. Delivery arrangements targeted more frequently clinical integration (n = 13), and care in proximity, community or online-telephone based (n = 15). Interventions reported investments in the role of users, through self-management support (n = 16), and in coordination, through multidisciplinary teams (n = 9) and continuity of care (n = 8). Implementation strategies targeted educational and training activities (n = 12), and less often, mechanisms of iterative improvement (n = 3). At the level of organizational design and governance, interventions mobilised users and communities through representation, at boards and committees, and through consultancy, along different phases of the design process (n = 11).

Conclusion: The data advance important lessons and considerations to take steps forward from disease-focused care to integrated care at two critical levels: design and implementation. Multidisciplinary work, continuity of care, and meaningful engagement of users seem crucial to attain care that is comprehensive and more proximal, within or cross organizations, or sectors. Promising practices are advanced at the level of design,

implementation, and evaluation, that set integration as a continued process of improvement and value professionals and users' knowledge as assets along those phases.

Trial registration: PROSPERO number CRD42020194117.

Keywords: Care coordination; Change management; Continuity of care; Coproduction; HIV infection; Integrated care; Learning health systems; Multimorbidity; People-centred care; Self-management.

Conflict of interest statement

The authors declare no competing interests.

- 76 references
- 1 figure

BMC Med

. 2023 Aug 15;21(1):309.
doi: 10.1186/s12916-023-02970-z.

Impact of data source choice on multimorbidity measurement: a comparison study of 2.3 million individuals in the Welsh National Health Service

Clare MacRae[1,2], Daniel Morales[3,4], Stewart W Mercer[5,6], Nazir Lone[6], Andrew Lawson[6,7], Emily Jefferson[3], David McAllister[8], Marjan van den Akker[9,10,11], Alan Marshall[12], Sohan Seth[13], Anna Rawlings[14], Jane Lyons[14], Ronan A Lyons[14], Amy Mizen[14], Eleojo Abubakar[8], Chris Dibben[15], Bruce Guthrie[5,6]
Affiliations expand

- PMID: 37582755

- PMCID: PMC10426056

- DOI: 10.1186/s12916-023-02970-z

Free PMC article

Abstract

Background: Measurement of multimorbidity in research is variable, including the choice of the data source used to ascertain conditions. We compared the estimated prevalence of multimorbidity and associations with mortality using different data sources.

Methods: A cross-sectional study of SAIL Databank data including 2,340,027 individuals of all ages living in Wales on 01 January 2019. Comparison of prevalence of multimorbidity and constituent 47 conditions using data from primary care (PC), hospital inpatient (HI), and linked PC-HI data sources and examination of associations between condition count and 12-month mortality.

Results: Using linked PC-HI compared with only HI data, multimorbidity was more prevalent (32.2% versus 16.5%), and the population of people identified as having multimorbidity was younger (mean age 62.5 versus 66.8 years) and included more women (54.2% versus 52.6%). Individuals with multimorbidity in both PC and HI data had stronger associations with mortality than those with multimorbidity only in HI data (adjusted odds ratio 8.34 [95% CI 8.02-8.68] versus 6.95 (95%CI 6.79-7.12] in people with ≥ 4 conditions). The prevalence of conditions identified using only PC versus only HI data was significantly higher for 37/47 and significantly lower for 10/47: the highest PC/HI ratio was for depression (14.2 [95% CI 14.1-14.4]) and the lowest for aneurysm (0.51 [95% CI 0.5-0.5]). Agreement in ascertainment of conditions between the two data sources varied considerably, being slight for five (kappa < 0.20), fair for 12 (kappa 0.21-0.40), moderate for 16 (kappa 0.41-0.60), and substantial for 12 (kappa 0.61-0.80) conditions, and by body system was lowest for mental and behavioural disorders. The percentage agreement, individuals with a condition identified in both PC and HI data, was lowest in anxiety (4.6%) and highest in coronary artery disease (62.9%).

Conclusions: The use of single data sources may underestimate prevalence when measuring multimorbidity and many important conditions (especially mental and behavioural disorders). Caution should be used when interpreting findings of research examining individual and multiple long-term conditions using single data sources. Where available, researchers using electronic health data should link primary care and hospital inpatient data to generate more robust evidence to support evidence-based healthcare planning decisions for people with multimorbidity.

Keywords: Electronic health records; Epidemiology; Multimorbidity.

Conflict of interest statement

The authors declare that they have no competing interests.

- 40 references
- 3 figures

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

FULL TEXT LINKS

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

1
Respir Res
.
2023 Aug 19;24(1):205.
doi: 10.1186/s12931-023-02510-6.

Rhinovirus infection induces secretion of endothelin-1 from airway epithelial cells in both in vitro and in vivo models

Alane Blythe C Dy[1], Jason Girkin[2], Antonella Marrocco[1], Adam Collison[2], Chimwemwe Mwase[1], Michael J O'Sullivan[1], Thien-Khoi N Phung[1], Joerg Mattes[2], Cynthia Koziol-White[3], James E Gern[4], Yury A Bochkov[4], Nathan W Bartlett[2], Jin-Ah Park[5]
Affiliations expand

- PMID: 37598152

- DOI: 10.1186/s12931-023-02510-6

Abstract

Background: Rhinovirus (RV) infection of airway epithelial cells triggers asthma exacerbations, during which airway smooth muscle (ASM) excessively contracts. Due to ASM contraction, airway epithelial cells become mechanically compressed. We previously reported that compressed human bronchial epithelial (HBE) cells are a source of endothelin-1 (ET-1) that causes ASM contraction. Here, we hypothesized that epithelial sensing of RV by TLR3 and epithelial compression induce ET-1 secretion through a TGF-β receptor (TGFβR)-dependent mechanism.

Methods: To test this, we used primary HBE cells well-differentiated in air-liquid interface culture and two mouse models (ovalbumin and house dust mite) of allergic airway disease (AAD). HBE cells were infected with RV-A16, treated with a TLR3 agonist (poly(I:C)), or exposed to compression. Thereafter, EDN1 (ET-1 protein-encoding gene) mRNA expression and secreted ET-1 protein were measured. We examined the role of TGFβR in ET-1 secretion using either a pharmacologic inhibitor of TGFβR or recombinant TGF-β1 protein. In the AAD mouse models, allergen-sensitized and allergen-challenged mice were subsequently infected with RV. We then measured ET-1 in bronchoalveolar lavage fluid (BALF) and airway hyperresponsiveness (AHR) following methacholine challenge.

Results: Our data reveal that RV infection induced EDN1 expression and ET-1 secretion in HBE cells, potentially mediated by TLR3. TGFβR activation was partially required for ET-1 secretion, which was induced by RV, poly(I:C), or compression. TGFβR activation alone was sufficient to increase ET-1 secretion. In AAD mouse models, RV induced ET-1 secretion in BALF, which positively correlated with AHR.

Conclusions: Our data provide evidence that RV infection increased epithelial-cell ET-1 secretion through a TGFβR-dependent mechanism, which contributes to bronchoconstriction during RV-induced asthma exacerbations.

Keywords: Asthma exacerbations; Bronchoconstriction; Epithelial endothelin-1; Mechanical compression; Rhinovirus infection.

- 54 references

SUPPLEMENTARY INFO

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2

Ann Epidemiol

. 2023 Aug 18;S1047-2797(23)00155-2.
doi: 10.1016/j.annepidem.2023.08.003. Online ahead of print.

Age at Menarche and Asthma Onset among US Girls and Women: Findings from NHANES, 2001–2018

Li Cai[1], Xun Li[1], Lan Qiu[1], Yaqi Wang[2], Li Wu[3], Xiaojie Wu[4], Ruijun Xu[2], Yuewei Liu[2], Yun Zhou[5]

Affiliations expand

- PMID: 37598789

- DOI: 10.1016/j.annepidem.2023.08.003

Abstract

Objectives: Our study aimed to quantitatively estimate the association of age at menarche with the risk of childhood- and adult-onset asthma separately.

Methods: A retrospective cohort study of 24,282 US girls and women aged less than 80 years was conducted using continuous NHANES data from 2001-2018, and Cox

proportional hazards regression models with censoring ages of 19 and 79 years were employed to separately estimate hazard ratios of childhood- and adult-onset asthma associated with age at menarche.

Results: Each one-year increase in age at menarche was significantly associated with a 16% (hazard ratio (HR) = 0.84; 95% confidence interval (CI): 0.77-0.91) decrease in the risk of childhood-onset asthma. Compared with age at menarche of 12-14 years, we observed a 56% (HR = 1.56; 95% CI: 1.19-2.04) increased risk of childhood-onset asthma for early menarche (age at menarche < 12 years) and a 40% (HR = 0.60; 95% CI: 0.32-1.10) decreased risk for late menarche (age at menarche ≥15 years). Race, family income, BMI, education and a family history of asthma did not modify these associations. No significant association was noted between age at menarche and adult-onset asthma.

Conclusion: These results demonstrate that early menarche may represent a risk factor for childhood-onset asthma in the US, indicating the need for timely and effective management of individuals with early menarche to prevent asthma.

Keywords: National Health and Nutrition Examination Survey; US population; adult-onset asthma; childhood-onset asthma; menarche.

Conflict of interest statement

Declaration of Competing Interest All authors have reviewed and approved the submission of the manuscript. None of the authors has any conflicts of interest in the matter. Conflict of Interest All authors declare that they have no conflicts of interest.

Int Arch Allergy Immunol

. 2023 Aug 18;1-7.

doi: 10.1159/000532068. Online ahead of print.

Risk Factors for Abnormal Small Airway Function Indicators in Nasal Polyp Patients with and without Asthma

Jing Guo[1,2,3], Jianwei Wang[1,2,3], Xinjun Xu[1,2,3], Yujuan Yang[1,2,3], Pengyi Yu[1,2,3], Zhen Liu[1,2,3], Jiayu Cao[1,2,3], Qintai Yang[4], Yu Zhang[1,2,3], Xicheng Song[1,2,3]
Affiliations expand

- PMID: 37598674

- DOI: 10.1159/000532068

Abstract

Introduction: Small airway dysfunction (SAD) is associated with type 2 inflammation in patients who have non-asthmatic chronic rhinosinusitis with nasal polyps (CRSwNPs); however, the risk factors for abnormal small airway function indicators in CRSwNP patients with and without asthma remain unclear.

Methods: We retrospectively analyzed 41 asthmatic and 109 non-asthmatic CRSwNP patients. Clinical characteristics were compared between groups, correlations between small airway function and clinical parameters were calculated, and independent risk factors for every small airway indicator were identified in each group.

Results: Asthmatic CRSwNP patients had significantly reduced small airway function, and the proportion of patients with SAD was higher in asthmatic CRSwNP patients (65.85%) than in patients without asthma (9.17%). With regard to specific airway function indicators, age and a patient's blood eosinophil (%) were identified as independent risk factors for lower FEF50% %pred and FEF25-75% pred, with age being an independent risk factor for FEF75% %pred in asthmatic CRSwNP patients. In non-asthmatic CRSwNP patients, allergic rhinitis comorbidity was found to be an independent risk factor for FEF50% %pred, FEF75% %pred, and FEF25-75% %pred.

Conclusion: Physicians should pay greater attention to risk factors for abnormal small airway function indicators in patients with CRSwNPs to prevent the occurrence of SAD.

Keywords: Allergic rhinitis; Asthma; Chronic rhinosinusitis with nasal polyps; Eosinophil; Small airway dysfunction.

Cancer Epidemiol

. 2023 Aug 18;86:102439.
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Lung cancer in nonsmokers- A risk factor analysis

Denise Albano[1], Ankit Dhamija[2], Yunhan Liao[3], Allison Mclarty[2], Hannah Talavera[2], Esther K Kim[2], Mark Ashamalla[4]
Affiliations expand

- PMID: 37598649

- DOI: 10.1016/j.canep.2023.102439

Abstract

Institutions: STONY BROOK MEDICAL CENTERRATIONALE: Lung Cancer screening for the high-risk smoking population has been proven to save lives. However, in 2022, 20% of newly diagnosed lung cancers (47,300) were in nonsmokers. These patients were found to be diagnosed at later stages. This may be at least partly due to not meeting criteria for and participating in current lung cancer screening. This study aims to describe characteristics of a never smoker patient population to help identify common risk factors which might merit inclusion in lung cancer screening and thus improve patient outcomes.

Methods: This retrospective single center study included never-smoker patients diagnosed with lung nodules and never-smoker patients diagnosed with lung cancer from 2016 to 2022. Data was obtained from the Stony Brook Medical Center electronic medical record. 16,056 patients were identified as never-smokers who were asked by the medical assistant

if they ever smoked in their lifetime. Patients were eliminated if they had any smoking history up to first diagnosis date. Demographics, radiology, histology, diagnosis dates, comorbidities, smoking status, and exposures collected through ICD10 codes and not self-reported, were investigated.

Results: Of 16,056 never-smoking patients, 9315 (58.02%) were females diagnosed with lung nodules and 6741 (41.98%) were males diagnosed with lung nodules. The univariate analysis showed significant differences between gender, age at nodule diagnosis, and patients with and without comorbidities including chronic obstructive pulmonary disease (COPD), hypertension (HTN), and family history (FHX) of lung cancer. The percentage of lung cancer patients among females was significantly higher than among males. Patients having lung cancer were older. The percentages of lung cancer patients with these comorbidities were significantly higher than those without. However, there was no significant difference found between patients with and without diabetes mellitus (DM). The multivariable logistic regression suggested that age at nodule diagnosis and comorbidities including COPD (which included asthma, emphysema and chronic bronchitis) and family history of lung cancer were significantly associated with lung cancer. Older patients and patients with those comorbidities had a higher risk of developing cancer than those who were younger or without those comorbidities. The study excluded HTN and included age at nodule diagnosis in the logistic regression model as HTN was found to be protective against lung cancer due to age at lung nodule diagnosis. Please refer to the appendix for further details.

Conclusion: Never-smoker patients who were older and with COPD and Family History of lung cancer had higher risk of developing lung cancer than younger patients without these comorbidities. In this study, gender had no impact on outcome.

Keywords: Lung neoplasm (D008175); NLM class WF 658.

Conflict of interest statement

Declaration of Competing Interest All authors do not have any financial and or personal relationships with other people or organizations that could inappropriately influence their work. NONE.

5
J Asthma
.
. 2023 Aug 18;1-11.
doi: 10.1080/02770903.2023.2248485. Online ahead of print.

In symptomatic patients on as-needed inhaled corticosteroids-formoterol, VAS asthma is associated with small airways resistance

Ilgim Vardaloglu[1], Bernardo Sousa-Pinto[2,3], Jean Bousquet[4,5,6], Peter Dodek[7], Anna Bedbrook[6,8], Mert Karatas[9], Bilun Gemicioglu[1]
Affiliations expand

- PMID: 37594413

- DOI: 10.1080/02770903.2023.2248485

Abstract

Objectives: Impulse oscillometry (IOS) can demonstrate small airways disease even when spirometry values are normal. However, it is unknown if absence of symptoms excludes increased small airways resistance in asthma patients. We aimed to correlate symptoms (assessed through visual analogue scales) with measures of small airways resistance in patients with asthma and to determine whether less symptomatic patients have increased small airways resistance.**Methods:** We conducted a single centre, prospective cohort study. We included controlled asthma patients on as-needed inhaled corticosteroids-formoterol. Patients were evaluated on their symptom VASs, Spirometry and IOS (with R5-R20% measuring small airways resistance) which were measured both in periods when they were less symptomatic and symptomatic. Symptoms were assessed using MASK-air®, an mHealth app that includes a daily monitoring questionnaire with validated VASs. We correlated MASK-air VASs with small airways resistance.**Results:** We assessed 29 patients. There was a significant correlation between VAS asthma and R5-R20% in symptomatic periods (r = 0.43; 95%CI = 0.13;0.68, p = 0.019), but not in less symptomatic periods (0.04; 95%CI-0.40;0.46; p = 0.825). In less symptomatic periods, patients presenting with low VAS asthma (VAS < 30) displayed a lower median R5-R20% than the remainder (0.26 versus

0.35), as well as a lower R5% (0.13 versus 0.15) ($p < 0.001$). In 68.9% of less symptomatic patients, R5-R20 values remained higher than normal values.**Conclusion:** In symptomatic patients on as-needed inhaled corticosteroids-formoterol, VAS asthma was associated with small airways resistance. However, even if these patients are less symptomatic, small airways resistance may be higher than normal. Since SAD significantly affects asthma control, patients should be carefully followed-up even in less symptomatic periods.

Keywords: Airway resistance; Asthma; Patient Reported Outcome Measures; Symptom assessment.

Cardiol Rev

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doi: 10.1097/CRD.0000000000000600. Online ahead of print.

Asthma and Cardiovascular Diseases: Uncovering Common Ground in Risk Factors and Pathogenesis

Kanishk Aggarwal[1], Vasu Bansal[1], Ramsha Mahmood[2], Sai Gautham Kanagala[3], Rohit Jain[4]

Affiliations expand

- PMID: 37594265

- DOI: 10.1097/CRD.0000000000000600

Abstract

Asthma and cardiovascular diseases (CVDs) are the 2 common and complex health problems with a substantial global impact. Epidemiological studies indicate that asthma

and CVDs are common, with evidence supporting their cooccurrence. Inflammation, oxidative stress, obesity, metabolic syndrome, smoking, secondhand smoke exposure, physical inactivity, and environmental exposures are all risk factors for asthma and CVDs. In addition, inflammatory and immunological pathways, autonomic dysfunction, endothelial dysfunction, thrombosis, coagulation, and common genetic risk factors contribute to the asthma-CVD relationship. Asthmatic individuals have higher morbidity and mortality rates related to CVDs and high-risk factors. Techniques such as screening for CVDs in asthma patients, pharmaceutical therapy, and lifestyle changes are critical for effectively managing these comorbid illnesses. Understanding the link between asthma and CVD is necessary for integrated and clinical management approaches to enhance patient outcomes and lessen the burden of these related diseases.

Conflict of interest statement

Disclosure: The authors have no conflicts of interest to report.

- 84 references

Adv Ther

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. 2023 Aug 17.
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Understanding the Clinical Implications of Individual Patient Characteristics and Treatment Choice on the Risk of

Exacerbation in Asthma Patients with Moderate–Severe Symptoms

Dave Singh[1], Sean Oosterholt[2], Ian Pavord[3], Gabriel Garcia[4], Abhijith Pg[5], Oscar Della Pasqua[6,7]
Affiliations expand

- PMID: 37589831

- DOI: 10.1007/s12325-023-02590-2

Abstract

Introduction: The assessment of future risk has become an important feature in the management of patients with asthma. However, the contribution of patient-specific characteristics and treatment choices to the risk of exacerbation is poorly understood. Here we evaluated the effect of interindividual baseline differences on the risk of exacerbation and treatment performance in patients receiving regular maintenance doses of inhaled corticosteroids (ICS) or ICS/long-acting beta-agonists (LABA) combination therapy.

Methods: Exacerbations and changes to asthma symptoms 5-item Asthma Control Questionnaire (ACQ-5) were simulated over a 12-month period using a time-to-event and a longitudinal model developed from phase III/IV studies in patients with moderate-severe asthma (N = 16,282). Simulations were implemented to explore treatment performance across different scenarios, including randomised designs and real-world settings. Treatment options included regular dosing with ICS monotherapy [fluticasone propionate (FP)] and combination therapy [fluticasone propionate/salmeterol (FP/SAL) or budesonide/formoterol (BUD/FOR)]. Exacerbation rate was analysed using the log-rank test. The cumulative incidence of events was summarised stratified by treatment.

Results: Being a woman, smoker, having higher baseline ACQ-5 and body mass index (BMI) and lower forced expiratory volume in the first second (FEV_1) are associated with increased exacerbation risk ($p < 0.01$). This risk is bigger in winter because of the seasonal variation effect. Across the different scenarios, the use of FP/SAL resulted in a 10% lower annual incidence of exacerbations relative to FP or regular dosing BUD/FOR, independently of baseline characteristics. Similar differences in the annual incidence of exacerbations were also observed between treatments in obese patients (BMI ≥ 25-35 kg/m^2) ($p < 0.01$) and in patients who do not achieve symptom control on FP monotherapy.

Conclusions: Individual baseline characteristics and treatment choices affect future risk. Achieving comparable levels of symptom control whilst on treatment does not imply

comparable risk reduction, as shown by the lower exacerbation rates in FP/SAL vs. BUD/FOR-treated patients. These factors should be considered as a basis for personalised clinical management of patients with moderate-severe asthma.

Keywords: ACQ-5; Asthma exacerbation; Clinical trial simulations; Fluticasone propionate; Future risk; ICS/LABA combination therapy; Salmeterol; Symptom control; Treatable traits.

Plain language summary

The goal of this project was to demonstrate that individual baseline characteristics can affect the risk of exacerbation as well as the overall treatment response in patients receiving regular maintenance doses of inhaled corticosteroids, given as monotherapy or in combination with long-acting beta-agonists. Using computer simulations based on a drug–disease model previously developed from a large pool of patients with moderate–severe asthma symptoms (N = 16,282), we describe how demographic and clinical baseline patient characteristics at the time of treatment start correlate with the risk of exacerbation. Our results indicate that poor symptom control, limited lung function, obesity, smoking and sex are associated with significant increase in the incidence of asthma attacks. Such an effect is augmented in winter because of the contribution of seasonal variation. This analysis also allowed us to assess how different treatments modify or reduce the annual incidence of moderate to severe attacks. In addition, simulated scenarios showed that combination therapy with fluticasone propionate/salmeterol results in 10% fewer asthma attacks relative to budesonide/formoterol combination therapy. Such a difference may be associated with corticosteroid-specific properties, which vary between inhaled corticosteroids. Consequently, even though comparable level of immediate relief and symptom control may be achieved whilst on treatment, these effects do not imply the same long-term reduction in the risk of exacerbation. These factors should be considered as a basis for personalised clinical management of patients with moderate–severe asthma.

- 45 references

SUPPLEMENTARY INFO

Grant supportexpand

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8
J Asthma
.
. 2023 Aug 17;1-10.
doi: 10.1080/02770903.2023.2244579. Online ahead of print.

Serum levels of interleukin-33, soluble ST2 and IgE in patients with asthma: a case-control study

Himadri Singh[1], Alkesh Khurana[2], Ashok Kumar[1], Rohit Saluja[3]
Affiliations expand

- PMID: 37548422

- DOI: 10.1080/02770903.2023.2244579

Abstract

Introduction: Interleukins play a very important role in the pathophysiology of asthma. Interleukin-33 (IL-33) is a partially explored cytokine in asthma. It binds with a specific receptor called suppression of tumorigenicity 2 (ST2). The study aims to evaluate the serum levels of IL-33, sST2 and IgE in asthmatic patients and healthy controls and its further association with the forced expiratory volume in one second (FEV 1%) and absolute eosinophil count.

Materials and methods: We enrolled 100 asthmatic patients and 57 healthy subjects for the study. We measured serum levels of IgE, IL-33, and sST2. Based on serum IgE levels, patients were divided into allergic and non-allergic groups. Statistical analysis was done by using Graph pad prism software 8.

Results: We found significantly elevated levels of IL-33 and IgE in asthmatic patients as compared to healthy subjects. However, sST2 levels were significantly lower in asthmatic patients than in healthy subjects. FEV1% values were decreased in uncontrolled asthmatic patients. In addition, serum levels of IL-33 were significantly correlated with the IgE. Furthermore, we found a significant correlation between IL-33 and AEC in allergic asthmatic patients.

Conclusion: In this study, we reported elevated IL-33 and IgE levels and decreased sST2 levels in asthmatic patients compared to healthy controls. IL-33 and sST2 may act as inflammatory biomarkers for allergic diseases such as asthma.

Keywords: FEV1%; IL-33; asthma; sST2.

Eur Respir J

. 2023 Aug 17;62(2):2300700.
doi: 10.1183/13993003.00700-2023. Print 2023 Aug.

Revisiting asthma pharmacotherapy: where do we stand and where do we want to go?

Mario Cazzola[1], Clive P Page[2], Maria Gabriella Matera[3], Paola Rogliani[4], Nicola A Hanania[5]
Affiliations expand

- PMID: 37474159

- DOI: 10.1183/13993003.00700-2023

Abstract

Several current guidelines/strategies outline a treatment approach to asthma, which primarily consider the goals of improving lung function and quality of life and reducing symptoms and exacerbations. They suggest a strategy of stepping up or down treatment, depending on the patient's overall current asthma symptom control and future risk of exacerbation. While this stepwise approach is undeniably practical for daily practice, it does not always address the underlying mechanisms of this heterogeneous disease. In the last

decade, there have been attempts to improve the treatment of severe asthma, such as the addition of a long-acting antimuscarinic agent to the traditional inhaled corticosteroid/long-acting β_2-agonist treatment and the introduction of therapies targeting key cytokines. However, despite such strategies several unmet needs in this population remain, motivating research to identify novel targets and develop improved therapeutic and/or preventative asthma treatments. Pending the availability of such therapies, it is essential to re-evaluate the current conventional "one-size-fits-all" approach to a more precise asthma management. Although challenging, identifying "treatable traits" that contribute to respiratory symptoms in individual patients with asthma may allow a more pragmatic approach to establish more personalised therapeutic goals.

Conflict of interest statement

Conflict of interest: M. Cazzola participated as a faculty member and advisor in scientific meetings and courses under the sponsorship of Abdi Ibrahim, Alkem, Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi Farmaceutici, Cipla, GlaxoSmithKline, Glenmark, Lallemand, Mankind Pharma, Menarini Group, Mundipharma, Novartis, Pfizer, Recipharm, Sanofi, Teva, Verona Pharma and Zambon, and is or was a consultant to ABC Farmaceutici, AstraZeneca, Chiesi Farmaceutici, GlaxoSmithKline, Lallemand, Novartis, Ockham Biotech, Recipharm, Verona Pharma and Zambon. C.P. Page has acted as a consultant to Eurodrug, Recipharm, Glycosynnovation and PrEP Biopharma, and also holds equity in Verona Pharma. M.G. Matera participated as a faculty member and advisor in scientific meetings and courses under the sponsorship of ABC Farmaceutici, Almirall, AstraZeneca, Chiesi Farmaceutici, GlaxoSmithKline and Novartis, was a consultant to Chiesi Farmaceutici and GlaxoSmithKline, and her department was funded by GlaxoSmithKline and Novartis. P. Rogliani has participated as a faculty member and advisor in scientific meetings and courses under the sponsorship of Almirall, AstraZeneca, Biofutura, Boehringer Ingelheim, Chiesi Farmaceutici, GlaxoSmithKline, Menarini Group, Mundipharma, Novartis, Recipharm, Sanofi and Zambon, and her department was funded by Almirall, Boehringer Ingelheim, Chiesi Farmaceutici, Novartis and Zambon. N.A. Hanania received honoraria for serving as advisor or consultant for GlaxoSmithKline, AstraZeneca, Sanofi, Regeneron, Amgen, Genentech, Novartis and Teva, and his institution received research grant support on his behalf from GlaxoSmithKline, Genentech, Sanofi, Teva, Novartis and AstraZeneca. The authors have no other relevant affiliations or financial involvement with any organisation or entity with a financial interest in, or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Eur Respir J

. 2023 Aug 17;62(2):2300442.
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European Respiratory Society statement on frailty in adults with chronic lung disease

Christian R Osadnik[1,2], Lisa J Brighton[3,4], Chris Burtin[5], Matteo Cesari[6], Lies Lahousse[7], Will D C Man[8,9,10], Alessandra Marengoni[11,12], Andreja Sajnic[13], Jonathan P Singer[14], Lies Ter Beek[15], Ioanna Tsiligianni[16], Janos T Varga[17,18], Stefano Pavanello[19], Matthew Maddocks[3]
Affiliations expand

- PMID: 37414420

- DOI: 10.1183/13993003.00442-2023

Abstract

Frailty is a complex, multidimensional syndrome characterised by a loss of physiological reserves that increases a person's susceptibility to adverse health outcomes. Most knowledge regarding frailty originates from geriatric medicine; however, awareness of its importance as a treatable trait for people with chronic respiratory disease (including asthma, COPD and interstitial lung disease) is emerging. A clearer understanding of frailty and its impact in chronic respiratory disease is a prerequisite to optimise clinical management in the future. This unmet need underpins the rationale for undertaking the present work. This European Respiratory Society statement synthesises current evidence and clinical insights from international experts and people affected by chronic respiratory conditions regarding frailty in adults with chronic respiratory disease. The scope includes coverage of frailty within international respiratory guidelines, prevalence and risk factors, review of clinical management options (including comprehensive geriatric care, rehabilitation, nutrition, pharmacological and psychological therapies) and identification of evidence gaps to inform future priority areas of research. Frailty is underrepresented in

international respiratory guidelines, despite being common and related to increased hospitalisation and mortality. Validated screening instruments can detect frailty to prompt comprehensive assessment and personalised clinical management. Clinical trials targeting people with chronic respiratory disease and frailty are needed.

Conflict of interest statement

Conflict of interest: The task force members report no conflicts of interest for the present work, but acknowledge the following roles and funding sources during the conduct of this work. C.R. Osadnik received a Rebecca L. Cooper Medical Research Foundation project grant (2020–21) and an education grant from GSK Australia, paid to his institution, and delivered an educational lecture for Novartis Australia, all outside of the present work. L.J. Brighton is supported by the NIHR Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust, and is funded by an Economic and Social Research Council Post-Doctoral Fellowship (ES/X005259/1). L. Lahousse reports external expert consultation for AstraZeneca and lectures for Chiesi and IPSA vzw, a non-profit organisation facilitating lifelong learning for healthcare providers, (to be) paid to her institution, outside this manuscript. W.D.C. Man is supported by National Institute for Health and Care Research (NIHR) Research for Patient Benefit awards (PB-PG-0816-20022 and PB-PG-0317-20032) and a NIHR Artificial Intelligence Award (AI_AWARD02204). A. Marengoni received fees for lectures provided to Vyvamed and Oliba. A. Sajnic reports advisory board membership for AstraZeneca and delivery of a lecture for Roche. J.P. Singer reports funding (NHLBI U01HL163242, U01HL145435, R01HL134851) and scientific advisory board membership for Altavant Sciences and Mallinckrodt Pharmaceuticals. I. Tsiligianni reports grants/advisory boards all unrelated to the current work from Novartis, GSK, Boehringer Ingelheim, AstraZeneca and Chiesi. J.T. Varga reports unrelated grants/advisory boards from Chiesi and Boehringer Ingelheim. S. Pavanello is president of Unione Trapiantati Polmone, Padua, Italy. M. Maddocks is supported by a National Institute for Health and Care Research (NIHR) Career Development Fellowship (CDF-2017–10-009) and the NIHR Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust. The remaining authors have no potential conflicts of interest to disclose.

SUPPLEMENTARY INFO

Grant supportexpand

Eur J Pharm Biopharm

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Inhalation powder development without carrier: how to engineer ultra-flying microparticles?

Anna Lechanteur[1], Eva Gresse[2], Luisa Orozco[3], Erwan Plougonven[4], Angélique Léonard[4], Nicolas Vandewalle[3], Geoffroy Lumay[3], Brigitte Evrard[2]
Affiliations expand

- PMID: 37595762

- DOI: 10.1016/j.ejpb.2023.08.010

Abstract

Particle engineering technologies have led to the commercialization of new inhaled powders like PulmoSol™ or PulmoSphere™. Such platforms are produced by spray drying, a well-known process popular for its versatility, thanks to wide-ranging working parameters. Whereas these powders contain a high drug-loading, we have studied a low-dose case, in optimizing the production of powders with two anti-asthmatic drugs, budesonide and formoterol. Using a Design of Experiments approach, 27 powders were produced, with varying excipient mixes (cyclodextrins, raffinose and maltodextrins), solution concentrations, and spray drying parameters in order to maximize deep lung deposition, measured through fine particle fraction (next generation impactor). Based on statistical analysis, two powders made of hydropropyl-β-cyclodextrin alone or mixed with raffinose and L-leucine were selected. Indeed, the two powders demonstrated very high fine particle fraction (>55%), considerably better than commercially available products. Deep lung deposition has been correlated to very fine particle size and lower microparticles interactions shown by laser diffraction assays at different working pressures, and particle morphometry. Moreover, the two drugs would be predicted to deposit homogeneously

into the lung according to impaction studies. Uniform delivery is fundamental to control symptoms of asthma. In this study, we develop carrier-free inhalation powders promoting very efficient lung deposition and demonstrate the high impact of inter-particular interactions intensity on their aerosolization behavior.

Keywords: DOE; DPI; inhalation; particle engineering; spray drying.

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.

J Allergy Clin Immunol

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Polygenic risk scores identify heterogeneity in asthma and chronic obstructive pulmonary disease

Matthew Moll[1], Joanne E Sordillo[2], Auyon J Ghosh[3], Lystra P Hayden[4], Gregory McDermott[5], Michael J McGeachie[6], Amber Dahlin[6], Anshul Tiwari[6], Monica G Manmadkar[6], Eric D Abston[7], Chandan Pavuluri[1], Aabida Saferali[6], Sofina Begum[6], John P Ziniti[6], Amund Gulsvik[8], Per S Bakke[8], Hugues Aschard[9], Carlos Iribarren[10], Craig P Hersh[1], Jeffrey A Sparks[5], Brian D Hobbs[1], Jessica A Lasky-Su[6], Edwin K Silverman[6], Scott T Weiss[6], Ann Chen Wu[2], Michael H Cho[1]

Affiliations expand

- PMID: 37595761

- DOI: 10.1016/j.jaci.2023.08.002

Abstract

Rationale: Asthma and chronic obstructive pulmonary disease (COPD) have distinct and overlapping genetic and clinical features.

Objectives: We hypothesized that polygenic risk scores (PRSs) for asthma (PRS_{Asthma}) and spirometry (FEV_1 and FEV_1/FVC; PRS_{spiro}) would demonstrate differential associations with asthma, COPD, and asthma-COPD overlap (ACO).

Methods: We developed and tested two asthma PRSs and applied the higher performing PRS_{Asthma} and a previously-published PRS_{spiro} to research (COPDGene and CAMP, with spirometry) and electronic-health record (EHR)-based (MGB Biobank and GERA) studies. We assessed the association of PRSs with COPD and asthma using modified random and binary effects meta-analyses, and ACO and asthma exacerbations in specific cohorts. Models were adjusted for confounders and genetic ancestry.

Measurements and main results: In meta-analyses of 102,477 participants, the PRS_{Asthma} (OR per SD 1.16 [95% CI: 1.14-1.19]) and PRS_{spiro} (OR per SD 1.19 [95% CI: 1.17-1.22]) both predicted asthma, while the PRS_{spiro} predicted COPD (OR per SD 1.25 [95% CI: 1.21-1.30]). However, results differed by cohort. The PRS_{spiro} was not associated with COPD in GERA and MGB. In COPDGene, the PRS_{Asthma} (OR per SD: Whites: 1.3; African Americans (AA): 1.2) and PRS_{spiro} (OR per SD: Whites: 2.2; AA: 1.6) were both associated with ACO. In GERA, the PRS_{Asthma} was associated with asthma exacerbations (OR 1.18) in whites; the PRS_{spiro} was associated with asthma exacerbations in white, LatinX, and East Asian participants.

Conclusions: Polygenic risk scores for asthma and spirometry are both associated with asthma-COPD overlap and asthma exacerbations. Genetic prediction performance differs in research versus EHR-based cohorts.

Keywords: asthma; asthma-COPD overlap; chronic obstructive pulmonary disease; heterogeneity; polygenic risk scores.

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Environ Pollut
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Short-term exposure to ultrafine particles and mortality and hospital admissions due to respiratory and cardiovascular diseases in Copenhagen, Denmark

Marie L Bergmann[1], Zorana J Andersen[1], Andreas Massling[2], Paula A Kindler[3], Steffen Loft[1], Heresh Amini[4], Thomas Cole-Hunter[1], Yuming Guo[5], Matija Maric[1], Claus Nordstrøm[2], Mahmood Taghavi[1], Stéphane Tuffier[1], Rina So[1], Jiawei Zhang[1], Youn-Hee Lim[6]
Affiliations expand

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Abstract

Ultrafine particles (UFP; particulate matter <0.1 μm in diameter) may be more harmful to human health than larger particles, but epidemiological evidence on their health effects is still limited. In this study, we examined the association between short-term exposure to UFP and mortality and hospital admissions in Copenhagen, Denmark. Daily concentrations of UFP (measured as particle number concentration in a size range 11-700 nm) and meteorological variables were monitored at an urban background station in central Copenhagen during 2002-2018. Daily counts of deaths from all non-accidental causes, as well as deaths and hospital admissions from cardiovascular and respiratory diseases were obtained from Danish registers. Mortality and hospital admissions associated with an

interquartile range (IQR) increase in UFP exposure on a concurrent day and up to six preceding days prior to the death or admission were examined in a case-crossover study design. Odds ratios (OR) with 95% confidence intervals (CI) per one IQR increase in UFP were estimated after adjusting for temperature and relative humidity. We observed 140,079 deaths in total, 236,003 respiratory and 342,074 cardiovascular hospital admissions between 2002 and 2018. Hospital admissions due to respiratory and cardiovascular diseases were significantly positively associated with one IQR increase in UFP (OR: 1.04 [95% CI: 1.01, 1.07], lag 0-4, and 1.02 [1.00, 1.04], lag 0-1, respectively). Among the specific causes, the strongest associations were found for chronic obstructive pulmonary disease (COPD) mortality and asthma hospital admissions and two-day means (lag 0-1) of UFP (OR: 1.13 [1.01, 1.26] and 1.08 [1.00, 1.16], respectively, per one IQR increase in UFP). Based on 17 years of UFP monitoring data, we present novel findings showing that short-term exposure to UFP can trigger respiratory and cardiovascular diseases mortality and morbidity in Copenhagen, Denmark. The strongest associations with UFP were observed with COPD mortality and asthma hospital admissions.

Keywords: Air pollution; Cardiovascular diseases; Mortality; Particle number concentration; Respiratory tract diseases; Ultrafine particles.

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.

14

Respir Med

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Impulse oscillometry defined small airway dysfunction in asthmatic patients with normal spirometry: Prevalence, clinical associations, and impact on asthma control

Marcello Cottini[1], Benedetta Bondi[2], Diego Bagnasco[3], Fulvio Braido[3], Giovanni Passalacqua[3], Anita Licini[1], Carlo Lombardi[4], Alvise Berti[5], Pasquale Comberiati[6], Massimo Landi[7], Enrico Heffler[8], Giovanni Paoletti[8]
Affiliations expand

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- DOI: 10.1016/j.rmed.2023.107391

Abstract

Background: The small-airway dysfunction (SAD), detected with impulse oscillometry (IOS) methods, has been recently better characterized in patients with asthma. However, little is known about SAD in asthmatic patients with normal spirometry (NS).

Objective: In this study, we aimed to investigate, in an unselected sample of 321 patients with physician-diagnosed asthma and NS, prevalence, clinical characterization, and impact on asthma control of IOS-defined SAD. As a secondary objective of the study, we focused on comparing the difference between IOS- and spirometry-defined SAD.

Methods: Consecutive patients with a previous diagnosis of asthma but normal spirometry at the moment of the enrollment were stratified by the presence of IOS-defined SAD (difference in resistance at 5 Hz and at 20 Hz [R5-R20] greater than 0.07 kPa x s x L^{-1}). We have also assessed the presence of SAD defined by spirometry, according to FEF 25-75 < 65% of the predicted. Clinical and laboratory features were collected, and univariable and multivariable analyses were used to analyze cross-sectional associations between clinical variables and outcomes (SAD).

Results: IOS-defined SAD was present in 54.1% of the cohort. In contrast, spirometry-defined SAD was present in only 10% of patients. Subjects with IOS-defined SAD showed less well-controlled asthma and a higher mean inhaled corticosteroid dosage use compared with subjects without SAD (both P < .001). Overweight (odds ratio [OR], 1.14;

95% CI, 1.05-1.23), exacerbation history (OR, 3.06; 95% CI, 1.34-6.97), asthma-related night awakenings (OR, 6.88; 95% CI, 2.13-22.23), exercise-induced asthma symptoms (OR, 33.5; 95% CI, 9.51-117.8), and controlled asthma (OR, 0.22; 95% CI, 0.06-0.84) were independently associated with SAD.

Conclusions: Asthmatic patients with IOS-defined SAD showed less well-controlled asthma, more severe exacerbations and higher mean inhaled corticosteroid dosage. We confirmed exercise-induced asthma, asthma-related night awakenings, exacerbation history, and overweight as independently associated with SAD, while showing well-controlled asthma as inversely associated. SAD may be overlooked by standard spirometry.

Conflict of interest statement

Declaration of competing interest All authors have no conflicts of interest to disclose about this paper.

Meta-Analysis

Sci Rep

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Efficacy and safety of inhaled heparin in asthmatic and chronic obstructive pulmonary disease patients: a systematic review and a meta-analysis

Rasha Ashmawy[1], Adel Zaki[2], Ayman Baess[3], Iman El Sayed[4]

Affiliations expand

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- PMCID: PMC10432425
- DOI: 10.1038/s41598-023-40489-8

Free PMC article

Abstract

Asthma and chronic obstructive pulmonary disease (COPD) are prevalent chronic respiratory disorders that cause significant morbidity and mortality. Some studies evaluated the use of inhaled unfractionated heparin (UFH) in the treatment of asthma and COPD. We aimed to synthesize the available evidence for the efficacy and safety of inhaled heparin in improving lung functions among asthmatic and COPD patients. A comprehensive search was performed using Pubmed, Embase, EBSCO, Scopus, Web of Science, Cochrane CENTRAL, WHO Clinical trials, clinicaltrials.gov, Iranian Clinical trials, Google Scholar, Research Gate, ProQuest Thesis, OVID, and medRxiv databases. Two independent reviewers included all pertinent articles according to PRISMA guidelines, and extract data independently. The two reviewers checked the quality of studies using the ROB2 tool. To determine the pooled effect estimate of the efficacy and safety of inhaled heparin, a meta-analysis was carried out using the R programming language. Publication bias was evaluated using Egger's regression test. The heterogeneity was explained using a meta-regression, and the quality of evidence was assessed by the GRADE approach. Twenty-six studies with a total of 581 patients were included in the qualitative analysis and 16 in the meta-analysis. The primary outcome was treatment success (improvement of lung function) that was measured by standardized mean differences (SMD) of the forced expiratory volume per second (FEV1) either per ml or percentage. Heparin has a large effect on both FEV1% and FEV1 ml when compared to the control group (SMD 2.7, 95% CI 1.00; 4.39; GRADE high, SMD 2.12, 95% CI - 1.49; 5.72: GRADE moderate, respectively). Secondary outcomes are other lung functions improving parameters such as PC20 (SMD 0.91, 95% CI - 0.15; 1.96). Meta-regression and subgroup analysis show that heparin type, dose, year of publication, study design, and quality of studies had a substantial effect. Regarding safety, inhaled heparin showed a good coagulation profile and mild tolerable side effects. Inhaled heparin showed improvement in lung functions either alone or when added to standard care. More large parallel RCTs are needed including COPD patients, children, and other types, and stages of asthmatic patients.

Conflict of interest statement

The authors declare no competing interests.

- 69 references
- 5 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

Review

BMJ Open
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Effect of monitoring adherence to regular inhaled corticosteroid (ICS) alone or in combination with a long-acting β2-agonist (LABA) using electronic methods on asthma outcomes: a narrative systematic review

Mohammed Almutairi[1,2], John F Marriott[3], Adel Mansur[3,4]
Affiliations expand

- PMID: 37586865

- PMCID: PMC10432637

- DOI: 10.1136/bmjopen-2023-074127

Free PMC article

Abstract

Objectives: To evaluate through a systematic review the effectiveness of electronic methods in monitoring adherence to regular inhaled corticosteroids (ICS) alone or in combination with long-acting β2-agonists (LABAs) and their effect on clinical outcomes.

Design: A narrative systematic review.

Data sources: MEDLINE, EMBASE, Cochrane Database of Systematic Reviews and Web of Science were searched through up to 10 July 2022.

Eligibility criteria: We included peer-reviewed studies of qualitative and quantitative outcomes that compared the effect of electronic methods to routine non-electronic monitoring intervention or placebo among children and adults with asthma on medication adherence rates to regular ICS alone or in combination with LABA, asthma control and asthma exacerbations.

Data extraction and synthesis: Data extraction was performed according to a predetermined sheet specific to the review objectives. The risk of bias was assessed using the Cochrane Risk of Bias Tool for randomised controlled trials and the Risk of Bias in Systematic Reviews tool for systematic reviews. Meta-analysis was not possible based on the findings of the scoping search; however, a narrative review was performed to allow for the grouping of results based on asthma inhaler adherence rates, asthma control and exacerbations.

Results: Six articles comprising 98 studies published from 1998 to 2022 in the USA, Canada and the UK were included. Compared with the control, electronic monitoring devices (EMDs) showed a 23% adherence improvement, mean difference (MD) of 23%, 95% CI 10.84 to 34.16, p=0.0002. Asthmatic children were 1.5 times more likely to be adherent using EMDs compared with non-EMD users (RR=1.5, 95% CI 1.19 to 1.9) (p<0.001). Mobile devices and text message reminders (MHealth) showed a 12% adherence improvement (MD 12%, 95% CI 6.22 to 18.03) (p<0.0001), alongside a small to medium improvement in asthma control (standardised mean difference (SMD) 0.31, 95% CI

0.17 to 0.44), small improvement in asthma-related quality of life (SMD 0.26) (p=0.007) and variable risk reduction in asthma exacerbations for digital health (risk ratio 0.53, 95% CI 0.32 to 0.91) (p=0.02) compared with EMDs, which showed insignificant differences (risk ratio 0.89, 95% CI 0.45 to 1.75) (p=0.72). Technologies combined yielded variable adherence effects, with an SMD for eHealth of 0.41, 95% CI 0.02 to 0.79, and MD for digital health was 14.66% higher than the control, 95% CI 7.74 to 21.57. Heterogeneity between studies was significant (eHealth I^2=98%, digital I^2=94%).

Conclusion: Electronic methods improved adherence to inhaled medications in asthma. EMDs appear to be the most effective technology, followed by mHealth. The adherence improvement was associated with a small clinical improvement. There was inconsistent overlapping of terminology describing electronic methods that require standardisation. Data on the cost-effectiveness of electronic devices and their utilisation in severe asthma are lacking and require further research.

Prospero registration number: CRD42022303069.

Keywords: Asthma; Information technology; Telemedicine.

Conflict of interest statement

Competing interests: AM declares no conflict of interest in relation to this work but has received personal and departmental funding from GSK, AZ, Teva, Chiesi, Novartis, BI for talks, advisory board, and educational grants.

- 39 references
- 2 figures

. 2023 Aug 16.
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The effect of a nurse-led home visit program on the care burden of caregivers of adults with asthma: A randomized controlled trial

Döndü Şanlıtürk[1], Sultan Ayaz-Alkaya[2]
Affiliations expand

- PMID: 37584900

- DOI: 10.1111/phn.13247

Abstract

Objective: This study aimed to determine the effect of a home visit program on the perceived care burden of family caregivers of adults with asthma.

Design: A single-blind randomized controlled trial.

Sample: The study was conducted with 30 participants in both the intervention and control groups.

Measurements: Care burden was measured via the Zarit Caregiver Burden Scale during the first interview at the pulmonology outpatient clinic and after the last home visit.

Intervention: A nurse-led home visit program with five visits over three months included education and health counseling with the intervention group. Control group received standard education given in the outpatient clinic.

Results: The mean Zarit Caregiver Burden Scale scores of the intervention group in the post-test were significantly lower than the control group.

Conclusions: The current study revealed that the nurse-led home visit program, including education and health counseling, was effective in reducing the care burden for family

caregivers of adults with asthma. Nurses can play an active role in preventing the negative effects of caregivers' burden of care, protecting their sense of control, and improving their health. Home visits integrated into the health care system could be effective in reducing the care burden of family members.

Keywords: adult; asthma; care burden; caregivers; education; follow-up; home visit.

- 28 references

Review

Allergy

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-
-

. 2023 Aug 16.
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An EAACI review: Go green in health care and research. Practical suggestions for sustainability in clinical practice, laboratories, and scientific meetings

Isabella Pali-Schöll[1,2], Kerstin Hermuth-Kleinschmidt[3], Stephanie Dramburg[4], Ioana Agache[5], Hanna Mayerhofer[1,2], Erika Jensen-Jarolim[1,2], Anna Goshua[6], Kari C Nadeau[7]
Affiliations expand

- PMID: 37584433

- DOI: 10.1111/all.15836

Abstract

Health care professionals (HCPs) and researchers in the health care sector dedicate their professional life to maintaining and optimizing the health of their patients. To achieve this, significant amounts of resources are used and currently it is estimated that the health care sector contributes to more than 4% of net greenhouse gas (GHG) emissions. GHG emissions adversely impact planetary health and consequently human health, as the two are intricately linked. There are many factors of health care that contribute to these emissions. Hospitals and research labs also use high amounts of consumables which require large amounts of raw materials and energy to produce. They are further responsible for polluting the environment via disposal of plastics, drug products, and other chemicals. To maintain and develop state-of-the-art best practices and treatments, medical experts exchange and update their knowledge on methods and technologies in the respective fields at highly specialized scientific meetings. These meetings necessitate thousands of attendants traveling around the globe. Therefore, while the goal of HCPs is to care for the individual, current practices have an enormous (indirect) impact on the health of the patients by their negative environmental impacts. There is an urgent need for HCPs and researchers to mitigate these detrimental effects. The installation of a sustainability-manager at health care facilities and research organizations to implement sustainable practices while still providing quality health care is desirable. Increased use of telemedicine, virtual/hybrid conferences and green chemistry have recently been observed. The benefits of these practices need to be evaluated and implemented as appropriate. With this manuscript, we aim to increase the awareness about the negative impacts of the health care system (including health care research) on planetary and human health. We suggest some easy and highly impactful steps and encourage health care professionals and research scientists of all hierarchical levels to immediately implement them in their professional as well as private life to counteract the health care sector's detrimental effects on the environment.

Keywords: asthma; education; environment; lung diseases; prevention; sustainability.

- 126 references

SUPPLEMENTARY INFO

Publication types, Grant supportexpand

FULL TEXT LINKS

Published Erratum

Clin Sci (Lond)

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Correction: New insights into the pathophysiology and therapeutic targets of asthma and comorbid chronic rhinosinusitis with or without nasal polyposis

No authors listed

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- PMCID: PMC10432874
- DOI: 10.1042/CS-2019-0281C_COR

Free PMC article

No abstract available

Keywords: airway remodelling; asthma; biologics; chronic rhinosinusitis; precision medicine; type 2 inflammation.

Erratum for

- New insights into the pathophysiology and therapeutic targets of asthma and comorbid chronic rhinosinusitis with or without nasal polyposis.
  Striz I, Golebski K, Strizova Z, Loukides S, Bakakos P, Hanania NA, Jesenak M, Diamant Z.Clin Sci (Lond). 2023 May 18;137(9):727-753. doi: 10.1042/CS20190281.PMID: 37199256 **Free PMC article.** Review.

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

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20

Eur Ann Otorhinolaryngol Head Neck Dis

-
-
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. 2023 Aug 15;S1879-7296(23)00097-2.
doi: 10.1016/j.anorl.2023.06.006. Online ahead of print.

Dupilumab in pediatric severe chronic rhinosinusitis with nasal polyps and asthma

M Bragança[1], A M Pereira[2], J L Plácido[3], L Amaral[3]
Affiliations expand

- PMID: 37591762

- DOI: 10.1016/j.anorl.2023.06.006

No abstract available

SUPPLEMENTARY INFO

Thorax

-
-
-

. 2023 Aug 15;thoraxjnl-2022-218670.
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Prospective study of e-cigarette use and respiratory symptoms in adolescents and young adults

Alayna P Tackett[1], Robert Urman[2], Jessica Barrington-Trimis[2], Feifei Liu[2], Hanna Hong[3], Mary Ann Pentz[2], Talat S Islam[2], Sandrah P Eckel[2], Meghan Rebuli[4], Adam Leventhal[2], Jonathan M Samet[5], Kiros Berhane[6], Rob McConnell[7]

Affiliations expand

- PMID: 37582630

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Abstract

Rationale: Electronic cigarette (e-cigarette) aerosol contains volatile aldehydes, including flavourings and oxidant metals with known pulmonary toxicity.

Objectives: To evaluate the associations of e-cigarette use with symptoms of wheeze, bronchitic symptoms and shortness of breath (SOB) across 4 years of prospective data.

Methods: Participants completed questionnaires on respiratory symptoms and past 30-day e-cigarette, cigarette and cannabis use in 2014 (wave 1; N=2094; mean age 17.3 years,

SD=0.6 years). Follow-up information was collected in 2015 (wave 2; n=1609), 2017 (wave 3; n=1502) and 2018 (wave 4; n=1637) using online surveys. Mixed-effects logistic regression models evaluated associations of e-cigarette use with respiratory symptoms.

Measurements and main results: Participants were mostly Hispanic white (51.8%) and evenly representative by sex (49.6% female; 50.4% male). Compared with never e-cigarette users, past 30-day e-cigarette users reported increased odds of wheeze (OR 1.81; 95% CI 1.28, 2.56), bronchitic symptoms (OR 2.06; 95% CI 1.58, 2.69) and SOB (OR 1.78; 95% CI 1.23, 2.57), adjusting for study wave, age, sex, race, lifetime asthma diagnosis and parental education. Effect estimates were attenuated (wheeze (OR 1.41; 95% CI 0.99, 2.01), bronchitic symptoms (OR 1.55; 95% CI 1.18, 2.05), SOB (OR 1.48; 95% CI 1.01, 2.18)), after adjusting additionally for current cigarette use, cannabis use and secondhand exposure to e-cigarettes/cigarettes/cannabis.

Conclusions: E-cigarette use in young adults was associated with respiratory symptoms, independent of combustible cannabis and cigarette exposures.

Keywords: Tobacco and the lung.

Conflict of interest statement

Competing interests: None declared.

Am J Respir Crit Care Med

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CC16: A Treatable Trait in Asthma?

Chloe I Bloom[1], Ian M Adcock[2]
Affiliations expand

- PMID: 37582203

- DOI: 10.1164/rccm.202307-1255ED

No abstract available

23

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An Evaluation of the Asthma Impact of the June, 2023 New York City Wildfire Air Pollution Episode

George Thurston[1], Wuyue Yu[2], David Luglio[3]
Affiliations expand

- PMID: 37582196

- DOI: 10.1164/rccm.202306-1073LE

Abstract

Not Applicable.

Keywords: Climate change; PM2.5; asthma; elemental constituents; wildfire air pollution.

Environ Sci Technol

. 2023 Aug 15;57(32):11750-11766.
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Indoor Airborne Microbiome and Endotoxin: Meteorological Events and Occupant Characteristics Are Important Determinants

Hesham Amin[1], Tina Šantl-Temkiv[2], Christine Cramer[3,4], Kai Finster[2], Francisco Gomez Real[1], Thorarinn Gislason[5], Mathias Holm[6], Christer Janson[7,8], Nils Oskar Jögi[1], Rain Jogi[9], Andrei Malinovschi[8], Ian P G Marshall[2], Lars Modig[10], Dan Norbäck[11], Rajesh Shigdel[1], Torben Sigsgaard[3], Cecilie Svanes[12,13], Hulda Thorarinsdottir[14], Inge M Wouters[15], Vivi Schlünssen[3], Randi J Bertelsen[1]

Affiliations expand

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- DOI: 10.1021/acs.est.3c01616

Free PMC article

Abstract

Airborne bacteria and endotoxin may affect asthma and allergies. However, there is limited understanding of the environmental determinants that influence them. This study investigated the airborne microbiomes in the homes of 1038 participants from five cities in Northern Europe: Aarhus, Bergen, Reykjavik, Tartu, and Uppsala. Airborne dust particles were sampled with electrostatic dust fall collectors (EDCs) from the participants' bedrooms. The dust washed from the EDCs' clothes was used to extract DNA and endotoxin. The DNA extracts were used for quantitative polymerase chain (qPCR) measurement and 16S rRNA gene sequencing, while endotoxin was measured using the kinetic chromogenic limulus amoebocyte lysate (LAL) assay. The results showed that households in Tartu and Aarhus had a higher bacterial load and diversity than those in Bergen and Reykjavik, possibly due to elevated concentrations of outdoor bacterial taxa associated with low precipitation and high wind speeds. Bergen-Tartu had the highest difference (ANOSIM R = 0.203) in β diversity. Multivariate regression models showed that α diversity indices and bacterial and endotoxin loads were positively associated with the occupants' age, number of occupants, cleaning frequency, presence of dogs, and age of the house. Further studies are needed to understand how meteorological factors influence the indoor bacterial community in light of climate change.

Keywords: 16S rRNA and occupants' age; Northern Europe; airborne microbiome; meteorological data.

Conflict of interest statement

The authors declare no competing financial interest.

- 86 references
- 6 figures

. 2023 Aug 15;S1933-0219(23)00054-5.
doi: 10.1016/j.mucimm.2023.07.002. Online ahead of print.

IL-33-induced neutrophilic inflammation and NETosis underlie rhinovirus-triggered exacerbations of asthma

Bodie Curren[1], Tufael Ahmed[2], Daniel R Howard[1], Md Ashik Ullah[3], Ismail Sebina[4], Ridwan B Rashid[1], Md Al Amin Sikder[1], Patricia Namubiru[1], Alec Bissell[3], Sylvia Ngo[3], David J Jackson[5], Marie Toussaint[6], Michael R Edwards[6], Sebastian L Johnston[6], Henry J McSorley[7], Simon Phipps[8]
Affiliations expand

- PMID: 37506849

- DOI: 10.1016/j.mucimm.2023.07.002

Abstract

Rhinovirus-induced neutrophil extracellular traps (NETs) contribute to acute asthma exacerbations; however, the molecular factors that trigger NETosis in this context remain ill-defined. Here, we sought to implicate a role for IL-33, an epithelial cell-derived alarmin rapidly released in response to infection. In mice with chronic experimental asthma (CEA), but not naïve controls, rhinovirus inoculation induced an early (1 day post infection; dpi) inflammatory response dominated by neutrophils, neutrophil-associated cytokines (IL-1α, IL-1β, CXCL1), and NETosis, followed by a later, type-2 inflammatory phase (3-7 dpi), characterised by eosinophils, elevated IL-4 levels, and goblet cell hyperplasia. Notably, both phases were ablated by HpARI (Heligmosomoides polygyrus Alarmin Release Inhibitor), which blocks IL-33 release and signalling. Instillation of exogenous IL-33 recapitulated the rhinovirus-induced early phase, including the increased presence of NETs in the airway mucosa, in a PAD4-dependent manner. Ex vivo IL-33-stimulated neutrophils from mice with CEA, but not naïve mice, underwent NETosis and produced greater amounts of IL-1α/β, IL-4, and IL-5. In nasal samples from rhinovirus-infected people with asthma, but not healthy controls, IL-33 levels correlated with neutrophil elastase and dsDNA. Our findings suggest that IL-33 blockade ameliorates the severity of an asthma

exacerbation by attenuating neutrophil recruitment and the downstream generation of NETs.

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.

Editorial

Am J Respir Crit Care Med

. 2023 Aug 15;208(4):356-357.
doi: 10.1164/rccm.202306-1082ED.

Postbronchodilator Reference Values: Should They Be the Norm?

Lewis J Smith[1]
Affiliations expand

- PMID: 37478330

- DOI: 10.1164/rccm.202306-1082ED

No abstract available

Comment on

- Consequences of Using Post- or Prebronchodilator Reference Values in Interpreting Spirometry.
  Malinovschi A, Zhou X, Andersson A, Backman H, Bake B, Blomberg A, Caidahl K, Eriksson MJ, Eriksson Ström J, Hamrefors V, Hjelmgren O, Janson C, Karimi R, Kylhammar D, Lindberg A, Lindberg E, Liv P, Olin AC, Shalabi A, Sköld CM, Sundström J, Tanash H, Torén K, Wollmer P, Zaigham S, Östgren CJ, Engvall JE.Am J Respir Crit Care Med. 2023 Aug 15;208(4):461-471. doi: 10.1164/rccm.202212-2341OC.PMID: 37339507

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

Am J Respir Crit Care Med
. 2023 Aug 15;208(4):472-486.
doi: 10.1164/rccm.202303-0534OC.

A Single-Cell Atlas of Small Airway Disease in Chronic Obstructive Pulmonary Disease: A Cross-Sectional Study

Steven Booth[1,2], Aileen Hsieh[1,2], Leila Mostaco-Guidolin[3], Hyun-Kyoung Koo[1,2], Keith Wu[1,2], Fatemeh Aminazadeh[1,2], Chen Xi Yang[1], Daniela Quail[4], Yuhong Wei[4], Joel D Cooper[5], Peter D Paré[1], James C Hogg[1,6], Dragoş M Vasilescu[1,6], Tillie-Louise Hackett[1,2]
Affiliations expand

- PMID: 37406359

- DOI: 10.1164/rccm.202303-0534OC

Abstract

Rationale: Emerging data demonstrate that the smallest conducting airways, terminal bronchioles, are the early site of tissue destruction in chronic obstructive pulmonary disease (COPD) and are reduced by as much as 41% by the time someone is diagnosed with mild (Global Initiative for Chronic Obstructive Lung Disease [GOLD] stage 1) COPD. **Objectives:** To develop a single-cell atlas that describes the structural, cellular, and extracellular matrix alterations underlying terminal bronchiole loss in COPD. **Methods:** This cross-sectional study of 262 lung samples derived from 34 ex-smokers with normal lung function (n = 10) or GOLD stage 1 (n = 10), stage 2 (n = 8), or stage 4 (n = 6) COPD was performed to assess the morphology, extracellular matrix, single-cell atlas, and genes associated with terminal bronchiole reduction using stereology, micro-computed tomography, nonlinear optical microscopy, imaging mass spectrometry, and transcriptomics. **Measurements and Main Results:** The lumen area of terminal bronchioles progressively narrows with COPD severity as a result of the loss of elastin fibers within alveolar attachments, which was observed before microscopic emphysematous tissue destruction in GOLD stage 1 and 2 COPD. The single-cell atlas of terminal bronchioles in COPD demonstrated M1-like macrophages and neutrophils located within alveolar attachments and associated with the pathobiology of elastin fiber loss, whereas adaptive immune cells (naive, CD4, and CD8 T cells, and B cells) are associated with terminal bronchiole wall remodeling. Terminal bronchiole pathology was associated with the upregulation of genes involved in innate and adaptive immune responses, the interferon response, and the degranulation of neutrophils. **Conclusions:** This comprehensive single-cell atlas highlights terminal bronchiole alveolar attachments as the initial site of tissue destruction in centrilobular emphysema and an attractive target for disease modification.

Keywords: COPD; elastin; micro–computed tomography; single-cell atlas; small airways disease.

Comment in

- Unraveling the Distal Lung Destruction in Emphysema.
  Petrache I.Am J Respir Crit Care Med. 2023 Aug 15;208(4):357-358. doi: 10.1164/rccm.202307-1198ED.PMID: 37450936 No abstract available.

SUPPLEMENTARY INFO

J Allergy Clin Immunol Pract

. 2023 Aug 14;S2213-2198(23)00918-2.

doi: 10.1016/j.jaip.2023.08.015. Online ahead of print.

Mepolizumab reduces systemic corticosteroid use in chronic rhinosinusitis with nasal polyps

Geoffrey Chupp[1], Isam Alobid[2], Njira L Lugogo[3], Harsha H Kariyawasam[4], Arnaud Bourdin[5], Adam M Chaker[6], Steven G Smith[7], Ana R Sousa[8], Bhabita Mayer[9], Robert H Chan[10], Andrea Matucci[11]

Affiliations expand

- PMID: 37586475

- DOI: 10.1016/j.jaip.2023.08.015

Abstract

Background: Systemic corticosteroids (SCS) are associated with short- and long-term adverse effects.

Objective: To assess mepolizumab efficacy according to prior SCS use and characterize mepolizumab's SCS-sparing capabilities, in patients with severe chronic rhinosinusitis with nasal polyps (CRSwNP).

Methods: In the randomized, double-blind, Phase III SYNAPSE trial (NCT03085797), adults with severe CRSwNP eligible for repeat sinus surgery despite standard of care treatment received mepolizumab (100 mg subcutaneously) or placebo every 4 weeks for 52 weeks. The impact of prior SCS courses (0/1/>1) on mepolizumab versus placebo treatment responses (changes from baseline in total endoscopic NP [Week 52], nasal obstruction visual analog scale [Weeks 49-52], and 22-item Sino-Nasal Outcome Test total [Week 52] scores) was analyzed post hoc. To characterize mepolizumab's SCS-sparing capabilities, time-to-first SCS course for NP (prespecified) and total prednisolone-equivalent oral corticosteroid (OCS) dose by patient baseline characteristics (post hoc, in patients with ≥1 SCS course during SYNAPSE) were assessed up to Week 52.

Results: Mepolizumab versus placebo improved treatment responses, irrespective of prior SCS use. By Week 52, the probability of requiring SCS for NP (Kaplan-Meier estimate[95% confidence interval]) was lower with mepolizumab (25.4%[20.0, 32.1]) versus placebo (37.5%[31.1, 44.6]). In patients requiring ≥1 dose of SCS, total (mean[standard deviation] mg/year) prednisolone-equivalent OCS dose was lower with mepolizumab (438.9[350.40]) versus placebo (505.2[455.091]), overall and irrespective of prior sinus surgeries, blood eosinophil count, or comorbidities.

Conclusion: Mepolizumab is associated with clinical benefits in patients with severe CRSwNP regardless of prior SCS and has a SCS-sparing effect.

Keywords: aspiring-exacerbated respiratory disease (AERD); asthma; mepolizumab; refractory disease; severe chronic rhinosinusitis with nasal polyps; subgroup analysis; systemic corticosteroids.

Expert Rev Respir Med

. 2023 Aug 14.

doi: 10.1080/17476348.2023.2247973. Online ahead of print.

Evaluating as-needed inhaled corticosteroid strategies in asthma: Expanding the benefits to mild asthma

Tommaso Bigoni[1], Franco Alfano[1], Federico Baraldi[1], Marco Contoli[1], Alberto Papi[1]
Affiliations expand

- PMID: 37578053

- DOI: 10.1080/17476348.2023.2247973

Abstract

Introduction: Adherence to regular anti-inflammatory treatment is commonly low, and short-acting β2 agonist (SABA) overuse is common in patients with asthma, leading to an increased risk of asthma-related adverse events.

Areas covered: Given the pivotal role of inflammation in asthma, multiple as-needed inhaled corticosteroid (ICS)-containing therapies have been developed, leading to a reduction in asthma exacerbations and improvement in symptom control. Currently, as-needed ICS/formoterol is one of the most commonly available formulations; however, other combinations such as ICS/SABA have been shown to be superior to as-needed SABA alone. Therefore, we performed a comprehensive review of the available scientific literature to enhance the advantages and disadvantages of each combination in clinical practice.

Expert opinion: The future direction we foresee in asthma management consists of abandoning as-needed short-acting bronchodilators in favor of as-needed ICS-containing therapies. Each patient is unique and differs from others; consequently, a single option will not fit everyone. Patients' and physicians' awareness of this perspective can be reached through the development of multiple therapeutic options suitable for each condition that can be found in 'real life'.

Keywords: Asthma; ICS; Inflammation; Mild; SABA; Treatment; as-needed.

Book

Zafirlukast

Amareen Dhaliwal[1], Tushar Bajaj[2]
In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan.
2023 Aug 14.
Affiliations expand

- PMID: 32491776

- Bookshelf ID: NBK557844

Excerpt

Zafirlukast belongs to the leukotriene receptor antagonist (LTRA) class of medications and is utilized for managing and treating chronic asthma. The medication is available in 10 mg and 20 mg chewable tablets approved by the U.S. Food and Drug Administration (FDA) for use in adults and children 5 or older. Zafirlukast is also used as an off-label medication to manage chronic urticaria, prevent exercise-induced bronchospasm, and treat allergic rhinitis. As per the Global Initiative for Asthma (GINA) guidelines, LTRA, including montelukast or zafirlukast, is an essential controller therapy for patients who cannot tolerate inhaled corticosteroids (ICS). This activity reviews the mechanism of action, adverse event profile, indications, effects, contraindications, and other crucial factors relevant to utilizing zafirlukast as an agent in managing and prophylaxis of chronic asthma.

Conflict of interest statement

Disclosure: Amareen Dhaliwal declares no relevant financial relationships with ineligible companies.

Disclosure: Tushar Bajaj declares no relevant financial relationships with ineligible companies.

- 31 references

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

StatPearls [Internet]

UNIMORE

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Book

Omalizumab

Calvin Kumar[1], Patrick M. Zito[2]

In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan.
2023 Aug 14.

Affiliations expand

- PMID: 31424767

- Bookshelf ID: NBK545183

Free Books & Documents

Excerpt

<p>Omalizumab received initial approval from the U.S. Food and Drug Administration (FDA) in 2003 for the treatment of moderate-to-severe asthma. Subsequently, in 2014, the drug was also approved for use in patients with chronic idiopathic or spontaneous urticaria in the United States and Europe. Omalizumab is a recombinant humanized

immunoglobulin G1 (IgG1) monoclonal anti-IgE antibody utilized to treat allergic asthma and chronic urticaria. This medication works by interacting with the high-affinity receptor Fc-epsilon-RI, typically found on eosinophils, mast cells, and basophils, therefore playing a critical role in preventing the allergic cascade. As a result, omalizumab plays a vital role in managing moderate-to-severe IgE-mediated asthma and, more recently, in treating chronic urticaria. This activity will comprehensively cover the indications, contraindications, mechanisms of action, pharmacokinetics, adverse effects, warnings, precautions, and monitoring requirements of omalizumab. In addition, this activity will also provide updates on some of the critical studies implemented primarily for asthma and include information on urticarial reactions.</p>

Conflict of interest statement

Disclosure: Calvin Kumar declares no relevant financial relationships with ineligible companies.
Disclosure: Patrick Zito declares no relevant financial relationships with ineligible companies.

- 33 references

EMS Prehospital Evaluation and Treatment of Asthma in Children

Jennifer N. Fishe[1], Onyinyechukwu Okorji[2], Kathryn Blake
In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan.
2023 Aug 14.
Affiliations expand

- PMID: 30480949

- Bookshelf ID: NBK534210

Free Books & Documents

Excerpt

Asthma is the most common chronic childhood disease and a frequent reason for pediatric emergency medical treatment. This article will review emergency medical services' (EMS) prehospital assessment and management of acute pediatric asthma exacerbations.

Conflict of interest statement

Disclosure: Jennifer Fishe declares no relevant financial relationships with ineligible companies.
Disclosure: Onyinyechukwu Okorji declares no relevant financial relationships with ineligible companies.
Disclosure: Kathryn Blake declares no relevant financial relationships with ineligible companies.

- 20 references

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

StatPearls [Internet]
UNIMORE
Proceed to details
Cite

Ann Allergy Asthma Immunol

. 2023 Aug 12;S1081-1206(23)00567-7.
doi: 10.1016/j.anai.2023.08.006. Online ahead of print.

Retrospective Analysis and Biologic Asthma Response Score reveal roadmap for switching biologics in severe asthma

Moritz Z Kayser[1], Ben L Jülicher[2], Tobias Welte[3], Jan Fuge[3], Hendrik Suhling[2]
Affiliations expand

- PMID: 37580014

- DOI: 10.1016/j.anai.2023.08.006

No abstract available

J Asthma

. 2023 Aug 12;1-9.
doi: 10.1080/02770903.2023.2241905. Online ahead of print.

Cost-effectiveness and resource use analysis of patients with asthma before and after treatment with mepolizumab in a real-life setting

Javier Domínguez-Ortega[1], Daniel Laorden[2], Francisca Vílchez-Sánchez[1], David Bañas-Conejero[3], Santiago Quirce[1]
Affiliations expand

- PMID: 37503953

- DOI: 10.1080/02770903.2023.2241905

Abstract

Objective: To define the cost-effectiveness and health resource use of mepolizumab in a cohort of patients with severe eosinophilic asthma in real-life conditions in Spain.

Methods: This was an observational, retrospective, single-center study. Patients included were diagnosed with severe eosinophilic asthma and treated with mepolizumab 100 mg subcutaneous (SC) 4-weekly for 12 months. Outcomes evaluated: incremental cost-effectiveness ratio (ICER), number of exacerbations, disease control with the Asthma Control Test (ACT), Asthma Quality of Life Questionnaire (AQLQ), and direct and indirect cost per patient.

Results: 12 months after mepolizumab initiation, a significant decrease in exacerbations was shown, from a mean (standard deviation [SD]) of 3.1 (2.6) to 0.7 (1.5), an increase from 4.9 (0.4) to 6.1 (0.5) in AQLQ, and from 14.9 (5.7) to 21.5 (3.9) in ACT scores. The number of cortico-dependent patients significantly decreased from 53.3% to 13.3% during this period. There was a significant decrease of 94% in the cost of hospitalization, from a mean (SD) of €4063.9 (5423.9) pretreatment to €238.6 (1306.9) post-treatment (p = 0.0003). Total costs decreased significantly from a median of €2,423.1 (1,512.8; 9,320.9) pretreatment to €1,177.5 (965.0; 1,737.8) post-treatment if mepolizumab was excluded. ICER per exacerbation avoided was €3606.9, per 3-point ACT score increase €3934.8, and per 0.5-point AQLQ score increase €3606.9.

Conclusions: Mepolizumab improves control of asthma and quality of life in patients with severe diseases in a cost-effectiveness range. The number of exacerbations decreased, and

there was a clear reduction in primary care visits and hospitalizations. Further economic analyses of biological therapies for asthma are required.

Keywords: Treatment; economics; management/control.

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

1
Int Arch Allergy Immunol
. 2023 Aug 18;1-7.
doi: 10.1159/000532068. Online ahead of print.

Risk Factors for Abnormal Small Airway Function Indicators in Nasal Polyp Patients with and without Asthma

Jing Guo[1,2,3], Jianwei Wang[1,2,3], Xinjun Xu[1,2,3], Yujuan Yang[1,2,3], Pengyi Yu[1,2,3], Zhen Liu[1,2,3], Jiayu Cao[1,2,3], Qintai Yang[4], Yu Zhang[1,2,3], Xicheng Song[1,2,3]
Affiliations expand

- PMID: 37598674

- DOI: 10.1159/000532068

Abstract

Introduction: Small airway dysfunction (SAD) is associated with type 2 inflammation in patients who have non-asthmatic chronic rhinosinusitis with nasal polyps (CRSwNPs); however, the risk factors for abnormal small airway function indicators in CRSwNP patients with and without asthma remain unclear.

Methods: We retrospectively analyzed 41 asthmatic and 109 non-asthmatic CRSwNP patients. Clinical characteristics were compared between groups, correlations between small airway function and clinical parameters were calculated, and independent risk factors for every small airway indicator were identified in each group.

Results: Asthmatic CRSwNP patients had significantly reduced small airway function, and the proportion of patients with SAD was higher in asthmatic CRSwNP patients (65.85%) than in patients without asthma (9.17%). With regard to specific airway function indicators, age and a patient's blood eosinophil (%) were identified as independent risk factors for lower FEF50% %pred and FEF25-75% pred, with age being an independent risk factor for FEF75% %pred in asthmatic CRSwNP patients. In non-asthmatic CRSwNP patients, allergic rhinitis comorbidity was found to be an independent risk factor for FEF50% %pred, FEF75% %pred, and FEF25-75% %pred.

Conclusion: Physicians should pay greater attention to risk factors for abnormal small airway function indicators in patients with CRSwNPs to prevent the occurrence of SAD.

Keywords: Allergic rhinitis; Asthma; Chronic rhinosinusitis with nasal polyps; Eosinophil; Small airway dysfunction.

2

Pulm Ther

. 2023 Aug 14.

doi: 10.1007/s41030-023-00238-8. Online ahead of print.

A Clinical Study to Assess the Efficacy and Safety of MP-AzeFlu Nasal Spray in Comparison to Commercially Available Azelastine Hydrochloride and

Fluticasone Propionate Nasal Sprays in Chinese Volunteers with Allergic Rhinitis

Bing Zhou[1], Lei Cheng[2,3], Jing Pan[4], Huizhong Wang[5], Yongde Jin[6], Changqing Zhao[7], Peng Lin[8], Guolin Tan[9], Hongyan Fang[10], Hua Zhang[11], Huifang Zhou[12], Yaowu Dong[13], Hans Christian Kuhl[14], Rajesh Kumar Ramalingam[15], Duc Tung Nguyen[16]
Affiliations expand

- PMID: 37580498

- DOI: 10.1007/s41030-023-00238-8

Free article

Abstract

Introduction: The objective of the present study was to evaluate the efficacy and safety of MP-AzeFlu nasal spray in comparison to commercially available azelastine hydrochloride and fluticasone propionate sprays in Chinese patients with moderate-to-severe allergic rhinitis (AR).

Methods: We conducted a 14-day multicenter, randomized, double-blind, active controlled prospective clinical study in adult and adolescent patients with AR, who had moderate-to-severe symptoms. The primary efficacy endpoint was the change from baseline in combined 12-h reflective total nasal symptom score (rTNSS) (morning [AM] + afternoon [PM]). The safety profile of the study medications was assessed through the recording, reporting, and analysis of baseline medical conditions, adverse events (AEs), vital signs, and focused nasal examination. Three hundred patients per treatment group were randomized, which led to a total sample size estimation of 900 patients.

Results: MP-AzeFlu group showed significantly higher symptom reduction for the entire 2-week treatment period in rTNSS when compared with the AZE group (LS mean difference: - 1.96; 95% CI: - 2.53, - 1.39; p < 0.0001), or the FLU group (LS mean difference: - 0.98; 95% CI: - 1.55, - 0.41; p = 0.0007). The results of adult RQLQ showed improvement in QoL in all treatment groups. Except for dysgeusia (bitter taste) that was reported by more patients (13 [4.3%]) in the MP-AzeFlu group, the incidence of all other TEAEs in the MP-AzeFlu group was comparable or even lower than in other treatment groups.

Conclusions: MP-AzeFlu, when administered as one spray per nostril twice daily for 14 days, alleviated AR symptoms in Chinese patients with moderate-to-severe AR.

Trial registration: Clinicaltrials.gov; NCT03599791, Registered June 29, 2018, retrospectively registered, https://clinicaltrials.gov/ct2/show/NCT03599791 .

Keywords: Allergic rhinitis; Azelastine; Fixed-dose combination; Fluticasone; Seasonal allergic rhinitis.

- 23 references

SUPPLEMENTARY INFO

Associated dataexpand

FULL TEXT LINKS

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3

Neurochem Res

. 2023 Aug 14.
doi: 10.1007/s11064-023-04012-9. Online ahead of print.

Metformin Improves Comorbid Depressive Symptoms in Mice with Allergic Rhinitis by Reducing Olfactory Bulb Damage

Hao Lv[1,2], Ziang Gao[1,2,3], Yunfei Wang[1,2], Siyuan Chen[1,2], Peiqiang Liu[1,2,3], Yulie Xie[1,2], Mengting Guan[1,2], Jianchao Cong[1,2], Yu Xu[4,5,6,7]

Affiliations expand

- PMID: 37574530

- DOI: 10.1007/s11064-023-04012-9

Abstract

Allergic rhinitis (AR) is a widespread disease that is frequently comorbid with depression. However, the mechanisms and treatments for depression in AR remain underexplored. Metformin, a widely used antidiabetic drug, has shown antidepressant effects. The aim of this study was to explore the effects and potential mechanisms of metformin on depression-like behaviors in an AR mouse model. In the present study, mice were sensitized and challenged with ovalbumin (OVA) to induce AR. Results showed that mice with AR exhibited significant depression-like behavior which was attenuated by metformin. In addition, the levels of expression of synaptic plasticity markers (anti-microtubule-associated protein 2, synaptophysin, postsynaptic density protein 95), neurogenesis markers (doublecortin and Ki-67), and brain-derived neurotrophic factor were decreased in the olfactory bulb (OB) of mice with AR, while metformin ameliorated all these alterations and reduced apoptosis in the OB of these mice. Furthermore, it enhanced the phosphorylation of AMP-activated kinase (AMPK) and the levels of ten-eleven translocation 2 (TET2) and 5-hydroxymethylcytosine in the OB. In conclusion, our findings suggest that metformin might be a viable strategy for treating AR-related depression, possibly by modulating neuroplasticity, neurogenesis, apoptosis, and BDNF signaling in the OB via the AMPK/TET2 pathway.

Keywords: Allergic rhinitis; Depression; Metformin; Olfactory bulb; Ten-eleven translocation 2.

- 58 references

SUPPLEMENTARY INFO

Grant supportexpand

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Book

Zafirlukast

Amareen Dhaliwal[1], Tushar Bajaj[2]

In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan.
2023 Aug 14.
Affiliations expand

- PMID: 32491776

- Bookshelf ID: NBK557844

Excerpt

Zafirlukast belongs to the leukotriene receptor antagonist (LTRA) class of medications and is utilized for managing and treating chronic asthma. The medication is available in 10 mg and 20 mg chewable tablets approved by the U.S. Food and Drug Administration (FDA) for use in adults and children 5 or older. Zafirlukast is also used as an off-label medication to manage chronic urticaria, prevent exercise-induced bronchospasm, and treat allergic rhinitis. As per the Global Initiative for Asthma (GINA) guidelines, LTRA, including montelukast or zafirlukast, is an essential controller therapy for patients who cannot tolerate inhaled corticosteroids (ICS). This activity reviews the mechanism of action, adverse event profile, indications, effects, contraindications, and other crucial factors relevant to utilizing zafirlukast as an agent in managing and prophylaxis of chronic asthma.

Conflict of interest statement

Disclosure: Amareen Dhaliwal declares no relevant financial relationships with ineligible companies.
Disclosure: Tushar Bajaj declares no relevant financial relationships with ineligible companies.

- 31 references

5

Sci Rep

. 2023 Aug 12;13(1):13125.

doi: 10.1038/s41598-023-39987-6.

Distinction between rhinitis alone and rhinitis with asthma using interactomics

Daniel Aguilar[1], Nathanaël Lemonnier[2], Erik Melén[3 4], Mariona Bustamante[5 6 7], Olena Gruzieva[8 9], Stefano Guerra[10], Thomas Keil[11 12 13], Gerard H Koppelman[14], Juan C Celedón[15], Josep M Antó[5 6 7], Jean Bousquet[16 17 18 19]

Affiliations expand

- PMID: 37573373
- PMCID: PMC10423213
- DOI: 10.1038/s41598-023-39987-6

Abstract

The concept of "one-airway-one-disease", coined over 20 years ago, may be an over-simplification of the links between allergic diseases. Genomic studies suggest that rhinitis alone and rhinitis with asthma are operated by distinct pathways. In this MeDALL (Mechanisms of the Development of Allergy) study, we leveraged the information of the human interactome to distinguish the molecular mechanisms associated with two phenotypes of allergic rhinitis: rhinitis alone and rhinitis in multimorbidity with asthma. We observed significant differences in the topology of the interactomes and in the pathways associated to each phenotype. In rhinitis alone, identified pathways included cell cycle, cytokine signalling, developmental biology, immune system, metabolism of proteins and signal transduction. In rhinitis and asthma multimorbidity, most pathways were related to signal transduction. The remaining few were related to cytokine signalling, immune system or developmental biology. Toll-like receptors and IL-17-mediated signalling were identified in rhinitis alone, while IL-33 was identified in rhinitis in multimorbidity. On the other hand, few pathways were associated with both phenotypes, most being associated with signal transduction pathways including estrogen-stimulated signalling. The only immune system pathway was FceRI-mediated MAPK activation. In conclusion, our findings suggest that rhinitis alone and rhinitis and asthma multimorbidity should be considered as two distinct diseases.

Conflict of interest statement

DA reports personal fees from MASK-AIR SAS, outside the submitted work. JB reports personal fees from Cipla, Menarini, Mylan, Novartis, Purina, Sanofi-Aventis, Teva, Uriach, other from KYomed-Innov, other from Mask-air-SAS, outside the submitted work. JCC reports other from GSK, other from Merck, other from Pharmavite, outside the submitted work. GHK reports grants from Netherlands Lung Foundation, TEVA, VERTEX, GSK, Ubbo Emmius Foundation, European Union, Zon MW (Vici Grant), outside the submitted work; and GHK participated in advisory boards to GSK, AZ and Pure-IMS (Money to institution). The other authors have no COIs to disclose, outside the submitted work.

- 54 references
- 4 figures

Review

Eur J Immunol

. 2023 Aug 12;e2149510.
doi: 10.1002/eji.202149510. Online ahead of print.

Mesenchymal stromal cells and their small extracellular vesicles in allergic diseases: from immunomodulation to therapy

Ya-Qi Peng[1,2], Xiao-Hui Deng[1,3], Zhi-Bin Xu[1], Zi-Cong Wu[1], Qing-Ling Fu[1,3]
Affiliations expand

- PMID: 37572379

- DOI: 10.1002/eji.202149510

Abstract

Mesenchymal stromal cells (MSCs) have long been considered a potential tool for treatment of allergic inflammatory diseases, owing to their immunomodulatory characteristics. In recent decades, the medical utility of MSCs has been evaluated both in vitro and in vivo, providing a foundation for therapeutic applications. However, the existing limitations of MSC therapy indicate the necessity for novel therapies. Notably, small extracellular vesicles (sEV) derived from MSCs have emerged rapidly as candidates instead of their parental cells. The acquisition of abundant and scalable MSC-sEV is a obstacle for clinical applications. The potential application of MSC-sEV in allergic diseases has attracted increasing attention from researchers. By carrying biological microRNAs or active proteins, MSC-sEV can modulate the function of various innate and adaptive immune cells. In this

review, we summarise the recent advances in the immunomodulatory properties of MSCs in allergic diseases, the cellular sources of MSC-sEV, and the methods for obtaining high quality human MSC-sEV. In addition, we discuss the immunoregulatory capacity of MSCs and MSC-sEV for the treatment of asthma, atopic dermatitis, and allergic rhinitis, with a special emphasis on their immunoregulatory effects and the underlying mechanisms of immune cell modulation.

Keywords: Allergy; Immune cells; Immunomodulation; Mesenchymal stromal cells; Small extracellular vesicles.

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

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

1

Case Reports

Respirol Case Rep

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. 2023 Aug 16;11(9):e01203.
doi: 10.1002/rcr2.1203. eCollection 2023 Sep.

Atypical distal tracheal fibrous bridge and bronchial stenosis in an adult patient with bronchopulmonary dysplasia

Ishaq J Wadiwala[1], Alejandra Yu Lee-Mateus[2], Bakr Alhayek[3], David Abia-Trujillo[2], Ryan Chadha[4], Britney N Hazelett[2], Sebastian Fernandez-Bussy[2]
Affiliations expand

- PMID: 37593371
- PMCID: PMC10427834
- DOI: 10.1002/rcr2.1203

Free PMC article

Abstract

Tracheobronchial stenosis (TBS) in adults derives from congenital and acquired conditions, including prolonged mechanical intubation, expiratory central airway collapse, infectious or inflammatory disease, and malignancy. The most common clinical presentation is shortness of breath, recurrent infections, and chronic cough. TBS is usually diagnosed via computed tomography or bronchoscopy, with the latter doubling as a therapeutic tool. We present a case of an atypical fibrotic bridge connecting the walls of the distal trachea and fibrotic bronchial stenosis treated with electrocautery knife and balloon dilation, in an adult patient with bronchopulmonary dysplasia.

Keywords: bronchial stenosis; bronchoscopy; electrocautery knife; fibrotic bridge.

Conflict of interest statement

None declared.

- 6 references
- 2 figures

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

Proceed to details

Cite

Cryobiology
.
. 2023 Aug 17;104569.
doi: 10.1016/j.cryobiol.2023.104569. Online ahead of print.

Effects of spray cryotherapy on cough receptors and airway microenvironment in a canine model of chronic bronchitis

Long Liang[1], Jushan Zhang[1], Hongxia Duan[2], Xuan Li[1], Shuanshuan Xie[3], Changhui Wang[4]
Affiliations expand

- PMID: 37597598

- DOI: 10.1016/j.cryobiol.2023.104569

Abstract

The aim of this study was to explore the effects of spray cryotherapy (SCT) on cough receptors and airway microenvironment in a canine model of chronic bronchitis. We examined the expression of transient receptor potential vanilloid 1/4 (TRPV1/4) and the neuropeptides substance P (SP) and calcitonin gene-related peptide (CGRP) at the gene and protein levels before and after SCT. In addition, we explored whether TRPV1/4 could regulate inflammatory factors via mediator adenosine triphosphate (ATP). The levels of ATP and cytokines in alveolar lavage fluid and cell supernatant were measured using ELISA. SCT effectively downregulated the expression of TRPV1/4 and SP/CGRP in canine airway tissues with chronic bronchitis and reduced the levels of inflammatory mediators and cytokines that affect cough receptor sensitivity, achieving cough relief. TRPV1/4 - ATP - inflammatory cytokines axis has been demonstrated at the cellular level, which in turn modulate the milieu of the airways and promote the formation of a cough feedback loop. Our study has fully revealed the specific mechanism of SCT in treating cough in a canine model of chronic bronchitis, providing a solid theoretical basis for future clinical treatment.

Keywords: Airway microenvironment; Chronic bronchitis; Neuropeptides; Spray cryotherapy; TRPs.

Conflict of interest statement

Declaration of competing interest All authors declare that they have no competing interests.

3

Rheumatol Int

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. 2023 Aug 15.
doi: 10.1007/s00296-023-05395-2. Online ahead of print.

PET FDG CT is useful for giant-cell arteritis with isolated cough

Florent L Besson[1], Arsene Mekinian[2]
Affiliations expand

- PMID: 37581686

- DOI: 10.1007/s00296-023-05395-2

Abstract

Giant cell arteritis (GCA) is a chronic vasculitis of large- and medium-sized vessels. The most frequent symptoms are temporal headaches, scalp tenderness, jaw claudication and polymyalgia rheumatica in 35% of patients. Atypical presentation with dry cough is very

rare and could be isolated making the diagnosis difficult. Initial imaging including PET-CT could be helpful. Literature review yielded 13 case reports with available data and one case series which focused on cough and which were all be included in this study. Most of the cases included males (n = 8), with mostly isolated cough or associated to fever and weight loss. Angio-CT of aortic wall was mostly normal, whereas FDG PET-CT showed in all available cases abnormal arterial thoracic uptake. Temporal artery biopsy was almost suggestive of GCA in all available cases. Cough was steroid responsive usually within few days in all cases without any need of combined therapy. Giant cell arteritis is the most common large-vessel vasculitis over the age of 50 in western countries. Isolated dry cough is extremely rare and encountered in less than 5% of cases.

Keywords: Case report; Cough; Giant cell arteritis; Literature review; Outcome.

- 17 references

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

Proceed to details

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4

Randomized Controlled Trial

Am J Respir Crit Care Med

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. 2023 Aug 15;208(4):417-427.
doi: 10.1164/rccm.202303-0458OC.

Icenticaftor, a CFTR Potentiator, in COPD: A Multicenter, Parallel-Group, Double-Blind Clinical Trial

Fernando J Martinez[1], Gerard J Criner[2], Christian Gessner[3], Margret Jandl[4], Fernando Scherbovsky[5], Masaharu Shinkai[6], Thomas M Siler[7], Claus F Vogelmeier[8], Robert Voves[9], Jadwiga A Wedzicha[10], Christian Bartels[11], Ivan Bottoli[11], Stuart Byiers[11], Pamela Cardenas[12], Joerg H Eckert[11], Florian S Gutzwiller[11], Barbara Knorr[12], Mahavir Kothari[13], Rutvick Parlikar[13], Ana-Maria Tanase[11], Frits M E Franssen[14]
Affiliations expand

- PMID: 37411039

- DOI: 10.1164/rccm.202303-0458OC

Abstract

Rationale: CFTR (cystic fibrosis transmembrane conductance regulator) dysfunction is associated with mucus accumulation and worsening chronic obstructive pulmonary disease (COPD) symptoms. **Objectives:** The aim of this phase IIb dose-finding study was to compare a CFTR potentiator, icenticaftor (QBW251), with placebo in patients with COPD and chronic bronchitis. **Methods:** Patients with COPD on triple therapy for at least three months were randomized to six treatment arms (icenticaftor 450, 300, 150, 75, or 25 mg or placebo twice daily [b.i.d.]) in a 24-week, multicenter, parallel-group, double-blind study. The primary endpoint was change from baseline in trough FEV_1 after 12 weeks. Secondary endpoints included change from baseline in trough FEV_1 and Evaluating Respiratory Symptoms in COPD (E-RS) total and cough and sputum scores after 24 weeks. Multiple comparison procedure-modeling was conducted to characterize dose-response relationship. Rescue medication use, exacerbations, and change in serum fibrinogen concentration after 24 weeks were assessed in exploratory and *post hoc* analyses, respectively. **Measurements and Main Results:** Nine hundred seventy-four patients were randomized. After 12 weeks of icenticaftor treatment, no dose-response relationship for change from baseline in trough FEV_1 was observed; however, it was observed for E-RS cough and sputum score. A dose-response relationship was observed after 24 weeks for trough FEV_1, E-RS cough and sputum and total scores, rescue medication use, and fibrinogen. A dose of 300 mg b.i.d. was consistently the most effective. Improvements for 300 mg b.i.d. versus placebo were also seen in pairwise comparisons of these endpoints. All treatments were well tolerated. **Conclusions:** The primary endpoint was negative, as icenticaftor did not improve trough FEV_1 over 12 weeks. Although the findings must be interpreted with caution, icenticaftor improved trough FEV_1; reduced cough, sputum, and rescue medication use; and lowered fibrinogen concentrations at 24 weeks. Clinical trial registered with www.clinicaltrials.gov (NCT04072887).

Keywords: CFTR dysfunction; CFTR potentiator; COPD; chronic bronchitis; icenticaftor.

Comment in

- Icenticaftor, Novel Therapy for COPD: This Glass Is Half Full.
  Rennard SI.Am J Respir Crit Care Med. 2023 Aug 15;208(4):346-348. doi: 10.1164/rccm.202307-1175ED.PMID: 37437299 No abstract available.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated data, Grant supportexpand

FULL TEXT LINKS

Proceed to details
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ERJ Open Res
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. 2023 Aug 14;9(4):00167-2023.
doi: 10.1183/23120541.00167-2023. eCollection 2023 Jul.

Modified-release morphine or placebo for chronic breathlessness: the MABEL trial protocol

Kathryn Date[1], Bronwen Williams[1], Judith Cohen[1], Nazia Chaudhuri[2], Sabrina Bajwah[3], Mark Pearson[4], Irene Higginson[3], John Norrie[5], Catriona Keerie[5], Sharon Tuck[5], Peter Hall[5], David Currow[6], Marie Fallon[7], Miriam Johnson[4]
Affiliations expand

- PMID: 37583966

- PMCID: PMC10423982

- DOI: 10.1183/23120541.00167-2023

Abstract

Chronic breathlessness, a persistent and disabling symptom despite optimal treatment of underlying causes, is a frightening symptom with serious and widespread impact on patients and their carers. Clinical guidelines support the use of morphine for the relief of chronic breathlessness in common long-term conditions, but questions remain around clinical effectiveness, safety and longer term (>7 days) administration. This trial will evaluate the effectiveness of low-dose oral modified-release morphine in chronic breathlessness. This is a multicentre, parallel group, double-blind, randomised, placebo-controlled trial. Participants (n=158) will be opioid-naïve with chronic breathlessness due to heart or lung disease, cancer or post-coronavirus disease 2019. Participants will be randomised 1:1 to 5 mg oral modified-release morphine/placebo twice daily and docusate/placebo 100 mg twice daily for 56 days. Non-responders at Day 7 will dose escalate to 10 mg morphine/placebo twice daily at Day 15. The primary end-point (Day 28) measure will be worst breathlessness severity (previous 24 h). Secondary outcome measures include worst cough, distress, pain, functional status, physical activity, quality of life, and early identification and management of morphine-related side-effects. At Day 56, participants may opt to take open-label, oral modified-release morphine as part of usual care and complete quarterly breathlessness and toxicity questionnaires. The study is powered to be able to reject the null hypothesis and an embedded normalisation process theory-informed qualitative substudy will explore the adoption of morphine as a first-line pharmacological treatment for chronic breathlessness in clinical practice if effective.

Conflict of interest statement

Conflict of interest: K. Date has nothing to disclose. B. Williams has nothing to disclose. J. Cohen has nothing to disclose. N. Chaudhuri has nothing to disclose. S. Bajwah reports a payment from Boehringer Ingelheim for a lecture given on breathlessness to the Denmark Respiratory Society, outside the submitted work. M. Pearson reports a National Institute for Health Research (NIHR) Health Technology Assessment (HTA) grant (17/34/01) to his institution, for the current study. I. Higginson reports grants from the Medical Research Foundation, the NIHR Global Health Research Group on Global Health and Palliative Care (GHAP), Cicely Saunders International, the NIHR, Health Data Research UK, the Alzheimer's Society, the Medical Research Council, and Marie Curie Cancer Care, outside the submitted work. J. Norrie reports an NIHR/HTA grant to his institution, for the current study. C. Keerie has nothing to disclose. S. Tuck has nothing to disclose. P. Hall reports an NIHR grant, for the current study; and institutional research funding from Lilly, Eisai, Novartis, Merck, Gilead, Sanofi, Roche and SeaGen, outside the submitted work. D. Currow reports grants from the National Health and Medical Research Council (Australia) to his institution (University of Wollongong); grants to his institution (Flinders University) and personal

royalties/licenses from Mayne Pharma International Pty Ltd; participation on the Anamorelin Advisory Board for Helsinn Pharmaceuticals; and roles in the Chris O'Brien Lifehouse Board (unpaid), the NSW Health Pathology Board (paid) and the Dust Diseases Board NSW (paid); all outside the submitted work. M. Fallon has nothing to disclose. M. Johnson reports that she is the clinical advisor to Mayne Pharma and an observer in the Open (blinded) DMEC for this study.

- 49 references
- 1 figure

Randomized Controlled Trial

BMC Pulm Med

. 2023 Aug 14;23(1):298.

doi: 10.1186/s12890-023-02587-1.

Complexity in clinical diagnoses of acute exacerbation of chronic obstructive pulmonary disease

Alexandre J Pratt[1], Andrew Purssell[2], Tinghua Zhang[3], Vanessa P J Luks[3,4], Xavier Bauza[5], Sunita Mulpuru[3,4], Miranda Kirby[5], Shawn D Aaron[3,4], Juthaporn Cowan[6,7]

Affiliations expand

- PMID: 37580731

- PMCID: PMC10426055

- DOI: 10.1186/s12890-023-02587-1

Free PMC article

Abstract

Background: Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is a clinical syndrome with various causes. It is not uncommon that COPD patients presenting with dyspnea have multiple causes for their symptoms including AECOPD, pneumonia, or congestive heart failure occurring concurrently.

Methods: To identify clinical, radiographic, and laboratory characteristics that might help distinguish AECOPD from another dominant disease in patients with a history of COPD, we conducted a retrospective cohort study of hospitalized patients with admitting diagnosis of AECOPD who were screened for a prospective randomized controlled trial from Sep 2016 to Mar 2018. Clinical characteristics, course in hospital, and final diagnosis at discharge were reviewed and adjudicated by two authors. The final diagnosis of each patient was determined based on the synthesis of all presenting signs and symptoms, imaging, and laboratory results. We adhered to AECOPD diagnosis definitions based on the GOLD guidelines. Univariate and multivariate analyses were performed to identify any associated features of AECOPD with and without other acute processes contributing to dyspnea.

Results: Three hundred fifteen hospitalized patients with admitting diagnosis of AECOPD were included. Mean age was 72.5 (SD 10.6) years. Two thirds (65.4%) had spirometry defined COPD. The most common presenting symptom was dyspnea (96.5%), followed by cough (67.9%), and increased sputum (57.5%). One hundred and eighty (57.1%) had a final diagnosis of AECOPD alone whereas 87 (27.6%) had AECOPD with other conditions and 48 (15.2%) did not have AECOPD after adjudication. Increased sputum purulence (OR 3.35, 95%CI 1.68-6.69) and elevated venous pCO2 (OR 1.04, 95%CI 1.01 - 1.07) were associated with a diagnosis of AECOPD but these were not associated with AECOPD alone without concomitant conditions. Radiographic evidence of pleural effusion (OR 0.26, 95%CI 0.12 - 0.58) was negatively associated with AECOPD with or without other conditions while radiographic evidence of pulmonary edema (OR 0.31; 95%CI 0.11 - 0.91) and lobar pneumonia (OR 0.13, 95%CI 0.07 - 0.25) suggested against the diagnosis of AECOPD alone.

Conclusion: The study highlighted the complexity and difficulty of AECOPD diagnosis. A more specific clinical tool to diagnose AECOPD is needed.

Keywords: Acute exacerbation; Chronic obstructive pulmonary disease; Diagnosis.

Conflict of interest statement

JC received honoraria from GSK, Merck, Sanofi Genzyme, Takeda, CSL Behring, Biogen unrelated to this work. MK is a consultant for VIDA Diagnostics Inc. (Coralville, IA, USA). AJP, AP, TZ, VL, XB, SM, SDA do not have competing interests.

- 21 references
- 1 figure

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

Book

EMS Field Identification Of Chronic Obstructive Pulmonary Disease (COPD)

Kevin McLendon[1], Peter F. Edemekong[2]
In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan.
2023 Aug 14.
Affiliations expand

- PMID: 29630282

- Bookshelf ID: NBK493230

Excerpt

Chronic obstructive pulmonary disease (COPD) is a common co-morbidity and cause of new complaints. Rapid recognition, assessment, and treatment are paramount to patient outcomes. Gone are the days of definitive airway management as first-line therapy. The scope of practice has expanded and the expectation of medical care to prevent respiratory

collapse or failure along with it. With an aging population who spent much of their youth with high prevalence of smoking, COPD is a diagnosis that continues to rise as evidenced by the incidence of EMS calls and emergency room (ER) visits. Patients do not always recognize the diagnosis of COPD due to lack of medical access, desire to seek medical attention, or insufficient medical literacy. There is a clear increased predominance of COPD in lower-income areas with the above-increased risk factors. This care burden often lands on those providing emergency care. If the patient has a known diagnosis and is either known to you or can communicate thier diagnosis of COPD, it becomes straightforward to recognize their clinical condition. However, if they are unable, do not know, or have confounding disease processes, then it falls to the clinician to determine the etiology of the complaint and plan rapid, appropriate treatment.

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) recognizes COPD as the fourth leading cause of death worldwide, and it is expected to assume the number 3 spot by 2020. Most often, the reported complaint will be respiratory, for example, shortness of breath, difficulty breathing, dyspnea, or a cough. Additionally, it may also be complaints of chest pain, fever, or other broad complaints. If the patient is not in a life-threating condition, appropriate history and physical can guide the diagnosis and subsequent treatment. There are differential diagnosis that must be accurately assessed, as incorrect diagnosis can increase strain on a failing system and cause a rapid patient decline.

Conflict of interest statement

Disclosure: Kevin McLendon declares no relevant financial relationships with ineligible companies.
Disclosure: Peter Edemekong declares no relevant financial relationships with ineligible companies.

- 8 references

Cite

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8

Book

Hydromorphone

Karl R. Abi-Aad[1], Armen Derian[1]
In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan.
2023 Aug 14.
Affiliations expand

- PMID: 29261877

- Bookshelf ID: NBK470393

Excerpt

Hydromorphone belongs to the opioid class of medications and is utilized to effectively manage and treat moderate-to-severe acute pain and severe chronic pain in patients. The drug exerts its analgesic effects by interacting with the mu-opioid receptors. Moreover, hydromorphone also exerts its effects centrally at the medulla level, leading to respiratory depression and cough suppression. This activity reviews hydromorphone's indications, actions, and contraindications as a crucial pain management agent. This activity also highlights the pharmacodynamics, pharmacokinetics, interactions, adverse event profile, potential toxicity, and monitoring recommendations of hydromorphone, which are crucial for healthcare providers to enhance their competence when caring for patients with moderate-to-severe acute pain and severe chronic pain.

Conflict of interest statement

Disclosure: Karl Abi-Aad declares no relevant financial relationships with ineligible companies.
Disclosure: Armen Derian declares no relevant financial relationships with ineligible companies.

- 13 references

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

StatPearls [Internet]

UNIMORE

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

1

Editorial

Epigenomics

. 2023 Aug 16.
doi: 10.2217/epi-2023-0252. Online ahead of print.

ncRNAs as biomarkers and therapeutic targets for bronchiectasis

Catherine M Greene[1]
Affiliations expand

- PMID: 37584220

- DOI: 10.2217/epi-2023-0252

No abstract available

Keywords: biomarker; bronchiectasis; circular RNA; diagnostic; lncRNA; microRNA; noncoding RNA; therapeutic.

Observational Study

PLoS One

. 2023 Aug 15;18(8):e0286832.
doi: 10.1371/journal.pone.0286832. eCollection 2023.

Follow-up evaluation of pulmonary function and computed tomography findings in chronic kidney disease patients after COVID-19 infection

Solos Jaturapisanukul[1], Nadwipa Yuangtrakul[1], Dearada Wangcharoenrung[1], Krongkan Kanchanarat[1], Kan Radeesri[1], Jakravoot Maneerit[1], Anan Manomaipiboon[1], Khemika Rojtangkom[2], Chompoonuth Ananthanalapa[2], Siwaporn Rungrojthanakit[1], Peerawit Thinpangnga[1], Joshua Alvior[3], Thananda Trakarnvanich[1]

Affiliations expand

- PMID: 37582084

- PMCID: PMC10427007

- DOI: 10.1371/journal.pone.0286832

Free PMC article

Abstract

Pulmonary complications are common after SARS-CoV2- infection. However, data on pulmonary sequelae of COVID-19 after recovery in dialysis patients are limited. We determined the prevalence of abnormal lung function tests and CT findings and investigate the association factors impacting pulmonary dysfunction. This prospective observational cohort study enrolled 100 patients with stage 5 chronic kidney disease (CKD) undergoing dialysis who had recovered from COVID-19 for ≥3 months. Pulmonary function test (PFT) and chest computed tomography (CT) were performed. Demographic data and laboratory results were recorded. The mean patient age was 55.15 ± 12.84 years. Twenty-one patients (21%) had severe COVID-19, requiring mechanical ventilation or oxygen supplementation. Pulmonary function tests revealed a restrictive pattern in 41% (95% confidence interval [CI], 31.73-50.78;) and an obstructive pattern in 7.29% (95% CI, 3.19-13.25) patients. The severe group showed PFT test results similar to the non-severe group, with three patients showing severe obstructive lung disease. The CT scan findings included reticulation (64%), multifocal parenchymal band (43%), ground glass opacities (32%), and bronchiectasis (28%). The median total CT score was 3 (interquartile range, 1-8.5). The CT score and PFT findings showed no association with pulmonary dysfunction extent, except in bronchiectasis. Lung function indices were associated with abnormal CT findings. Abnormal CT findings (bronchiectasis, reticulation, and ground-glass opacities) was associated with higher oxygen requirements than normal CT findings ($p = 0.008$, bronchiectasis; $p = 0.041$, reticulation; $p = 0.032$, ground-glass appearance). Aside from CT findings and CRP levels, no significant lung abnormalities were observed in severe and non-severe patients. Some patients had residual symptoms at follow-up. The findings indicate persistence of both radiological and physiological abnormalities in dialysis patients after COVID-19. However, the prevalence of these abnormalities was comparable to that in the normal population; few patients experienced ongoing symptoms. Follow-up observations and evaluations are warranted. Trial registration. Clinicaltrials.gov Identifier: NCT05348759.

Conflict of interest statement

The authors declare no competing interests.

- 32 references
- 3 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated data, Grant supportexpand

FULL TEXT LINKS

Cite

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3

Editorial

Lancet Respir Med

. 2023 Aug 14;S2213-2600(23)00304-1.
doi: 10.1016/S2213-2600(23)00304-1. Online ahead of print.

New developments in bronchiectasis

The Lancet Respiratory Medicine

- PMID: 37591297

- DOI: 10.1016/S2213-2600(23)00304-1

No abstract available

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

Orphanet J Rare Dis
. 2023 Aug 12;18(1):243.
doi: 10.1186/s13023-023-02830-2.

The prevalence of bronchiectasis in patients with alpha-1 antitrypsin deficiency: initial report of EARCO

Robert A Stockley[1], Anita Pye[2], Joshua De Soyza[2], Alice M Turner[2], Marc Miravitlles[3]; EARCO study investigators
Collaborators, Affiliations expand

- PMID: 37573351
- PMCID: PMC10422747
- DOI: 10.1186/s13023-023-02830-2

Free PMC article

Abstract

Background: Although bronchiectasis has been recognised as a feature of some patients with Alpha1-Antitrypsin deficiency the prevalence and characteristics are not widely known. We wished to determine the prevalence of bronchiectasis and patient characteristics. The first cohort of patients recruited to the EARCO (European Alpha1 Research Collaboration) International Registry data base by the end of 2021 was analysed for radiological evidence of both emphysema and bronchiectasis as well as baseline demographic features.

Results: Of the first 505 patients with the PiZZ genotype entered into the data base 418 (82.8%) had a reported CT scan. There were 77 (18.4%) with a normal scan and 38 (9.1%) with bronchiectasis alone. These 2 groups were predominantly female never smokers and had lung function in the normal range. The remaining 303 (72.5%) ZZ patients all had emphysema on the scan and 113 (27%) had additional evidence of bronchiectasis.

Conclusions: The data indicates the bronchiectasis alone is a feature of 9.1% of patients with the PiZZ genotype of Alpha1-antitrypsin deficiency but although emphysema is the dominant lung pathology bronchiectasis is also present in 27% of emphysema cases and may require a different treatment strategy.

Keywords: Alpha-1 antitrypsin deficiency; Bronchiectasis; Emphysema; Prevalence.

Conflict of interest statement

Marc Miravitlles has received speaker fees from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, Menarini, Kamada, Takeda, Zambon, CSL Behring, Specialty Therapeutics, Janssen, Grifols and Novartis, consulting fees from AstraZeneca, Atriva Therapeutics, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, CSL Behring, Inhibrx, Ferrer, Menarini, Mereo Biopharma, Spin Therapeutics, ONO Pharma, Palobiofarma SL, Takeda, Novartis, Novo Nordisk, Sanofi, Zambon and Grifols and research grants from Grifols. Alice M Turner has received either grants or speaker fees from AstraZeneca, GlaxoSmithKline, Boehringer Ingelheim, Chiesi, CSL Behring, Takeda, Vertex and Grifols Biotherapeutics. Robert A Stockley has received research grants from Mereo BioPharma and CSL Behring, consulting fees from Mereo BioPharma, CSL Behring, Vertex, Inhibrx and chairs the DSMB for Takeda.

- 29 references
- 2 figures