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EXPECT SOME OVERLAP WITH PREVIOUS DELIVERY DUE TO 1 OCT 2022 ONSET DATE

COPD

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Rev Port Cardiol

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. 2022 Oct;41(10):853-861.

doi: 10.1016/j.repc.2021.06.027. Epub 2022 Jul 29.

Beta-blocker use in patients with heart failure with preserved ejection fraction and sinus rhythm

[Article in English, Portuguese]

[Francesc Formiga](#)¹, [David Chivite](#)², [Julio Nuñez](#)³, [Ma Carmen Moreno García](#)⁴, [Luis Manzano](#)⁵, [José Carlos Arévalo-Lorido](#)⁶, [Jose Manuel Cerqueiro](#)⁷, [Álvaro García Campos](#)⁸, [Joan Carles Trullàs](#)⁹, [Manuel Montero-Pérez-Barquero](#)¹⁰, [RICA Investigators group](#)

Affiliations expand

- PMID: 36207068
- DOI: [10.1016/j.repc.2021.06.027](https://doi.org/10.1016/j.repc.2021.06.027)

Abstract

Introduction: Beta-adrenergic receptor blockers (beta-blockers) are frequently used for patients with heart failure (HF) with preserved ejection fraction (HFpEF), although evidence-based recommendations for this indication are still lacking. Our goal was to assess which clinical factors are associated with the prescription of beta-blockers in patients discharged after an episode of HFpEF decompensation, and the clinical outcomes of these patients.

Methods: We assessed 1078 patients with HFpEF and in sinus rhythm who had experienced an acute HF episode to explore whether prescription of beta-blockers on discharge was associated with one-year all-cause mortality or the composite endpoint of one-year all-cause death or HF readmission. We also examined the clinical factors associated with beta-blocker discharge prescription for such patients.

Results: At discharge, 531 (49.3%) patients were on beta-blocker therapy. Patients on beta-blockers more often had a prior diagnosis of hypertension and more comorbidity (including ischemic heart disease) and a better functional status, but less often a prior diagnosis of chronic obstructive pulmonary disease. These patients had a lower heart rate on admission and more often used angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, angiotensin receptor-neprilysin inhibitors and loop diuretics. One year after the index admission, 161 patients (15%) had died and 314 (29%) had experienced the composite endpoint. After multivariate adjustment, beta-blocker prescription was not associated with either all-cause mortality (HR=0.83 [95% CI 0.61-1.13]; p=0.236) or the composite endpoint (HR=0.98 [95% CI 0.79-1.23]; p=0.882).

Conclusion: In patients with HFpEF in sinus rhythm, beta-blocker use was not related to one-year mortality or mortality plus HF readmission.

Keywords: All-cause mortality; Beta-adrenergic receptor blockers; Bloqueadores dos recetores β -adrenérgicos; Fração de ejeção preservada; Heart failure; Heart failure readmission; Insuficiência cardíaca; Mortalidade global; Preserved ejection fraction; Reinternamento por insuficiência cardíaca.

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Association between right ventricular dysfunction and adverse cardiac events in mild COPD patients

[Giuseppe Armentaro](#)^{#1}, [Corrado Pelaia](#)^{#2}, [Velia Cassano](#)¹, [Sofia Miceli](#)¹, [Raffaele Maio](#)¹, [Maria Perticone](#)¹, [Daniele Pastori](#)³, [Pasquale Pignatelli](#)³, [Francesco Andreozzi](#)¹, [Francesco Violi](#)³, [Giorgio Sesti](#)⁴, [Angela Sciacqua](#)¹

Affiliations expand

- PMID: 36203411
- DOI: [10.1111/eci.13887](https://doi.org/10.1111/eci.13887)

Abstract

Background: Lung hyperinflation and systemic inflammation are currently believed to be the most important causes of right heart alterations in chronic obstructive pulmonary disease (COPD) patients. A multicenter observational study was performed to assess the morphological and functional parameters of right ventricle (RV) in COPD subjects, as well as to evaluate the potential prognostic impact on the development of major cardiovascular adverse events (MACEs).

Methods: For this retrospective study, from January 1, 2010 to December 31, 2021, we enrolled COPD patients on the basis of their airflow limitation. In particular, we selected subjects spanning across GOLD 1 and 2 functional stages. Clinical, laboratory, and functional parameters were collected at baseline. Echocardiography was routinely performed in all COPD patients. RV dysfunction was defined on the basis of tricuspid annular plane systolic excursion (TAPSE) values. MACE occurrence (non-fatal ischemic stroke, non-fatal myocardial infarction, cardiac revascularization or coronary bypass surgery, and cardiovascular death) was evaluated during a median follow-up of 55 (36-72) months.

Results: Among the 749 enrolled patients, 408 subjects had a TAPSE value ≥ 20 mm, while the remaining 341 had a TAPSE value < 20 mm. In patients with TAPSE ≥ 20 mm the observed MACEs were 1.9 events/100 patient-year, while in the group with a worse right heart function there were 4.2 events/100 patient-year ($p < 0.0001$). The multivariate analysis model confirmed the association between RV dysfunction and MACE. Indeed, a 1 mm-increase in TAPSE value and the intake of long-acting β_2 -receptor agonists (LABA)/long-acting muscarinic antagonist (LAMA) inhaled therapy were protective factors for the onset of MACE, while the presence of diabetes mellitus and high values of both uric acid (UA) and systolic pulmonary arterial pressure (S-PAP) enhanced the risk of MACE in study participants.

Conclusions: The results of this study showed that in patients with mild COPD there is an association between right heart dysfunction and the risk of MACE during follow-up.

Keywords: COPD; MACE; TAPSE; oxidative stress; right heart.

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BMJ Open Respir Res

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. 2022 Oct;9(1):e001385.

doi: 10.1136/bmjresp-2022-001385.

Small airway function measured using forced expiratory flow between 25% and 75% of vital capacity and its relationship to airflow limitation in symptomatic ever-smokers: a cross-sectional study

[Nowaf Y Alobaidi](#)^{1,2,3}, [Mohammed Almeshari](#)^{1,4}, [James Stockley](#)⁵, [Robert Andrew Stockley](#)⁵, [Elizabeth Sapey](#)^{6,7}

Affiliations expand

- PMID: 36202407
- PMCID: [PMC9540854](#)
- DOI: [10.1136/bmjresp-2022-001385](#)

Free PMC article

Abstract

Background: Chronic obstructive pulmonary disease (COPD) is diagnosed and its severity graded by traditional spirometric parameters (forced expiratory volume in 1 s (FEV₁)/forced vital capacity (FVC) and FEV₁, respectively) but these parameters are considered insensitive for identifying early pathology. Measures of small airway function, including forced expiratory flow between 25% and 75% of vital capacity (FEF₂₅₋₇₅), may be more valuable in the earliest phases of COPD. This study aimed to determine the prevalence of low FEF₂₅₋₇₅ in ever-smokers with and without airflow limitation (AL) and to determine whether FEF₂₅₋₇₅ relates to AL severity.

Method: A retrospective analysis of lung function data of 1458 ever-smokers suspected clinically of having COPD. Low FEF₂₅₋₇₅ was defined by z-score < -0.8345 and AL was defined by FEV₁/FVC z-scores < -1.645. The severity of AL was evaluated using FEV₁ z-scores. Participants were placed into three groups: normal FEF₂₅₋₇₅/ no AL (normal FEF₂₅₋₇₅/AL-); low FEF₂₅₋₇₅/ no AL (low FEF₂₅₋₇₅/AL-) and low FEF₂₅₋₇₅/ AL (low FEF₂₅₋₇₅/AL+).

Results: Low FEF₂₅₋₇₅ was present in 99.9% of patients with AL, and 50% of those without AL. Patients in the low FEF₂₅₋₇₅/AL- group had lower spirometric measures (including FEV₁, FEF₂₅₋₇₅/FVC and FEV₃/FVC) than those in the normal FEF₂₅₋₇₅/AL- group. FEF₂₅₋₇₅ decreased with AL severity. A logistic regression model demonstrated that in the absence of AL, the presence of low FEF₂₅₋₇₅ was associated with lower FEV₁ and FEV₁/FVC even when smoking history was accounted for.

Conclusions: Low FEF₂₅₋₇₅ is a physiological trait in patients with conventional spirometric AL and likely reflects early evidence of impairment in the small airways when spirometry is within the 'normal range'. FEF₂₅₋₇₅ likely identifies a group of patients with early evidence of pathological lung damage who warrant careful monitoring and reinforced early intervention to abrogate further lung injury.

Keywords: COPD epidemiology; Lung Physiology; Respiratory Measurement.

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Conflict of interest statement

Competing interests: None declared.

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- [6 figures](#)

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BMC Pulm Med

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. 2022 Oct 5;22(1):376.

doi: 10.1186/s12890-022-02137-1.

[Prognostic value of lymphocyte count for in-hospital mortality in patients with severe AECOPD](#)

[Yanlu Hu](#)¹, [Huanyu Long](#)¹, [Yang Cao](#)², [Yanfei Guo](#)³

Affiliations [expand](#)

- PMID: 36199131

- PMCID: [PMC9533979](#)
- DOI: [10.1186/s12890-022-02137-1](#)

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Abstract

Background: Patients with severe acute exacerbations of chronic obstructive pulmonary disease often have a poor prognosis. Biomarkers can help clinicians personalize the assessment of different patients and mitigate mortality. The present study sought to determine if the lymphocyte count could act as a risk factor for mortality in individuals with severe AECOPD.

Methods: A retrospective study was carried out with 458 cases who had severe AECOPD. For analysis, patients were divided into two groups on the basis of lymphocyte count: $< 0.8 \times 10^9/L$ and $\geq 0.8 \times 10^9/L$.

Results: Patients who fulfilled the criteria for inclusion were enrolled, namely 458 with a mean age of 78.2 ± 8.2 years. Of these patients, 175 had a low lymphocyte count. Compared to patients with normal lymphocyte counts, those with low counts were older (79.2 ± 7.4 vs. 77.5 ± 8.6 years, $p = 0.036$), had lower activities of daily living scores on admission (35.9 ± 27.6 vs. 47.5 ± 17.1 , $p < 0.001$), and had a greater need for home oxygen therapy (84.6 vs. 72.1% , $p = 0.002$). Patients with low lymphocytes had higher mortality rates during hospitalization (17.1 vs. 7.1% , $p = 0.001$), longer hospital stay (median [IQR] 16 days [12-26] vs. 14 days [10-20], $p = 0.002$) and longer time on mechanical ventilation (median [IQR] 11.6 days [5.8-18.7] vs. 10.9 days [3.8-11.6], $p < 0.001$). The logistic regression analysis showed lymphocyte count $< 0.8 \times 10^9/L$ was an independent risk factor associated with in-hospital mortality (OR 2.74, 95%CI 1.33-5.66, $p = 0.006$).

Conclusion: Lymphocyte count could act as a predictor of mortality in patients with severe AECOPD.

Keywords: Biomarker; Chronic obstructive pulmonary disease; Exacerbation; Lymphocyte count; Mortality.

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Conflict of interest statement

The authors declare that they have no competing interests.

- [28 references](#)
- [2 figures](#)

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Sci Rep

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. 2022 Oct 5;12(1):16674.

doi: 10.1038/s41598-022-21038-1.

Effects of tiotropium on the risk of coronary heart disease in patients with COPD: a nationwide cohort study

[Jiyoung Shin](#)¹, [Jin Hwa Lee](#)²

Affiliations expand

- PMID: 36198721
- PMCID: [PMC9535029](#)
- DOI: [10.1038/s41598-022-21038-1](#)

Free PMC article

Abstract

Inhaled long-acting muscarinic antagonist (LAMA) is recommended for the treatment of chronic obstructive pulmonary disease (COPD). However, there is still concern that LAMA may cause cardiovascular adverse events in COPD patients. Therefore, this study aimed to determine whether the administration of tiotropium, the first commercially available LAMA, could increase the risk of coronary heart disease (CHD) in COPD patients through a nationwide cohort study. We used the Korean National Health Insurance Service-National Sample Cohort (NHIS-NSC) database between 2002 and 2014 for the analysis. We applied a washout period of COPD diagnosis during 2002-2003 and excluded the patients who used an inhaler before the diagnosis of COPD. We also excluded patients who were diagnosed with CHD before inhaler use. Among a total of 5787 COPD patients, 1074 patients were diagnosed with CHD. In the Cox regression models with time-dependent tiotropium usage, we found that tiotropium significantly increased the risk of CHD in a subgroup of age [Formula: see text]55 years compared to non-users of tiotropium (adjusted hazard ratio [aHR], 1.24; 95% confidence interval [CI], 1.003-1.54). When analyzed by dividing into tertiles (high/middle/low) according to the cumulative tiotropium exposure, the high tertile exposure group of tiotropium was associated with a higher risk of CHD compared with the low tertile exposure group of tiotropium. Additionally, the risk of CHD was higher in the high tertile exposure group of tiotropium in the age 55 and older group and in the never smoker group. When prescribing tiotropium for COPD patients, particularly those over 55 years of age and never-smokers, it is desirable to evaluate the risk of CHD in advance and closely follow-up for CHD occurrence.

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Conflict of interest statement

The authors declare no competing interests.

- [36 references](#)
- [3 figures](#)

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ACS Sens

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. 2022 Oct 4.

doi: 10.1021/acssensors.2c01628. Online ahead of print.

Biodegradable Smart Face Masks for Machine Learning-Assisted Chronic Respiratory Disease Diagnosis

[Kaijun Zhang](#)¹, [Zhaoyang Li](#)¹, [Jianfeng Zhang](#)^{1,2}, [Dazhe Zhao](#)¹, [Yucong Pi](#)¹, [Yujun Shi](#)¹, [Renkun Wang](#)¹, [Peisheng Chen](#)³, [Chaojie Li](#)³, [Gangjin Chen](#)², [Iek Man Lei](#)¹, [Junwen Zhong](#)¹

Affiliations expand

- PMID: 36196484
- DOI: [10.1021/acssensors.2c01628](https://doi.org/10.1021/acssensors.2c01628)

Abstract

Utilizing smart face masks to monitor and analyze respiratory signals is a convenient and effective method to give an early warning for chronic respiratory diseases. In this work, a smart face mask is proposed with an air-permeable and biodegradable self-powered breath sensor as the key component. This smart face mask is easily fabricated, comfortable to use, eco-friendly, and has sensitive and stable output performances in real wearable conditions. To verify the practicability, we use smart face masks to record respiratory signals of patients with chronic respiratory diseases when the patients do not have obvious symptoms. With the assistance of the machine learning algorithm of the bagged decision tree, the accuracy for distinguishing the healthy group and three groups of chronic respiratory diseases (asthma, bronchitis, and chronic obstructive pulmonary disease) is up to 95.5%. These results indicate that the strategy of this work is feasible and may promote the development of wearable health monitoring systems.

Keywords: biodegradable; chronic respiratory disease diagnosis; machine learning; self-powered sensors; smart face mask.

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. 2022 Oct;51:486-489.

doi: 10.1016/j.clnesp.2022.06.109. Epub 2022 Jul 14.

Predictors of undernutrition in COPD patients

[Greta Lattanzi](#)¹, [Panaiotis Finamore](#)², [Claudio Pedone](#)², [Antonio Alma](#)³, [Simone Scarlata](#)², [Davide Onofrio Fontana](#)², [Yeganeh Manon Khazrai](#)⁴, [Raffaele Antonelli Incalzi](#)²

Affiliations expand

- PMID: 36184247
- DOI: [10.1016/j.clnesp.2022.06.109](https://doi.org/10.1016/j.clnesp.2022.06.109)

Abstract

Background & aims: Chronic obstructive pulmonary disease (COPD) is a chronic disease characterized by persistent respiratory symptoms and airflow limitation. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) report recommends smoking cessation, pharmacological therapy and pulmonary rehabilitation, but this clinical course can be negatively influenced by undernutrition, a condition documented in about 20% of COPD patients. An altered energy balance characterized by an insufficient intake of energy and nutrients is the primary cause of undernutrition, therefore the aim of this study is to investigate whether clinical and instrumental variables collected during a routine

respiratory assessment associate with an altered energy balance in order to identify COPD patients at higher risk of undernutrition worth of further assessment.

Methods: A total of forty-nine participants with a diagnosis of stable COPD were included in this mono-center and longitudinal study. Subjects underwent a multidimensional assessment including evaluation of medical history, evaluation of pulmonary function, evaluation of nutritional status, evaluation of energy intake and resting energy expenditure (REE) using EPIC questionnaire and indirect-calorimetry (IC), respectively, evaluation of physical impairment and mood status.

Results: The 24% of participants was at risk of undernutrition with a mean energy intake, total protein intake and lipid intake significantly lower than not at risk subjects, while REE was significantly higher. Age, sex, multimorbidity, disability and depression, and pulmonary function tests were not associated with a negative energy balance, with the exception of the Cumulative Illness Rating Scale (CIRS) severity index, which showed a significant association.

Conclusion: Clinical evaluation and pulmonary function tests are unable to reliably predict undernutrition in COPD patients, so a nutritional screening should always be forecast in this population based on an accurate evaluation of energy intake and expenditure and body composition.

Keywords: Chronic obstructive pulmonary disease; Clinical predictors; Undernutrition.

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Conflict of interest statement

Declaration of competing interest The authors declare no conflict of interest.

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Association of tobacco product use with chronic obstructive pulmonary disease (COPD) prevalence and incidence in Waves 1 through 5 (2013–2019) of the Population Assessment of Tobacco and Health (PATH) Study

[Laura M Paulin](#)¹, [Michael J Halenar](#)², [Kathryn C Edwards](#)², [Kristin Lauten](#)², [Cassandra A Stanton](#)², [Kristie Taylor](#)², [Dorothy Hatsukami](#)³, [Andrew Hyland](#)⁴, [Todd MacKenzie](#)⁵, [Martin C Mahoney](#)⁴, [Ray Niaura](#)⁶, [Dennis Trinidad](#)⁷, [Carlos Blanco](#)⁸, [Wilson M Compton](#)⁸, [Lisa D Gardner](#)⁹, [Heather L Kimmel](#)⁸, [Dana Lauterstein](#)⁹, [Daniela Marshall](#)^{8,10}, [James D Sargent](#)⁵

Affiliations expand

- PMID: 36183112
- PMCID: [PMC9526897](#)
- DOI: [10.1186/s12931-022-02197-1](#)

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Abstract

Background: We examined the association of non-cigarette tobacco use on chronic obstructive pulmonary disease (COPD) risk in the Population Assessment of Tobacco and Health (PATH) Study.

Methods: There were 13,752 participants ≥ 40 years with Wave 1 (W1) data for prevalence analyses, including 6945 adults without COPD for incidence analyses; W1-5 (2013-2019) data were analyzed. W1 tobacco use was modeled as 12 mutually-exclusive categories of past 30-day (P30D) single and polyuse, with two reference categories (current exclusive cigarette and never tobacco). Prevalence and incidence ratios of self-reported physician-diagnosed COPD were estimated using weighted multivariable Poisson regression.

Results: W1 mean (SE) age was 58.1(0.1) years; mean cigarette pack-years was similar for all categories involving cigarettes and exclusive use of e-cigarettes (all > 20), greater than exclusive cigar users (< 10); and COPD prevalence was 7.7%. Compared to P30D cigarette use, never tobacco, former tobacco, and cigar use were associated with lower COPD prevalence (RR = 0.33, (95% confidence interval-CI) [0.26, 0.42]; RR = 0.57, CI [0.47, 0.70]; RR = 0.46, CI [0.28, 0.76], respectively); compared to never tobacco use, all categories except cigar and smokeless tobacco use were associated with higher COPD prevalence (RR former = 1.72, CI [1.33, 2.23]; RR cigarette = 3.00, CI [2.37, 3.80]; RR e-cigarette = 2.22, CI [1.44, 3.42]; RR cigarette + e-cigarette = 3.10, CI [2.39, 4.02]; RR polycombusted = 3.37, CI [2.44, 4.65]; RR polycombusted plus noncombusted = 2.75, CI [1.99, 3.81]). COPD incidence from W2-5 was 5.8%. Never and former tobacco users had lower COPD risk compared to current cigarette smokers (RR = 0.52, CI [0.35, 0.77]; RR = 0.47, CI [0.32, 0.70], respectively). Compared to never use, cigarette, smokeless, cigarette plus e-cigarette, and polycombusted tobacco use were associated with higher COPD incidence (RR = 1.92, CI [1.29, 2.86]; RR = 2.08, CI [1.07, 4.03]; RR = 1.99, CI [1.29, 3.07]; RR = 2.59, CI [1.60, 4.21], respectively); exclusive use of e-cigarettes was not (RR = 1.36, CI [0.55, 3.39]).

Conclusions: E-cigarettes and all use categories involving cigarettes were associated with higher COPD prevalence compared to never use, reflecting, in part, the high burden of cigarette exposure in these groups. Cigarette-but not exclusive e-cigarette-use was also strongly associated with higher COPD incidence. Compared to cigarette use, only quitting tobacco was protective against COPD development.

Keywords: COPD; Cigarette; E-cigarette; Epidemiology; Prevention; Respiratory disease; Smoking-related lung disease; Tobacco.

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Conflict of interest statement

Martin C. Mahoney has provided expert testimony on the health effects of smoking in lawsuits filed against the tobacco industry. He has also received research support from Pfizer, Inc., for a clinical trial of smoking cessation, and has previously served on external advisory panels sponsored by Pfizer to promote smoking cessation in clinical settings. Raymond Niaura receives funding from the Food and Drug Administration Center for Tobacco Products via contractual mechanisms with Westat and the National Institutes of Health. Within the past 3 years, he has served as a paid consultant to the Government of Canada via a contract with Industrial Economics Inc. and has received an honorarium for a

virtual meeting from Pfizer Inc. Dr. Niaura was an unpaid grant reviewer for the Foundation for a Smoke Free World. Wilson Compton reports long-term stock holdings in General Electric, 3 M Company, and Pfizer Incorporated, unrelated to this article.

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Editorial

Ann Am Thorac Soc

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. 2022 Oct;19(10):1638-1639.

doi: 10.1513/AnnalsATS.202206-525ED.

[The Paradox of Obesity in Patients with Chronic Obstructive Pulmonary Disease](#)

[Abebaw Mengistu Yohannes](#)¹

Affiliations [expand](#)

- PMID: 36178401

- PMID: [PMC9528747](#)
- DOI: [10.1513/AnnalsATS.202206-525ED](#)

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No abstract available

Comment on

- [Physical Activity, Exercise Capacity, and Body Composition in U.S. Veterans with Chronic Obstructive Pulmonary Disease.](#)
Wan ES, Polak M, Goldstein RL, Lazzari AA, Kantorowski A, Garshick E, Moy ML. *Ann Am Thorac Soc.* 2022 Oct;19(10):1669-1676. doi: 10.1513/AnnalsATS.202111-1221OC.PMID: 35536690 Clinical Trial.
- [14 references](#)
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[Editorial](#)

Ann Am Thorac Soc

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. 2022 Oct;19(10):1636-1637.

doi: 10.1513/AnnalsATS.202207-609ED.

To β -Block or Not to β -Block: That Is Still the Question in Chronic Obstructive Pulmonary Disease

[Robert J Hancox](#)¹

Affiliations expand

- PMID: 36178400
- PMCID: [PMC9528739](#)
- DOI: [10.1513/AnnalsATS.202207-609ED](#)

Free PMC article

No abstract available

Comment on

- [Lung Function and the Risk of Exacerbation in the \$\beta\$ -Blockers for the Prevention of Acute Exacerbations of Chronic Obstructive Pulmonary Disease Trial.](#)
Parekh TM, Helgeson ES, Connett J, Voelker H, Ling SX, Lazarus SC, Bhatt SP, MacDonald DM, Mkorombindo T, Kunisaki KM, Fortis S, Kaminsky D, Dransfield MT. *Ann Am Thorac Soc.* 2022 Oct;19(10):1642-1649. doi: [10.1513/AnnalsATS.202109-1042OC](#). PMID: 35363600 Clinical Trial.
- [16 references](#)
- [1 figure](#)

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Editorial

Ann Am Thorac Soc

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. 2022 Oct;19(10):1640-1641.

doi: 10.1513/AnnalsATS.202207-591ED.

Peer Support and Chronic Obstructive Pulmonary Disease Self-Management: A Promising Approach?

Vincent S Fan^{1,2}, David B Coultas^{3,4}

Affiliations expand

- PMID: 36178399
- PMCID: [PMC9528742](#)
- DOI: [10.1513/AnnalsATS.202207-591ED](#)

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No abstract available

Comment on

- [Comparing Self-Management Programs with and without Peer Support among Patients with Chronic Obstructive Pulmonary Disease: A Clinical Trial.](#)
Aboumatar H, Garcia Morales EE, Jager LR, Naqibuddin M, Kim S, Saunders J, Bone L, Linnell J, McBurney M, Neiman J, Riley M, Robinson N, Rand C, Wise R. *Ann Am*

Thorac Soc. 2022 Oct;19(10):1687-1696. doi: 10.1513/AnnalsATS.202108-932OC.PMID: 35442179 Clinical Trial.

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Curr Med Res Opin

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. 2022 Oct 7;1-5.

doi: 10.1080/03007995.2022.2129229. Online ahead of print.

[Variation in costs due to virtual switching from free- to fixed-triple LABA/LAMA/ICS combinations among COPD patients: an analysis using a primary care database](#)

[Francesco Lapi](#)¹, [Ettore Marconi](#)¹, [Francesco Paolo Lombardo](#)², [Claudio Micheletto](#)³, [Claudio Cricelli](#)²

Affiliations expand

- PMID: 36154352

- DOI: [10.1080/03007995.2022.2129229](https://doi.org/10.1080/03007995.2022.2129229)

Abstract

Chronic obstructive pulmonary disease (COPD) is a condition with a relevant clinical and economic burden. Only 10% to 40% of COPD patients reporting a regular use of respiratory medications, including those who suffered from severe disease being prescribed with triple combination therapy, nominally long-acting beta agonist (LABA), long-acting muscarinic antagonist (LAMA) and inhaled corticosteroid (ICS). The recent market launch of fixed-triple LABA/LAMA/ICS therapy might contribute to improve medications adherence and costs containment, given the use of a single instead of two or three inhalers. Few data are available on costs due to triple therapy prescribed for COPD. In specific, there are no studies providing data on the potential costs saving whether COPD patients exposed to free-triple combination therapy were switched to fixed-triple combination. In this respect, we simulated some scenarios of virtual switching and calculated the related cost savings.

Keywords: COPD; LABA/LAMA/ICS; costs; triple therapy.

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Observational Study

Respir Med

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. 2022 Oct;202:106982.

doi: 10.1016/j.rmed.2022.106982. Epub 2022 Sep 9.

Luminal mucus plugs are spatially associated with airway wall thickening in severe COPD and asthma: A single-centered, retrospective, observational study

[Cecilia Tran](#)¹, [Gaurav Veer Singh](#)², [Ehsan Haider](#)³, [Colm Boylan](#)³, [Carmen Venegas](#)⁴, [Shaista Riaz](#)⁵, [Suad Al Duwaiki](#)⁵, [Moustafa Yehia](#)⁵, [Terence Ho](#)⁶, [Parameswaran Nair](#)⁶, [Sarah Svenningsen](#)⁶, [Miranda Kirby](#)⁷

Affiliations expand

- PMID: 36116144
- DOI: [10.1016/j.rmed.2022.106982](https://doi.org/10.1016/j.rmed.2022.106982)

Abstract

Background: Airway wall thickening and excess airway mucus occur in asthma and chronic obstructive pulmonary disease (COPD), but few studies have investigated the relationship between them. Our objective was to determine the association between computed tomography (CT) airway wall thickening in segmental airways proximal to airways with or without mucus plugging in patients with asthma and COPD.

Methods: Mucus plugging was scored using a CT bronchopulmonary segment-based scoring system in asthma and COPD patients. For each of the 19 segmental airways, a mucus plug was defined as complete occlusion of one or more of the daughter branches (sub-segmental airways) by mucus. CT airway measurements were generated for each of the 19 segmental airways: wall-area-percentage (WA%), lumen area (LA), and total airway count (TAC) (VIDA Diagnostics Inc.). Multivariable logistic regression models were constructed for the presence of mucus plugs with corresponding CT measurement and adjusted by covariates; each of the 19 segments was treated as a nested variable.

Results: A total of 33 participants were evaluated. Participants had a mean age of 60 ± 15 yrs and there were $n = 14$ (42%) males. There were 16 (48%) participants with a diagnosis of asthma and 17 (52%) with a COPD diagnosis. The mean FEV_1 was $53 \pm 21\%$ pred and FEV_1/FVC was $54 \pm 15\%$. The mean mucus score in all participants was 15 ± 4 (min = 0, max = 19). Multivariable logistic regression analysis showed the presence of

airway mucus was significantly associated with increased CT WA% ($\beta = 7.30$, $p = 0.004$) and reduced TAC ($\beta = -0.06$, $p = 0.045$).

Conclusions: There was increased airway wall thickness and reduced airway counts on CT in segments where there was a distal mucus plug compared to segments without mucus plugs in asthma and COPD.

Keywords: Airway wall thickening; Asthma; COPD; Computed tomography (CT); Imaging; Mucus plugs.

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Conflict of interest statement

Declaration of competing interest TH reports grants from Fisher and Paykel and personal fees from Sanofi, outside the submitted work. PN reports grants from AstraZeneca, Teva, Roche, Novartis, Sanofi and Foresee, and personal fees from AstraZeneca, Teva, Roche, Novartis, Merck and Equillium, outside the submitted work. SS reports grants from Cyclomedica and personal fees from AstraZeneca, Novartis, Polarean, and Arrowhead Pharmaceuticals, all outside the submitted work. All other authors do not have any potential conflicts of interest to declare.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS



[Proceed to details](#)

Cite

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 14

Lung

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. 2022 Oct;200(5):609-617.

doi: 10.1007/s00408-022-00568-5. Epub 2022 Sep 15.

Serum Creatinine/Cystatin C Ratio as a Predictor of In-hospital Mortality in Patients Hospitalized with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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Affiliations expand

- PMID: 36104573
- PMCID: [PMC9526688](#)
- DOI: [10.1007/s00408-022-00568-5](#)

Free PMC article

Abstract

Purpose: Low serum creatinine/cystatin C ratio (CCR) is associated with unfavorable characteristics in patients with chronic obstructive pulmonary disease (COPD); however, the relationship between CCR and in-hospital mortality of patients with acute exacerbation of COPD (AECOPD) is unexplored. Our objective was to assess the value of CCR for predicting in-hospital mortality of patients hospitalized with AECOPD.

Methods: Patients with AECOPD (n = 597) were retrospectively enrolled. Patient's clinical characteristics and laboratory tests, including serum cystatin C and creatinine, were reviewed. The prediction value of CCR was evaluated using area under the receiver operating characteristic curve (AUC) values. Factors potentially impacting in-hospital mortality were investigated using univariate and multivariate logistic regression analyses.

Results: Mortality rate during hospitalization was 10.05%. CCR was lower in non-surviving vs. survived patients (41.67 vs. 61.52, $P < 0.001$). AUC value for CCR for in-hospital mortality prediction was 0.79 [95% confidence interval (CI) 0.73-0.85]. On multivariate logistic regression analysis, in-hospital mortality was strongly associated with CCR < 52.27 [odds ratio (OR) 6.23, 95% CI (3.00-12.92), $P < 0.001$], age ≥ 81 years [OR 2.97, 95% CI

(1.20-7.37), $P = 0.019$], oxygenation index < 300 [OR 3.28, 95% CI (1.27-8.44), $P = 0.014$], CRP > 8 mg/L [OR 1.84, 95% CI (1.15-2.95), $P = 0.012$], and D-dimer > 500 ng/L [OR 5.19, 95% CI (1.51-17.79), $P = 0.009$].

Conclusions: CCR was significantly lower, and is a potential prognostic indicator, in patients with AECOPD who died during hospitalization.

Keywords: Acute exacerbation; Chronic obstructive pulmonary disease; Mortality; Serum creatinine/cystatin C ratio.

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Conflict of interest statement

The authors declare that they have no conflicts of interest for this work.

- [44 references](#)
- [3 figures](#)

SUPPLEMENTARY INFO

MeSH terms, Substances, Grant support[expand](#)

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J Cardiovasc Med (Hagerstown)

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. 2022 Oct 1;23(10):694-696.

doi: 10.2459/JCM.0000000000001327.

Ventilatory variability during cardiopulmonary exercise test is higher in heart failure and chronic obstructive pulmonary disease plus heart failure than in chronic obstructive pulmonary disease patients

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Affiliations expand

- PMID: 36099077
- DOI: [10.2459/JCM.0000000000001327](https://doi.org/10.2459/JCM.0000000000001327)

No abstract available

- [12 references](#)

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS



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☐ 16

Multicenter Study

Lung

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. 2022 Oct;200(5):601-607.

doi: 10.1007/s00408-022-00565-8. Epub 2022 Sep 5.

Trajectories of Severe Exacerbations of Chronic Obstructive Pulmonary Disease and Their Relationship with Mortality Risk

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Affiliations expand

- PMID: 36065068
- DOI: [10.1007/s00408-022-00565-8](https://doi.org/10.1007/s00408-022-00565-8)

Abstract

Purpose: Acute exacerbations of COPD (AECOPD) are important factors contributing to mortality risk. The rate of exacerbations varies overtime. An inconsistent pattern of exacerbation occurrence is a common finding. The mortality risk associated with such a pattern is not entirely clear. Our objective was to assess the risk of mortality associated with various possible patterns of AECOPD trajectories.

Methods: This is a multicenter historical cohort study. Four different exacerbation trajectories were defined according to the incidence of severe AECOPD requiring hospital admission 2 years before and after the date of the first visit to the respiratory clinic- Consistent non-exacerbators (NEx): no AECOPD before or after the index date; consistent exacerbators (Ex): at least one AECOPD both before and after the index date; converters to exacerbators (CONV-Ex): no exacerbations before and at least one AECOPD after the index date; converters to non-exacerbators (CONV-NEx): at least one AECOPD before the index date, and no exacerbations after said date. All-cause mortality risk for these trajectories was assessed.

Results: A total of 1713 subjects were included in the study: NEx: 1219 (71.2%), CONV-NEx: 225 (13.1%), CONV-Ex: 148 (8.6%), Ex: 121 (7.1%). After correcting for confounding variables, the group with the highest mortality risk was Ex. The CONV-Ex and CONV-Nex groups had a mortality risk between Ex and NEx, with no significant differences between them.

Conclusion: Different possible trajectories of severe AECOPD before and after a first specialized consultation are associated with different mortality risks. An inconsistent pattern of exacerbations has a mortality risk between Ex and NEx, with no clear differences between CONV-Ex and CONV-NEx.

Keywords: Exacerbations; Mortality; Prognosis; Pulmonary disease, chronic obstructive.

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- [17 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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☐ 17

J Heart Lung Transplant

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. 2022 Oct;41(10):1335-1347.

doi: 10.1016/j.healun.2022.08.007. Epub 2022 Aug 20.

[The International Thoracic Organ Transplant Registry of the](#)

International Society for Heart and Lung Transplantation: Thirty-ninth adult lung transplantation report-2022; focus on lung transplant recipients with chronic obstructive pulmonary disease

[Michael Perch¹](#), [Don Hayes¹](#), [Wida S Cherikh¹](#), [Andreas Zuckermann¹](#), [Michael O Harhay¹](#), [Eileen Hsich¹](#), [Luciano Potena¹](#), [Aparna Sadavarte¹](#), [Kelsi Lindblad¹](#), [Tajinder P Singh¹](#), [Josef Stehlik²](#), [International Society for Heart and Lung Transplantation¹](#)

Affiliations expand

- PMID: 36050206
- DOI: [10.1016/j.healun.2022.08.007](https://doi.org/10.1016/j.healun.2022.08.007)

No abstract available

Keywords: COPD; lung transplantation; morbidity; post-transplant survival; recipient characteristics; registry.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS



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Cite

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Review

Am J Physiol Cell Physiol

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. 2022 Oct 1;323(4):C974-C989.

doi: 10.1152/ajpcell.00292.2022. Epub 2022 Aug 22.

Impaired regenerative capacity contributes to skeletal muscle dysfunction in chronic obstructive pulmonary disease

[Ariel Jaitovich](#)¹

Affiliations expand

- PMID: 35993519
- PMCID: PMC9484993 (available on 2023-10-01)
- DOI: [10.1152/ajpcell.00292.2022](https://doi.org/10.1152/ajpcell.00292.2022)

Abstract

Locomotor skeletal muscle dysfunction is a relevant comorbidity of chronic obstructive pulmonary disease (COPD) and is strongly associated with worse clinical outcomes including higher mortality. Over the last decades, a large body of literature helped characterize the process, defining the disruptive muscle phenotype caused by COPD that involves reduction in muscle mass, force-generation capacity, fatigue-tolerance, and regenerative potential following injury. A major limitation in the field has been the scarcity of well-calibrated animal models to conduct mechanistic research based on loss- and gain-of-function studies. This article provides an overall description of the process, the tools available to mechanistically investigate it, and the potential role of mitochondrially driven metabolic signals on the regulation muscle regeneration after injury in COPD. Finally, a description of future avenues to further expand on the area is proposed based on very recent evidence involving mitochondrial metabolic cues affecting myogenesis.

Keywords: autophagy; chronic pulmonary diseases; myogenesis; pulmonary emphysema; satellite cells.

Conflict of interest statement

No conflicts of interest, financial or otherwise, are declared by the author.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

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Cite

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Eur J Radiol

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. 2022 Oct;155:110460.

doi: 10.1016/j.ejrad.2022.110460. Epub 2022 Aug 3.

Automated quantification of airway wall thickness on chest CT using retina U-Nets – Performance evaluation and application to a large cohort of chest CTs of COPD patients

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Affiliations expand

- PMID: 35963191

- DOI: [10.1016/j.ejrad.2022.110460](https://doi.org/10.1016/j.ejrad.2022.110460)

Abstract

Purpose: Airway wall thickening is a consequence of chronic inflammatory processes and usually only qualitatively described in CT radiology reports. The purpose of this study is to automatically quantify airway wall thickness in multiple airway generations and assess the diagnostic potential of this parameter in a large cohort of patients with Chronic Obstructive Pulmonary Disease (COPD).

Materials and methods: This retrospective, single-center study included a series of unenhanced chest CTs. Inclusion criteria were the mentioning of an explicit COPD GOLD stage in the written radiology report and time period (01/2019-12/2021). A control group included chest CTs with completely unremarkable lungs according to the report. The DICOM images of all cases (axial orientation; slice-thickness: 1 mm; soft-tissue kernel) were processed by an AI algorithm pipeline consisting of (A) a 3D-U-Net for det detection and tracing of the bronchial tree centerlines (B) extraction of image patches perpendicular to the centerlines of the bronchi, and (C) a 2D U-Net for segmentation of airway walls on those patches. The performance of centerline detection and wall segmentation was assessed. The imaging parameter average wall thickness was calculated for bronchus generations 3-8 (AWT₃₋₈) across the lungs. Mean AWT₃₋₈ was compared between five groups (control, COPD Gold I-IV) using non-parametric statistics. Furthermore, the established emphysema score %LAV-950 was calculated and used to classify scans (normal vs. COPD) alone and in combination with AWT₃₋₈. **RESULTS:** A total of 575 chest CTs were processed. Algorithm performance was very good (airway centerline detection sensitivity: 86.9%; airway wall segmentation Dice score: 0.86). AWT₃₋₈ was statistically significantly greater in COPD patients compared to controls (2.03 vs. 1.87 mm, $p < 0.001$) and increased with COPD stage. The classifier that combined %LAV-950 and AWT₃₋₈ was superior to the classifier using only %LAV-950 (AUC = 0.92 vs. 0.79).

Conclusion: Airway wall thickness increases in patients suffering from COPD and is automatically quantifiable. AWT₃₋₈ could become a CT imaging parameter in COPD complementing the established emphysema biomarker %LAV-950.

Clinical relevance statement: Quantitative measurements considering the complete visible bronchial tree instead of qualitative description could enhance radiology reports, allow for precise monitoring of disease progression and diagnosis of early stages of disease.

Keywords: Airway wall thickness; COPD; Computed tomography; Deep learning; Imaging biomarker; U-Net.

Conflict of interest statement

Declaration of Competing Interest The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Three co-authors are employees of Siemens Healthineers: Jonathan I. Sperl, Dominik Neumann, and Abishek Balachandran. They had no influence on the methodology of this study and on the published results. All other authors have no conflict of interest. This study did not receive funding.

SUPPLEMENTARY INFO

MeSH terms, Substances [expand](#)

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☐ 20

J Psychosom Res

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. 2022 Oct;161:111000.

doi: 10.1016/j.jpsychores.2022.111000. Epub 2022 Aug 4.

[Relationship between chronic obstructive pulmonary disease and cognition in an aging population](#)

[Stephanie Shea](#)¹, [Jayme M Palka](#)², [Alexandra Kulikova](#)³, [Carol S North](#)⁴, [E Sherwood Brown](#)⁵

Affiliations [expand](#)

- PMID: 35963125

- DOI: [10.1016/j.jpsychores.2022.111000](https://doi.org/10.1016/j.jpsychores.2022.111000)

Abstract

Objectives: Chronic obstructive pulmonary disease (COPD) is a common and severe respiratory illness. Prior research suggests that COPD may be associated with depression as well as cognitive impairment and increased risk of dementia. Many studies to date have been relatively small, have largely relied on global screening measures to identify cognitive impairment, and have not examined the potential role of comorbid depression on cognition. This cross-sectional study examined the relationship between COPD and multiple cognitive domains at two time points using data from a large longitudinal population database.

Methods: Linear multivariate analyses were conducted using secondary data from the Wisconsin Longitudinal Study to determine the effect of lifetime COPD and depressive symptom severity, assessed with the Center for Epidemiological Studies Depression Scale (CESD), on multiple cognitive outcomes.

Results: In both 2004 (n = 1608) and 2011 (n = 1743), lifetime COPD was found to be a non-significant predictor of all cognitive outcomes, while depressive symptom severity predicted significantly lower scores on the immediate recall and digit ordering tasks in 2004 and on all outcomes in 2011. Exploratory analyses in only those with lifetime COPD revealed COPD severity to be a non-significant factor for all outcomes in 2004 and 2011.

Conclusion: COPD was not significantly associated with cognition. Conversely, higher depressive symptom severity was significantly associated with poorer performance on additional cognitive tasks in 2011 compared to 2004, suggesting that depression may contribute to cognitive decline, dependent upon the context of aging.

Keywords: COPD; Cognition; Depression; Elderly.

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Conflict of interest statement

Declaration of Competing Interest The authors have no competing interests to report.

SUPPLEMENTARY INFO

MeSH termsexpand

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Comment

Cytokine

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. 2022 Oct;158:155995.

doi: 10.1016/j.cyto.2022.155995. Epub 2022 Aug 8.

COPD and the IL-33/ST2 axis targeted therapy: A role for vitamin D?

[Maria Maddalena Sirufo](#)¹, [Lina Maria Magnanini](#)², [Lia Ginaldi](#)¹, [Massimo De Martinis](#)³

Affiliations expand

- PMID: 35952594
- DOI: [10.1016/j.cyto.2022.155995](https://doi.org/10.1016/j.cyto.2022.155995)

No abstract available

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.

Comment on

- [Interleukin-33 \(IL-33\): A critical review of its biology and the mechanisms involved in its release as a potent extracellular cytokine.](#)
Cayrol C, Girard JP. *Cytokine*. 2022 Aug;156:155891. doi: 10.1016/j.cyto.2022.155891. Epub 2022 May 25. PMID: 35640416 Review.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances expand

FULL TEXT LINKS



[Proceed to details](#)

Cite

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☐ 22

Clinical Trial

Adv Ther

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. 2022 Oct;39(10):4692-4706.

doi: 10.1007/s12325-022-02268-1. Epub 2022 Aug 10.

[Effectiveness of Tiotropium/Olodaterol in the Real World: A Post Hoc Subgroup Analysis After the First Year of Use](#)

[Atsuyasu Sato](#)¹, [Ai Miyazaki](#)², [Shuhei Nakamura](#)²

Affiliations expand

- PMID: 35948844

- PMCID: [PMC9464735](#)
- DOI: [10.1007/s12325-022-02268-1](#)

Free PMC article

Abstract

Introduction: Real-world evidence is needed to optimize pharmacotherapy for chronic obstructive pulmonary disease (COPD). The effectiveness of inhaled tiotropium/olodaterol according to baseline symptoms and previous COPD treatment and predictors of response were assessed.

Methods: This was a post hoc analysis of a 52-week post-marketing surveillance study of tiotropium/olodaterol in 1255 Japanese patients with COPD of all severities. We analyzed change in total COPD Assessment Test (CAT) score and lung function (forced expiratory volume in 1 s [FEV₁] and forced vital capacity [FVC]). Patient subgroups were analyzed based on baseline CAT score (< 10 [n = 184], ≥ 10 [n = 507]) and previous COPD treatment (treatment-naïve [n = 407], previously treated [n = 848], treatment with long-acting muscarinic antagonist monotherapy [n = 161]).

Results: In the CAT ≥ 10 subgroup, tiotropium/olodaterol showed statistically significant improvements in mean total CAT score (- 6.2; 95% confidence interval [CI] - 7.2, - 5.1), FEV₁ (0.109 L; 95% CI 0.059, 0.159) and FVC (0.171 L; 95% CI 0.096, 0.245), which continued through Week 52. CAT score and lung function improvement were greatest in treatment-naïve patients: - 7.6 (95% CI - 9.2, - 6.1) mean total CAT score, 0.177 L (95% CI 0.076, 0.279) mean FEV₁ and 0.178 L (95% CI 0.036, 0.319) mean FVC. Baseline factors associated with treatment response (total CAT score improvement ≥ 2 points) were: shorter COPD duration (odds ratio [OR] 0.91; 95% CI 0.87, 0.96), total CAT score ≥ 10 (OR 3.86; 95% CI 2.46, 6.06) and treatment-naïve status (OR 1.86; 95% CI 1.12, 3.07). Baseline total CAT scores ≥ 13 predicted responses to tiotropium/olodaterol in all previous COPD treatment subgroups including treatment-naïve patients.

Conclusions: Tiotropium/olodaterol improved symptoms and lung function in Japanese COPD patients. Our results support the possible use of tiotropium/olodaterol in treatment-naïve patients and those with total CAT scores ≥ 10.

Trail registration: Clinicaltrials.gov Identifier for parent study: [NCT02850978](#).

Keywords: COPD; COPD Assessment Test; LAMA/LABA; Real world; Tiotropium/olodaterol; Treatment-naïve.

- [15 references](#)
- [4 figures](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated dataexpand

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☐ 23

Review

Cytokine

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. 2022 Oct;158:155982.

doi: 10.1016/j.cyto.2022.155982. Epub 2022 Aug 3.

Association between chronic obstructive pulmonary disease and periodontitis: The common role of innate immune cells?

[Yuanting Ouyang](#)¹, [Jiaohong Liu](#)¹, [Siyi Wen](#)¹, [Yixin Xu](#)², [Zhiyi Zhang](#)¹, [Yixing Pi](#)¹, [Ding Chen](#)¹, [Zhikang Su](#)¹, [Zitian Liang](#)¹, [Yan Wang](#)³, [Lvhuo Guo](#)⁴

Affiliations expand

- PMID: 35932499

- DOI: [10.1016/j.cyto.2022.155982](https://doi.org/10.1016/j.cyto.2022.155982)

Abstract

Innate immune cells are of broad interest in a variety of diseases. These cells include neutrophils, macrophages, dendritic cells and mast cells, etc. Innate immune cells are often mentioned in inflammatory diseases as the first line of defense against pathogens' invasion. As chronic obstructive pulmonary disease and periodontitis are inflammatory diseases, innate immune cells play an important role in the development of both diseases. COPD and periodontitis are common epidemic diseases with a very high prevalence, thus affecting a large number of people and also reducing the quality of life of patients. In addition, epidemiological studies suggested a link between the two, creating a co-morbid burden, but the mechanism of the link is yet to be explained. This article discusses the possible mechanism of the link between the two diseases in terms of innate immune cells and discusses possible future targeted therapies that could alleviate the burden on patients.

Keywords: Chronic obstructive pulmonary disease; Dendritic cells; Macrophages; Neutrophils; Periodontitis.

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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.

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Publication types, MeSH termsexpand

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Predicting 6-minute walking test outcomes in patients with chronic obstructive pulmonary disease without physical performance measures

[Daniel Romero](#)¹, [Dolores Blanco-Almazán](#)², [Willemijn Groenendaal](#)³, [Lien Lijnen](#)⁴, [Christophe Smeets](#)⁵, [David Ruttens](#)⁵, [Francky Catthoor](#)⁶, [Raimon Jané](#)²

Affiliations expand

- PMID: 35905697
- DOI: [10.1016/j.cmpb.2022.107020](https://doi.org/10.1016/j.cmpb.2022.107020)

Free article

Abstract

Background and objective: Chronic obstructive pulmonary disease (COPD) requires a multifactorial assessment, evaluating the airflow limitation and symptoms of the patients. The 6-min walk test (6MWT) is commonly used to evaluate the functional exercise capacity in these patients. This study aims to propose a novel predictive model of the major 6MWT outcomes for COPD assessment, without physical performance measurements.

Methods: Cardiopulmonary and clinical parameters were obtained from fifty COPD patients. These parameters were used as inputs of a Bayesian network (BN), which integrated three multivariate models including the 6-min walking distance (6MWD), the maximum HR (HR_{max}) after the walking, and the HR decay 3 min after (HRR_3). The use of BN allows the assessment of the patients' status by predicting the 6MWT outcomes, but also inferring disease severity parameters based on actual patient's 6MWT outcomes.

Results: Firstly, the correlation obtained between the estimated and actual 6MWT measures was strong ($R = 0.84$, $MAPE = 8.10\%$ for HR_{max}) and moderate ($R = 0.58$, $MAPE =$

15.43% for 6MWD and $R = 0.58$, $MAPE = 32.49\%$ for HRR_3), improving the classical methods to estimate 6MWD. Secondly, the classification of disease severity showed an accuracy of 78.3% using three severity groups, which increased up to 84.4% for two defined severity groups.

Conclusions: We propose a powerful two-way assessment tool for COPD patients, capable of predicting 6MWT outcomes without the need for an actual walking exercise. This model-based tool opens the way to implement a continuous monitoring system for COPD patients at home and to provide more personalized care.

Keywords: 6MWT; Bayesian networks; COPD; Physical capacity; Wearables.

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Conflict of interest statement

Declaration of Competing Interest None.

SUPPLEMENTARY INFO

MeSH termsexpand

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[Review](#)

Int J Cardiol Heart Vasc

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. 2022 Jul 19;42:101086.

doi: 10.1016/j.ijcha.2022.101086. eCollection 2022 Oct.

Dyspnea in patients with atrial fibrillation: Mechanisms, assessment and an interdisciplinary and integrated care approach

[Rachel M J van der Velden](#)¹, [Astrid N L Hermans](#)¹, [Nikki A H A Pluymaekers](#)¹, [Monika Gawalko](#)^{1,2,3}, [Adrian Elliott](#)⁴, [Jeroen M Hendriks](#)^{4,5}, [Frits M E Franssen](#)^{6,7,8}, [Annelies M Slats](#)⁹, [Vanessa P M van Empel](#)¹, [Isabelle C Van Gelder](#)¹⁰, [Dick H J Thijssen](#)¹¹, [Thijs M H Eijsvogels](#)¹¹, [Carsten Leue](#)^{12,13}, [Harry J G M Crijns](#)¹, [Dominik Linz](#)^{1,4,14,15}, [Sami O Simons](#)^{7,8}

Affiliations expand

- PMID: 35873859
- PMCID: [PMC9304702](#)
- DOI: [10.1016/j.ijcha.2022.101086](#)

Free PMC article

Abstract

Atrial fibrillation (AF) is the most common sustained heart rhythm disorder and is often associated with symptoms that can significantly impact quality of life and daily functioning. Palpitations are the cardinal symptom of AF and many AF therapies are targeted towards relieving this symptom. However, up to two-third of patients also complain of dyspnea as a predominant self-reported symptom. In clinical practice it is often challenging to ascertain whether dyspnea represents an AF-related symptom or a symptom of concomitant cardiovascular and non-cardiovascular comorbidities, since common AF comorbidities such as heart failure and chronic obstructive pulmonary disease share similar symptoms. In addition, therapeutic approaches specifically targeting dyspnea have not been well validated. Thus, assessing and treating dyspnea can be difficult. This review describes the latest knowledge on the burden and pathophysiology of dyspnea in AF patients. We discuss the role of heart rhythm control interventions as well as the management of AF risk factors and comorbidities with the goal to achieve maximal relief of dyspnea. Given the different and often complex mechanistic pathways leading to dyspnea, dyspneic AF patients will likely profit from an integrated multidisciplinary approach to tackle all factors and mechanisms involved. Therefore, we propose an interdisciplinary and integrated care pathway for the work-up of dyspnea in AF patients.

Keywords: Atrial fibrillation; Comorbidities; Dyspnea; Exercise intolerance; Mechanisms; Symptom assessment.

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Conflict of interest statement

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.

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Intern Emerg Med

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. 2022 Oct;17(7):2119-2127.

doi: 10.1007/s11739-022-03048-z. Epub 2022 Jul 20.

[The predictive value of modified risk scores in patients with acute exacerbation of COPD: a retrospective cohort study](#)

Affiliations expand

- PMID: 35854207
- PMCID: [PMC9296366](#)
- DOI: [10.1007/s11739-022-03048-z](#)

Free PMC article

Abstract

This study aims to evaluate the performance of CREWS (Chronic Respiratory Early Warning Score), S-NEWS (Salford-National Early Warning Score), qNEWS (Quick National Early Warning Score), NEWS (National Early Warning Score), and qSOFA (Quick Sequential Organ Failure Assessment) scores in predicting mortality, intensive care unit (ICU) admission and the need for mechanical ventilation (MV) of patients presented with acute exacerbations of chronic obstructive pulmonary disease (AECOPD). This retrospective cohort study was conducted in the emergency department of a tertiary hospital between January 1 and December 31, 2019. The patients with AECOPD and aged ≥ 18 were included. Patients who were transferred from another center and whose data could not be reached were excluded. Demographic information, comorbid diseases, variables of the scores, laboratory results, and outcomes were recorded. A total of 575 consecutive patients were included. The 30-day mortality, ICU admission, and MV need rate were 5.7% (n = 33), 9.6% (n = 55), and 13.7% (n = 79), respectively. Each score had moderate-to-excellent performance in predicting MV need and ICU admission, while their performance in predicting mortality was poor. CREWS is the most successful score in predicting 30-day mortality (AUC 0.695), ICU admission (AUC 0.841), and MV need (AUC 0.924). ICU admission, age, and creatinine levels were associated with mortality ($p < 0.05$). All scores have better performance in predicting ICU admission and MV need than mortality. ICU admission, age, and creatinine levels may be the predictors of mortality among AECOPD patients.

Keywords: Acute exacerbation; Chronic obstructive pulmonary disease; Chronic respiratory disease; Early warning score; Emergency.

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Conflict of interest statement

The authors declare that they did not have any potential conflicts of interest with regard to this research, or the authorship and publication of this article.

- [29 references](#)
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Ann Allergy Asthma Immunol

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. 2022 Oct;129(4):490-496.

doi: 10.1016/j.anai.2022.06.028. Epub 2022 Jul 11.

[Plasma immunoglobulin E and risk of exacerbation and mortality in chronic obstructive pulmonary disease: A contemporary population-based cohort](#)

[Yunus Çolak](#)¹, [Truls S Ingebrigtsen](#)², [Børge G Nordestgaard](#)³, [Jacob L Marott](#)⁴, [Peter Lange](#)⁵, [Jørgen Vestbo](#)⁶, [Shoaib Afzal](#)⁷

Affiliations expand

- PMID: 35835293

- DOI: [10.1016/j.anai.2022.06.028](https://doi.org/10.1016/j.anai.2022.06.028)

Free article

Abstract

Background: Novel biomarkers and targeted treatments are needed for patients with chronic obstructive pulmonary disease (COPD).

Objective: To test the hypothesis that high plasma immunoglobulin (Ig)E concentrations associate with increased risk of exacerbation and mortality in individuals with COPD in the general population.

Methods: Among 46,598 adults in the Copenhagen General Population Study, we included 1559 with COPD, defined as forced expiratory volume in 1 second/forced vital capacity < 0.70 and forced expiratory volume in 1 second < 80% predicted in individuals aged ≥ 40 years with chronic respiratory symptoms and smoking exposure ≥ 10 pack-years, and without asthma. We assessed risk of future severe exacerbation and all-cause mortality according to baseline plasma IgE ≥ 76 IU/mL, a clinical cutoff for omalizumab treatment in severe asthma.

Results: During 14 years of follow-up (median, 6.9; interquartile range, 3.4), we recorded 224 severe exacerbations and 434 deaths in 1559 individuals with COPD. Individuals with COPD with IgE ≥ 76 IU/mL vs those with < 76 IU/mL had a multivariable adjusted hazard ratio (HR) of 1.43 (95% confidence interval, 1.07-1.89) for severe exacerbation and 1.30 (1.05-1.62) for all-cause mortality. Compared with individuals with IgE < 76 IU/mL and blood eosinophils < 300 cells/ μ L, the multivariable adjusted HR for severe exacerbation was 1.12 (0.76-1.67) for those with IgE < 76 IU/mL and blood eosinophils ≥ 300 cells/ μ L, 1.62 (1.17-2.24) for IgE ≥ 76 IU/mL and blood eosinophils < 300 cells/ μ L, and 1.06 (0.63-1.77) for those with IgE ≥ 76 IU/mL and blood eosinophils ≥ 300 cells/ μ L. Corresponding HRs for all-cause mortality were 1.27 (0.99-1.63), 1.47 (1.14-1.88), and 1.17 (0.83-1.64), respectively.

Conclusion: High plasma IgE was associated with an increased risk of severe exacerbation and all-cause mortality in individuals with COPD in the general population, independent of blood eosinophils.

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Review

Tuberc Respir Dis (Seoul)

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. 2022 Oct;85(4):289-301.

doi: 10.4046/trd.2022.0074. Epub 2022 Jul 13.

Long-Term Outcome of Chronic Obstructive Pulmonary Disease: A Review

[Yong Suk Jo](#)¹

Affiliations expand

- PMID: 35822318
- DOI: [10.4046/trd.2022.0074](https://doi.org/10.4046/trd.2022.0074)

Free article

Abstract

Chronic obstructive pulmonary disease (COPD) is a chronic airway inflammation characterized by fixed airflow limitation and chronic respiratory symptoms, such as cough, sputum, and dyspnea. COPD is a progressive disease characterized by a decline in lung function. During the natural course of the disease, acute deterioration of symptoms

leading to hospital visits can occur and influence further disease progression and subsequent exacerbation. Moreover, COPD is not only restricted to pulmonary manifestations but can present with other systemic diseases as comorbidities or systemic manifestations, including lung cancer, cardiovascular disease, pulmonary hypertension, sarcopenia, and metabolic abnormalities. These pulmonary and extrapulmonary conditions lead to the aggravation of dyspnea, physical inactivity, decreased exercise capacity, functional decline, reduced quality of life, and increased mortality. In addition, pneumonia, which is attributed to both COPD itself and an adverse effect of treatment (especially the use of inhaled and/or systemic steroids), can occur and lead to further deterioration in the prognosis of COPD. This review summarizes the long-term outcomes of patients with COPD. In addition, recent studies on the prediction of adverse outcomes are summarized in the last part of the review.

Keywords: Chronic Obstructive Pulmonary Disease; Exacerbation; Lung Function; Mortality; Outcome.

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Tuberc Respir Dis (Seoul)

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. 2022 Oct;85(4):302-312.

doi: 10.4046/trd.2022.0029. Epub 2022 Jul 13.

Phenotype of Chronic Obstructive Pulmonary Disease Based on Computed Tomography-Defined Underlying Pathology

[Won-Dong Kim](#)¹

Affiliations [expand](#)

- PMID: 35822317
- DOI: [10.4046/trd.2022.0029](https://doi.org/10.4046/trd.2022.0029)

Free article

Abstract

Chronic obstructive pulmonary disease (COPD) is a complex and heterogeneous disease. Not all patients with COPD respond to available drugs. Identifying respondents to therapy is critical to delivering the most appropriate treatment and avoiding unnecessary medication. Recognition of individual patients' dominant characteristics by phenotype is a useful tool to better understand their disease and tailor treatment accordingly. To look for a suitable phenotype, it is important to understand what makes COPD complex and heterogeneous. The pathology of COPD includes small airway disease and/or emphysema. Thus, COPD is not a single disease entity. In addition, there are two types (panlobular and centrilobular) of emphysema in COPD. The coexistence of different pathological subtypes could be the reason for the complexity and heterogeneity of COPD. Thus, it is necessary to look for the phenotype based on the difference in the underlying pathology. Review of the literature has shown that clinical manifestation and therapeutic response to pharmacological therapy are different depending on the presence of computed tomography-defined airway wall thickening in COPD patients. Defining the phenotype of COPD based on the underlying pathology is encouraging as most clinical manifestations can be distinguished by the presence of increased airway wall thickness. Pharmacological therapy has shown significant effect on COPD with airway wall thickening. However, it has limited use in COPD without an airway disease. The phenotype of COPD based on the underlying pathology can be a useful tool to better understand the disease and adjust treatment accordingly.

Keywords: Centrilobular Emphysema; Chronic Obstructive Pulmonary Disease; Emphysema; Panlobular Emphysema; Phenotype; Small Airway Disease.

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Editorial

Am J Med

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. 2022 Oct;135(10):1147-1149.

doi: 10.1016/j.amjmed.2022.06.001. Epub 2022 Jul 9.

COPD Readmission: The Missing Link

[Smita Pakhale](#)¹, [Nina Huynh](#)², [Saania Tariq](#)²

Affiliations expand

- PMID: 35820455
- DOI: [10.1016/j.amjmed.2022.06.001](https://doi.org/10.1016/j.amjmed.2022.06.001)

No abstract available

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Atherosclerosis

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. 2022 Oct;358:60-67.

doi: 10.1016/j.atherosclerosis.2022.06.1010. Epub 2022 Jun 14.

[The frailty risk trajectory associated with kidney and cardiovascular morbidities among patients with incident diabetes: A population-based study](#)

[Jui Wang](#)¹, [Szu-Ying Lee](#)², [Chia-Ter Chao](#)³, [Jenq-Wen Huang](#)⁴, [Kuo-Liong Chien](#)¹

Affiliations expand

- PMID: 35798572
- DOI: [10.1016/j.atherosclerosis.2022.06.1010](https://doi.org/10.1016/j.atherosclerosis.2022.06.1010)

Abstract

Background and aims: Frailty denotes the increased vulnerability to stressors/insults associated with aging or diseases, and has high incidence in patients with diabetes mellitus

(DM). We hypothesized that chronic kidney disease (CKD) and non-kidney morbidities in patients with newly diagnosed DM might modulate their risk of developing incident frailty.

Methods: From the Longitudinal Cohort of Diabetes Patients, we identified 322,109 patients with newly diagnosed DM, and classified them into those without CKD, with CKD before and after DM. We used Kaplan-Meier analyses and Cox proportional hazard regression to analyze associations between CKD or non-kidney morbidities and the risk of incident frailty. We further analyzed the year-to-year trend of frailty risk brought by CKD or non-kidney morbidities.

Results: Patients with DM but without CKD ($n = 249,752$; 77.5%), with CKD prior to ($n = 23,829$; 7.4%), and after DM ($n = 48,528$; 15.1%) were enrolled. Those with CKD, regardless of onset timing, had a significantly higher risk of developing frailty than those without (for onset prior to DM, hazard ratio (HR) 1.235, 95% confidence interval (CI) 1.11-1.38; for onset after DM, HR 1.386, 95% CI 1.21-1.59). The risk was more prominent early after the diagnosis of DM was made. Patients with chronic obstructive pulmonary disease, liver, and cardiovascular morbidities all had a significantly higher risk of frailty than those without, with cerebrovascular accident carrying the most prominent risk elevation (HR 4.059, 95% CI 3.73-4.42).

Conclusions: CKD regardless of onset timing relative to DM predicted a higher risk of incident frailty, while non-kidney morbidities including cardiovascular morbidities, similarly increased frailty risk among incident diabetic patients.

Keywords: Chronic kidney disease; Diabetes mellitus; Diabetic kidney disease; Frail phenotype; Frailty; Heart failure.

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. 2022 Oct;304:103941.

doi: 10.1016/j.resp.2022.103941. Epub 2022 Jun 28.

Exertional Dyspnoea responses reported in the Dyspnoea Challenge and measures of disease severity in COPD

[Craig R Aitken](#)¹, [James R Walsh](#)², [Glenn M Stewart](#)³, [Surendran Sabapathy](#)⁴, [Lewis Adams](#)⁵, [Norman R Morris](#)³

Affiliations expand

- PMID: 35777721
- DOI: [10.1016/j.resp.2022.103941](https://doi.org/10.1016/j.resp.2022.103941)

Abstract

Background: The Dyspnoea Challenge has been developed to facilitate the field-based measure of exertional dyspnoea(ED). To further validate the test, we aimed to; investigate the relationship between end-exercise ED, generated by a fixed-intensity Dyspnoea Challenge(DC_{FIX}), and measures of disease severity (Forced expiratory volume in 1 s(FEV₁), six-minute walk distance(6MWD), breathing reserve(\dot{V}_E /MVV), modified medical research council dyspnoea scale (mMRC), Body-mass index, airflow Obstruction, Dyspnoea, and Exercise (BODE index) and compare the physiological response of the DC_{FIX} to a six-minute walk test(6MWT).

Methods: Thirty-two individuals (15 female) with COPD (GOLD II-IV) (age: 69.7 ± 9.4 yrs; FEV₁: 49.1 ± 18.2 %) performed 2×6MWT and 2xDC_{FIX} at a treadmill speed of 3 km h⁻¹ and gradient of 4 %. The intensity of ED was measured using the modified Borg dyspnoea scale at baseline and end-exercise with heart rate (HR) and oxygen saturation (S_pO₂) monitored continuously. During 1×6MWT and 1xDC_{FIX} pulmonary gas exchange, cardiac output (\dot{Q}) and dynamic hyperinflation were measured.

Results: End-exercise ED measured during the DC_{FIX} was not correlated to FEV₁, but moderately correlated to; 6MWD(r_s = -0.54, P < .01), \dot{V}_E /MVV (r_s = 0.46, P = .02), mMRC(r_s =

0.45, $P = .01$), and the BODE index ($r_s = 0.53$, $P < .01$). When comparing the DC_{FIX} and 6MWT, participants walked to comparable levels of oxygen consumption ($P = .38$), ventilation ($P = .37$), \dot{Q} ($P = .20$), \dot{V}_E/MVV ($P = .83$), maximum HR percentages ($P = .67$) and dynamically hyperinflated to a similar degree ($P = .37$).

Conclusions: The Dyspnoea Challenge is correlated to different parameters of disease severity and produces a similar physiological and ED response to that of the 6MWT with the added benefit of being appropriate for longitudinal assessment of ED.

Keywords: COPD; Disease severity; Exercise; Exertional dyspnoea; Test; Treadmill.

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Respirology

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. 2022 Oct;27(10):844-853.

doi: 10.1111/resp.14309. Epub 2022 Jun 15.

[Effectiveness of influenza and pneumococcal vaccines on chronic obstructive pulmonary disease exacerbations](#)

[Yan Li](#)¹, [Pingshu Zhang](#)², [Zhijie An](#)¹, [Chenyan Yue](#)¹, [Yamin Wang](#)¹, [Yunqiu Liu](#)³, [Xiaodong Yuan](#)², [Ying Ma](#)², [Keli Li](#)¹, [Zundong Yin](#)¹, [Liye Wang](#)³, [Huaqing Wang](#)¹

Affiliations expand

- PMID: 35705329
- DOI: [10.1111/resp.14309](https://doi.org/10.1111/resp.14309)

Abstract

Background and objective: Single-study evidence of separate and combined effectiveness of influenza and pneumococcal vaccination in patients with chronic obstructive pulmonary disease (COPD) is limited. To fill this gap, we studied the effectiveness of trivalent seasonal influenza vaccine (TIV) and 23-valent pneumococcal polysaccharide vaccine (PPSV23), separately and together, at preventing adverse COPD outcomes.

Methods: Our study used a self-controlled, before-and-after cohort design to assess the effectiveness of TIV and PPSV23 in COPD patients. Patients were recruited from hospitals in Tangshan City, Hebei Province, China. Subjects self-selected into one of the three vaccination schedules: TIV group, PPSV23 group and TIV&PPSV23 group. We used a physician-completed, medical record-verified questionnaire to obtain data on acute exacerbations of COPD (AECOPD), pneumonia and related hospitalization. Vaccine effectiveness was determined by comparing COPD outcomes before and after vaccination, controlling for potential confounding using Cox regression.

Results: We recruited 474 COPD patients, of whom 109 received TIV, 69 received PPSV23 and 296 received TIV and PPSV23. Overall effectiveness for preventing AECOPD, pneumonia and related hospitalization were respectively 70%, 59% and 58% in the TIV group; 54%, 53% and 46% in the PPSV23 group; and 72%, 73% and 69% in the TIV&PPSV23 group. The vaccine effectiveness without COVID-19 non-pharmaceutical intervention period were 84%, 77% and 88% in the TIV group; 63%, 74% and 66% in the PPSV23 group; and 82%, 83% and 91% in the TIV&PPSV23 group.

Conclusion: Influenza vaccination and PPSV23 vaccination, separately and together, can effectively reduce the risk of AECOPD, pneumonia and related hospitalization. Effectiveness for preventing AECOPD was the greatest.

Keywords: 23-valent pneumococcal polysaccharide vaccine; acute exacerbations of chronic obstructive pulmonary disease; hospitalization; immunization; pneumonia; trivalent seasonal influenza vaccine; vaccine effectiveness.

Comment in

- [Vaccination in patients with COPD: COVID has raised the bar.](#)
Waterer G. *Respirology*. 2022 Oct;27(10):799-800. doi: 10.1111/resp.14331. Epub 2022 Jul 18. PMID: 35852029 **Free PMC article.**
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Radiology

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. 2022 Oct;305(1):199-208.

doi: 10.1148/radiol.212071. Epub 2022 Jun 7.

[Deep Learning Prediction of Survival in Patients with Chronic Obstructive Pulmonary Disease Using Chest Radiographs](#)

[Ju Gang Nam](#) ^{#1}, [Hye-Rin Kang](#) ^{#1}, [Sang Min Lee](#) ¹, [Hyungjin Kim](#) ¹, [Chanyoung Rhee](#) ¹, [Jin Mo Goo](#) ¹, [Yeon-Mok Oh](#) ¹, [Chang-Hoon Lee](#) ^{#1}, [Chang Min Park](#) ^{#1}

Affiliations [expand](#)

- PMID: 35670713
- DOI: [10.1148/radiol.212071](https://doi.org/10.1148/radiol.212071)

Abstract

Background Preexisting indexes for predicting the prognosis of chronic obstructive pulmonary disease (COPD) do not use radiologic information and are impractical because they involve complex history assessments or exercise tests. **Purpose** To develop and to validate a deep learning-based survival prediction model in patients with COPD (DLSP) using chest radiographs, in addition to other clinical factors. **Materials and Methods** In this retrospective study, data from patients with COPD who underwent postbronchodilator spirometry and chest radiography from 2011-2015 were collected and split into training ($n = 3475$), validation ($n = 435$), and internal test ($n = 315$) data sets. The algorithm for predicting survival from chest radiographs was trained (hereafter, DLSP_{CXR}), and then age, body mass index, and forced expiratory volume in 1 second (FEV₁) were integrated within the model (hereafter, DLSP_{integ}). For external test, three independent cohorts were collected ($n = 394, 416$, and 337). The discrimination performance of DLSP_{CXR} was evaluated by using time-dependent area under the receiver operating characteristic curves (TD AUCs) at 5-year survival. Goodness of fit was assessed by using the Hosmer-Lemeshow test. Using one external test data set, DLSP_{integ} was compared with four COPD-specific clinical indexes: BODE, ADO, COPD Assessment Test (CAT), and St George's Respiratory Questionnaire (SGRQ). **Results** DLSP_{CXR} had a higher performance at predicting 5-year survival than FEV₁ in two of the three external test cohorts (TD AUC: 0.73 vs 0.63 [$P = .004$]; 0.67 vs 0.60 [$P = .01$]; 0.76 vs 0.77 [$P = .91$]). DLSP_{CXR} demonstrated good calibration in all cohorts. The DLSP_{integ} model showed no differences in TD AUC compared with BODE (0.87 vs 0.80; $P = .34$), ADO (0.86 vs 0.89; $P = .51$), and SGRQ (0.86 vs 0.70; $P = .09$), and showed higher TD AUC than CAT (0.93 vs 0.55; $P < .001$). **Conclusion** A deep learning model using chest radiographs was capable of predicting survival in patients with chronic obstructive pulmonary disease. © RSNA, 2022 *Online supplemental material is available for this article.*

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Allergy

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. 2022 Oct;77(10):3137-3141.

doi: 10.1111/all.15401. Epub 2022 Jun 16.

Soluble ST2 enhances IL-33-induced neutrophilic and pro-type 2 inflammation in the lungs

[Masato Watanabe](#)¹, [Keitaro Nakamoto](#)¹, [Toshiya Inui](#)¹, [Mitsuru Sada](#)¹, [Kazuyuki Chibana](#)², [Chika Miyaoka](#)¹, [Yuki Yoshida](#)¹, [Jumpei Aso](#)¹, [Hiroki Nunokawa](#)¹, [Kojiro Honda](#)¹, [Masuo Nakamura](#)¹, [Masaki Tamura](#)¹, [Aya Hirata](#)¹, [Miku Oda](#)¹, [Saori Takata](#)¹, [Takeshi Saraya](#)¹, [Daisuke Kurai](#)³, [Haruyuki Ishii](#)¹, [Hajime Takizawa](#)¹

Affiliations expand

- PMID: 35661175
- DOI: [10.1111/all.15401](https://doi.org/10.1111/all.15401)

No abstract available

Keywords: COPD; asthma; asthma-COPD overlap; neutrophil; sputum.

- [6 references](#)

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Environ Res

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. 2022 Oct;213:113600.

doi: 10.1016/j.envres.2022.113600. Epub 2022 Jun 3.

Reductions in NO₂ and emergency room visits associated with California's goods movement policies: A quasi-experimental study

[Ying-Ying Meng](#)¹, [Dahai Yue](#)², [John Molitor](#)³, [Xiao Chen](#)⁴, [Jason G Su](#)⁵, [Michael Jerrett](#)⁶

Affiliations expand

- PMID: 35660569
- DOI: [10.1016/j.envres.2022.113600](https://doi.org/10.1016/j.envres.2022.113600)

Abstract

Introduction: This study examines whether the "Emission Reduction Plan for Ports and Goods Movement" in California reduced air pollution exposures and emergency room visits among California Medicaid enrollees with asthma and/or chronic obstructive pulmonary disease.

Method: We created a retrospective cohort of 5608 Medicaid enrollees from ten counties in California with data from 2004 to 2010. We grouped the patients into two groups: those living within 500 m of goods movement corridors (ports and truck-permitted freeways), and control areas (away from the busy truck or car permitted highways). We created annual air pollution surfaces for nitrogen dioxide and assigned them to enrollees' home

addresses. We used a quasi-experimental design with a difference-in-differences method to examine changes before and after the policy for cohort beneficiaries in the two groups.

Results: The reductions in nitrogen dioxide exposures and emergency room visits were greater for enrollees in goods movement corridors than those in control areas in post-policy years. We found that the goods movement actions were associated with 14.8% (95% CI, -24.0% to -4.4%; $P = 0.006$) and 11.8% (95% CI, -21.2% to -1.2%; $P = 0.030$) greater reduction in emergency room visits for the beneficiaries with asthma and chronic obstructive pulmonary disease, respectively, in the third year after California's emission reduction plan.

Conclusion: These findings indicate remarkable health benefits via reduced emergency room visits from the significantly improved air quality due to public policy interventions for disadvantaged and susceptible populations.

Keywords: Air pollution; Asthma; COPD; Emergency room visits.

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Ann Am Thorac Soc

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. 2022 Oct;19(10):1677-1686.

doi: 10.1513/AnnalsATS.202110-1174OC.

Adverse Effects, Smoking, Alcohol Consumption, and Quality of Life during Long-Term Oxygen Therapy: A Nationwide Study

Filip Björklund¹, Magnus Ekström^{1,2}

Affiliations expand

- PMID: 35657698
- PMCID: [PMC9528738](#)
- DOI: [10.1513/AnnalsATS.202110-1174OC](#)

Free PMC article

Abstract

Rationale: Long-term oxygen therapy (LTOT) is prescribed for at least 15 hours per day and often used by patients for several years, but knowledge is limited regarding adverse effects, risk exposures, and health-related quality of life (HrQoL) among those treated. **Objectives:** To determine the prevalence of adverse effects, smoking, and alcohol consumption and their relations to HrQoL among patients treated with LTOT. **Methods:** This was a cross-sectional survey of a randomized sample of adults with ongoing LTOT in the Swedish National Registry for Respiratory Failure (Swedevox). Patient characteristics and the prevalence of 26 prespecified adverse effects, smoking, and alcohol consumption, were compared between respondents with better and worse HrQoL on the chronic obstructive pulmonary disease assessment test. **Results:** A total of 151 respondents were included (mean age, 74.7 yr [standard deviation, 8.6 yr]; 58.9% women; median LTOT duration, 2.2 yr [interquartile range, 1.0-3.8 yr]). Characteristics upon starting LTOT were similar between respondents and nonrespondents. Active smoking was very rare ($n = 4$, 2.6%). For alcohol use, 67.2% of participants reported no consumption during an average week, whereas risk use was reported by 25.8% of men and 16.9% of women. The most prevalent adverse effects were reduced mobility or physical activity (70.9%), dry mouth (69.5%), congestion or nasal drip (61.6%), increased tiredness (57.0%), and dry nose (53.0%). Patients with higher numbers of total and systemic adverse effects experienced worse HrQoL, whereas no associations were found for smoking status or alcohol

consumption. The majority (54.8%) of adverse effects were untreated and unreported to health professionals. **Conclusions:** Adverse effects are common among patients with LTOT and are associated with worse HrQoL. As the majority of adverse effects had not been discussed or treated, structured assessment and management of risk exposures and adverse effects is warranted.

Keywords: HrQoL; LTOT; adverse effects; alcohol consumption; smoking.

- [34 references](#)
- [3 figures](#)

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Ann Am Thorac Soc

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. 2022 Oct;19(10):1661-1668.

doi: 10.1513/AnnalsATS.202112-1346OC.

[Race and Sex Differences in Mortality in Individuals with Chronic Obstructive Pulmonary Disease](#)

[Jamuna K Krishnan](#)¹, [Mangala Rajan](#)², [Samprit Banerjee](#)³, [Sonal G Mallya](#)², [MeiLan K Han](#)⁴, [David M Mannino](#)⁵, [Fernando J Martinez](#)¹, [Monika M Safford](#)²

Affiliations [expand](#)

- PMID: 35657680
- PMCID: PMC9528745 (available on 2023-10-01)
- DOI: [10.1513/AnnalsATS.202112-1346OC](https://doi.org/10.1513/AnnalsATS.202112-1346OC)

Abstract

Rationale: Despite differences in chronic obstructive pulmonary disease (COPD) comorbidities, race- and sex-based differences in all-cause mortality and cause-specific mortality are not well described. **Objectives:** To examine mortality differences in COPD by race-sex and underlying mechanisms. **Methods:** Medicare claims were used to identify COPD among REGARDS (Reasons for Geographic and Racial Differences in Stroke) cohort participants. Mortality rates were calculated using adjudicated causes of death. Hazard ratios (HRs) for mortality comparing race-sex groups were modeled with Cox proportional hazards regression. **Results:** In the 2,148-member COPD subcohort, 49% were women, and 34% were Black individuals; 1,326 deaths occurred over a median 7.5 years (interquartile range, 3.9-10.5 yr) follow-up. All-cause mortality per 1,000 person-years comparing Black versus White men was 101.1 (95% confidence interval [CI], 88.3-115.8) versus 93.9 (95% CI, 86.3-102.3; $P = 0.99$); comparing Black versus White women, all-cause mortality per 1,000 person-years was 74.2 (95% CI, 65.0-84.8) versus 70.6 (95% CI, 63.5-78.5; $P = 0.99$). Cardiovascular disease (CVD) was the leading cause-specific mortality among all race-sex groups. HR for CVD and chronic lung disease mortality were nonsignificant comparing Black versus White men. HR for CVD death was higher in Black compared with White women (HR, 1.44; 95% CI, 1.06-1.95), whereas chronic lung disease death was lower (HR, 0.44; 95% CI, 0.25-0.77). These differences were attributable to higher CVD risk factor burden among Black women. **Conclusions:** In the REGARDS COPD cohort, there were no race-sex differences in all-cause mortality. CVD was the most common cause of death for all race-sex groups with COPD. Black women with COPD had a higher risk of CVD-related mortality than White women. CVD comorbidity management, especially among Black individuals, may improve mortality outcomes.

Keywords: cardiovascular disease; chronic obstructive pulmonary disease; mortality; race.

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

FULL TEXT LINKS



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Ann Am Thorac Soc

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. 2022 Oct;19(10):1783-1787.

doi: 10.1513/AnnalsATS.202203-243RL.

Cause-Specific Death in Chronic Airway Obstruction and Restrictive Spirometric Pattern

[Helena Backman](#)¹, [Sami Sawalha](#)¹, [Ulf Nilsson](#)¹, [Linnea Hedman](#)¹, [Caroline Stridsman](#)¹, [Lowie E G W Vanfleteren](#)², [Bright I Nwaru](#)², [Nikolai Stenfors](#)¹, [Eva Rönmark](#)¹, [Anne Lindberg](#)¹

Affiliations [expand](#)

- PMID: 35657669
- DOI: [10.1513/AnnalsATS.202203-243RL](https://doi.org/10.1513/AnnalsATS.202203-243RL)

No abstract available

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Publication types, MeSH terms, Grant support[expand](#)

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Editorial

Am J Respir Crit Care Med

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. 2022 Oct 1;206(7):804-806.

doi: 10.1164/rccm.202205-0927ED.

Use of Computed Tomography Lung Densitometry as an Outcome Measure for Emphysema Progression: The Case of Losartan

[Marc Miravittles](#)¹, [Antonio Anzueto](#)²

Affiliations expand

- PMID: 35653703
- DOI: [10.1164/rccm.202205-0927ED](https://doi.org/10.1164/rccm.202205-0927ED)

No abstract available

Comment on

- [Clinical Trial of Losartan for Pulmonary Emphysema: Pulmonary Trials Cooperative Losartan Effects on Emphysema Progression Clinical Trial.](#)
Wise RA, Holbrook JT, Brown RH, Criner GJ, Dransfield MT, He J, Henderson RJ, Kaminsky DA, Kaner RJ, Lazarus SC, Make BJ, McCormack MC, Neptune ER, Que LG. *Am J Respir Crit Care Med.* 2022 Oct 1;206(7):838-845. doi: 10.1164/rccm.202201-0206OC. PMID: 35649189 Clinical Trial.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS



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Randomized Controlled Trial

Am J Respir Crit Care Med

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. 2022 Oct 1;206(7):838-845.

doi: 10.1164/rccm.202201-0206OC.

[Clinical Trial of Losartan for Pulmonary Emphysema: Pulmonary Trials Cooperative Losartan Effects on Emphysema Progression Clinical Trial](#)

[Robert A Wise](#)¹, [Janet T Holbrook](#)², [Robert H Brown](#)¹, [Gerard J Criner](#)³, [Mark T Dransfield](#)⁴, [Jiaxian He](#)², [Robert J Henderson](#)², [David A Kaminsky](#)⁵, [Robert J Kaner](#)⁶, [Stephen C Lazarus](#)⁷, [Barry J Make](#)⁸, [Meredith C McCormack](#)¹, [Enid R Neptune](#)¹, [Loretta G Que](#)⁹

Affiliations expand

- PMID: 35649189
- DOI: [10.1164/rccm.202201-0206OC](https://doi.org/10.1164/rccm.202201-0206OC)

Abstract

Rationale: There are no pharmacologic agents that modify emphysema progression in patients with chronic obstructive pulmonary disease (COPD). **Objectives:** To evaluate the efficacy of losartan, an angiotensin receptor blocker, to reduce emphysema progression. **Methods:** The trial was a multicenter, randomized, placebo-controlled trial conducted between May 2017 and January 2021. Eligible participants were aged ≥ 40 years, had moderate to severe airflow obstruction, ≥ 10 pack-years of smoking, mild-moderate emphysema on high-resolution computed tomography, and no medical indication for or intolerance of angiotensin receptor blockers. Treatment with losartan 100 mg daily or matching placebo (1:1) was randomly assigned. The primary outcome was emphysema progression on high-resolution computed tomography over 48 weeks. Secondary outcomes included the St George's Respiratory Questionnaire, the modified Medical Research Council dyspnea scale, the COPD Assessment Test, and the Physical Function-Short Form 20a. **Measurements and Main Results:** A total of 220 participants were enrolled; 58% were men, 19% were African American, and 24% were current smokers. The medians (interquartile ranges) for age were 65 (61-73) years and 48 (36-59) for percent predicted FEV₁ after bronchodilator use. The mean (95% confidence interval) percentage emphysema progression was 1.35% (0.67-2.03) in the losartan group versus 0.66% (0.09-1.23) in the placebo group ($P = \text{NS}$). **Conclusions:** Losartan did not prevent emphysema progression in people with COPD with mild-moderate emphysema. Clinical trial registered with www.clinicaltrials.gov ([NCT02696564](https://clinicaltrials.gov/ct2/show/study?term=NCT02696564)).

Keywords: angiotensin receptor blocker; clinical trial; emphysema; losartan; quantitative image analysis.

Comment in

- [Use of Computed Tomography Lung Densitometry as an Outcome Measure for Emphysema Progression: The Case of Losartan.](#)
Miravittles M, Anzueto A. *Am J Respir Crit Care Med*. 2022 Oct 1;206(7):804-806. doi: 10.1164/rccm.202205-0927ED. PMID: 35653703 No abstract available.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated data, Grant support [expand](#)

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Ann Allergy Asthma Immunol

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. 2022 Oct;129(4):461-466.

doi: 10.1016/j.anai.2022.05.024. Epub 2022 May 25.

Could transthoracic ultrasound be useful to suggest a small airways disease in severe uncontrolled asthma?

[Giulia Scioscia](#)¹, [Donato Lacedonia](#)¹, [Carla Maria Irene Quarato](#)², [Pasquale Tondo](#)¹, [Anna Del Colle](#)¹, [Marco Sperandeo](#)³, [Giovanna Elisiana Carpagnano](#)⁴, [Maria Pia Foschino Barbaro](#)¹

Affiliations expand

- PMID: 35643297
- DOI: [10.1016/j.anai.2022.05.024](https://doi.org/10.1016/j.anai.2022.05.024)

Abstract

Background: Transthoracic ultrasound (TUS) is an accepted complementary tool in the diagnostic process of several pleuro-pulmonary diseases. However, to the best of our knowledge, TUS findings in patients with severe asthma have never been systematically described.

Objective: To explore if TUS examination is a useful imaging method in suggesting the presence of a "small airways disease" in patients with severe uncontrolled asthma.

Methods: Seventy-two consecutive subjects with a diagnosis of severe uncontrolled asthma were enrolled. The presence of a "small airways disease" was assessed through the execution of pulmonary function tests. All the patients underwent a complete TUS examination and a chest high resolution computed tomography (HRCT), which was regarded as the reference standard for comparison with TUS findings.

Results: Pulmonary function tests results have confirmed a reduction in expiratory flows relative to the small airways and a condition of hyperinflation in 78% and 82% of our patients, respectively. The main signs observed in the TUS examination were a thickened and/or irregular pleural line and the lack or reduction of the "gliding sign." TUS showed high sensitivity and specificity in suggesting the presence of hyperinflation and distal airways inflammation according to the HRCT scan. K Cohen's coefficients showed substantial agreement between the 2 diagnostic tests.

Conclusion: TUS in patients with severe uncontrolled asthma can provide useful information on the state of the peripheral lung, suggesting the execution of a second-line HRCT scan for better assessment of eventual alterations that may represent the underlying causes of nonresponse to treatment.

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SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS



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Clinical Trial

Ann Am Thorac Soc

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. 2022 Oct;19(10):1669-1676.

doi: 10.1513/AnnalsATS.202111-1221OC.

Physical Activity, Exercise Capacity, and Body Composition in U.S. Veterans with Chronic Obstructive Pulmonary Disease

[Emily S Wan](#)^{1,2,3}, [Madeline Polak](#)¹, [Rebekah L Goldstein](#)¹, [Antonio A Lazzari](#)^{4,5}, [Ana Kantorowski](#)¹, [Eric Garshick](#)^{1,2,3}, [Marilyn L Moy](#)^{1,3}

Affiliations expand

- PMID: 35536690
- DOI: [10.1513/AnnalsATS.202111-1221OC](https://doi.org/10.1513/AnnalsATS.202111-1221OC)

Abstract

Rationale: Differences in body composition may contribute to variability in exercise capacity (EC) and physical activity (PA) in individuals with chronic obstructive pulmonary disease (COPD). Most studies have used bioimpedance-based surrogates of muscle (lean) mass; relatively few studies have included consideration of fat mass, and limited studies have been performed using dual X-ray absorptiometry (DXA) to assess body composition. **Objectives:** To determine whether DXA-assessed muscle (lean) and fat mass exhibit differential correlations with EC and PA in subjects with COPD. **Methods:** U.S. veterans with COPD (defined as forced expiratory volume in 1 second/forced vital capacity < 0.7 or emphysema on clinical chest computed tomography) had DXA-assessed body composition, EC (6-minute-walk distance), objective PA (average daily step counts), and self-reported PA measured at enrollment. Associations among EC, PA, and body composition were examined using Spearman correlations and multivariable models adjusted *a priori* for age, sex, race, and lung function. **Results:** Subjects ($n = 98$) were predominantly White (90%), obese (mean body mass index, 30.2 ± 6.2 kg/m²), and male (96%), with a mean age of 69.8 ± 7.9 years and moderate airflow obstruction (mean forced expiratory volume in 1 second percentage predicted, $68 \pm 20\%$). Modest inverse correlations of EC and PA with fat mass were observed (Spearman's rho range, -0.20 to -0.34), whereas measures of muscle (lean) mass were not significantly associated with EC or PA. The ratio of appendicular skeletal muscle mass (ASM) to weight, which considers both muscle (lean) and fat mass, was consistently associated with EC (8.4 [95% confidence interval, 2.9-13.8] meter increase in 6-minute walk distance per 1% increase in ASM-to-weight ratio), objective PA (194.8 [95% confidence interval, 15.2-374.4] steps per day per 1% increase in ASM-to-weight ratio), and self-reported PA in multivariable-adjusted models. **Conclusions:** DXA-assessed body composition measures that include consideration of both lean and fat mass are associated with cross-sectional EC and PA in COPD populations. Clinical trial registered with www.clinicaltrials.gov ([NCT02099799](https://www.clinicaltrials.gov/ct2/show/study?term=NCT02099799)).

Keywords: COPD; body composition; exercise tolerance; physical activity.

Comment in

- [The Paradox of Obesity in Patients with Chronic Obstructive Pulmonary Disease.](#)
Yohannes AM. Ann Am Thorac Soc. 2022 Oct;19(10):1638-1639. doi:
10.1513/AnnalsATS.202206-525ED.PMID: 36178401 **Free PMC article.** No abstract
available.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Associated data, Grant supportexpand

FULL TEXT LINKS



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Randomized Controlled Trial

Ann Am Thorac Soc

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. 2022 Oct;19(10):1642-1649.

doi: 10.1513/AnnalsATS.202109-1042OC.

[Lung Function and the Risk of Exacerbation in the \$\beta\$ -Blockers for the Prevention of Acute Exacerbations of Chronic Obstructive Pulmonary Disease Trial](#)

[Trisha M Parekh](#)¹, [Erika S Helgeson](#)², [John Connett](#)³, [Helen Voelker](#)³, [Sharon X Ling](#)³, [Stephen C Lazarus](#)⁴, [Surya P Bhatt](#)¹, [David M MacDonald](#)³, [Takudzwa Mkorombindo](#)¹, [Ken M Kunisaki](#)^{3,5}, [Spyridon Fortis](#)⁶, [David Kaminsky](#)⁷, [Mark T Dransfield](#)¹

Affiliations expand

- PMID: 35363600
- PMCID: PMC9528740 (available on 2023-10-01)
- DOI: [10.1513/AnnalsATS.202109-1042OC](https://doi.org/10.1513/AnnalsATS.202109-1042OC)

Abstract

Rationale: The BLOCK COPD (β -Blockers for the Prevention of Acute Exacerbations of Chronic Obstructive Pulmonary Disease) study found that metoprolol was associated with a higher risk of severe exacerbation. **Objectives:** To determine the mechanism underlying these results, we compared changes in lung function over the course of the study between treatment groups and evaluated whether baseline bronchodilator response or early reduction in forced expiratory volume in 1 second (FEV₁) or forced vital capacity (FVC) was associated with exacerbation risk. **Methods:** We compared changes in lung function (FEV₁ and FVC) over the treatment period between treatment groups using linear mixed-effect models. Cox proportional hazards models were used to evaluate the association between baseline bronchodilator responsiveness (FEV₁, FVC, and combined FEV₁ and FVC), early post-randomization (14 d) change in lung function, and the interaction between treatment assignment and these measures with risk of any or severe or very severe exacerbations. Negative binomial models were used to evaluate the relationship between bronchodilator responsiveness, the interaction between bronchodilator responsiveness and treatment assignment, and exacerbation rate. **Results:** Over the 336-day treatment period, individuals in the metoprolol group had a significantly greater decrease in logarithmic FEV₁ from baseline to visit on Day 28 than individuals in the placebo group. Individuals in the metoprolol group had a significantly greater decrease in FVC from baseline to visits on Days 14 and 28, and also a significantly greater decrease in logarithmic FVC from baseline to visits on Days 42 and 112 than individuals in the placebo group. There were no associations between early lung function reduction or interactions between lung function reduction and treatment assignment and time to any or severe or very severe exacerbations. There were no interactions between treatment arm and baseline bronchodilator responsiveness measures on risk or rate of exacerbations. However, those with baseline FVC bronchodilator responsiveness had a higher rate of severe or very severe exacerbations (adjusted rate ratio, 1.62; 95% confidence interval, 1.04–2.48). **Conclusions:** Metoprolol was associated with reduced lung function during the early part of the treatment period, but these effects were modest and did not persist. Early lung

function reduction and baseline bronchodilator responsiveness did not interact with the treatment arm to predict exacerbations; however, baseline FVC bronchodilator responsiveness was associated with a 60% higher rate of severe or very severe exacerbations. Clinical trial registered with www.clinicaltrials.gov ([NCT02587351](https://www.clinicaltrials.gov/ct2/show/study?term=NCT02587351)).

Keywords: COPD; bronchodilator response; exacerbations; spirometry; β -blockers.

Comment in

- [To \$\beta\$ -Block or Not to \$\beta\$ -Block: That Is Still the Question in Chronic Obstructive Pulmonary Disease.](#)
Hancox RJ. Ann Am Thorac Soc. 2022 Oct;19(10):1636-1637. doi: 10.1513/AnnalsATS.202207-609ED. PMID: 36178400 **Free PMC article.** No abstract available.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated data, Grant support [expand](#)

FULL TEXT LINKS



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J Thorac Cardiovasc Surg

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. 2022 Oct;164(4):1222-1233.e11.

doi: 10.1016/j.jtcvs.2021.11.086. Epub 2021 Dec 13.

[Lung transplantation for chronic obstructive pulmonary disease: A call to](#)

modify the lung allocation score to decrease waitlist mortality

[Travis D Hull¹](#), [Gregory A Leya¹](#), [Andrea L Axtell¹](#), [Philicia Moonsamy¹](#), [Asishana Osho¹](#), [David C Chang²](#), [Thoralf M Sundt¹](#), [Mauricio A Villavicencio³](#)

Affiliations expand

- PMID: 35016781
- DOI: [10.1016/j.jtcvs.2021.11.086](https://doi.org/10.1016/j.jtcvs.2021.11.086)

Abstract

Objective: Approximately 40% of lung transplants for chronic obstructive pulmonary disease (COPD) in the lung allocation score era are single lung transplantations (SLTs). We hypothesized that double lung transplantation (DLT) results in superior survival, but that mortality on the waitlist may compel clinicians to perform SLT. We investigated both waitlist mortality in COPD patients with restricted versus unrestricted listing preferences and posttransplant survival in SLT versus DLT to identify key predictors of mortality.

Methods: A retrospective analysis of waitlist mortality and posttransplant survival in patients with COPD was conducted using post-lung allocation score data from the United Network for Organ Sharing database between 2005 and 2018.

Results: Of 6740 patients with COPD on the waitlist, 328 (4.87%) died and 320 (4.75%) were removed due to clinical deterioration. Median survival on the waitlist was significantly worse in patients listed as restricted for DLT (4.39 vs 6.09 years; $P = .002$) compared with patients listed as unrestricted (hazard ratio, 1.34; 95% CI, 1.13-1.57). Factors that increase waitlist mortality include female sex, increased pulmonary artery pressure, and increased wait time. Median posttransplant survival was 5.3 years in SLT versus 6.5 years in DLT ($P < .001$). DLT recipients are younger, male patients with a higher lung allocation score. The survival advantage of DLT persisted in adjusted analysis (hazard ratio, 0.819; 95% CI, 0.741-0.905).

Conclusions: Restricted listing preference is associated with increased waitlist mortality, but DLT recipients have superior posttransplant survival. Because the lung allocation score does not prioritize COPD, concern for increased waitlist mortality with restricted listing preference may drive continued use of SLT despite better posttransplant survival in DLT.

Keywords: chronic obstruction pulmonary disease; double-lung transplantation; lung allocation score; lung transplantation; single-lung transplantation; waitlist mortality.

Comment in

- [Commentary: How best to dance tango in lung transplantation for chronic obstructive pulmonary disease?](#)

Van Raemdonck D, Ceulemans LJ, Vos R, Verleden GM. *J Thorac Cardiovasc Surg.* 2022 Oct;164(4):1234-1235. doi: 10.1016/j.jtcvs.2021.12.034. Epub 2021 Dec 24. PMID: 35000685 No abstract available.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS



ASTHMA

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Review

Trends Mol Med

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. 2022 Oct 5;S1471-4914(22)00217-9.

doi: 10.1016/j.molmed.2022.09.001. Online ahead of print.

[Asthma exacerbations: the Achilles heel of asthma care](#)

[Amanda McIntyre](#)¹, [William W Busse](#)²

Affiliations expand

- PMID: 36208987
- DOI: [10.1016/j.molmed.2022.09.001](https://doi.org/10.1016/j.molmed.2022.09.001)

Abstract

Asthma exacerbations significantly impact millions of patients worldwide to pose large disease burdens on affected patients, families, and health-care systems. Although numerous environmental factors cause asthma exacerbations, viral respiratory infections are the principal triggers. Advances in the pathophysiology of asthma have elucidated dysregulated protective immune responses and upregulated inflammation that create susceptibility and risks for exacerbation. Biologics for the treatment of severe asthma reduce rates of exacerbations and identify specific pathways of inflammation that contribute to altered pathophysiology, novel therapeutic targets, and informative biomarkers. Major steps to prevent exacerbations include the identification of molecular pathways whose blockage will prevent asthma attacks safely, predictably, and effectively.

Keywords: T2 inflammation; airway inflammation; asthma exacerbations; biologics; rhinovirus infections.

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Conflict of interest statement

Declaration of interests W.W.B. is a consultant for Sanofi, Regeneron, and GlaxoSmithKline.

SUPPLEMENTARY INFO

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[Review](#)

Environ Res

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. 2022 Oct 5;114489.

doi: 10.1016/j.envres.2022.114489. Online ahead of print.

Asthma triggered by extreme temperatures: From epidemiological evidence to biological plausibility

[Azhu Han](#)¹, [Shizhou Deng](#)¹, [Jiarui Yu](#)², [Yali Zhang](#)¹, [Bin Jalaludin](#)³, [Cunrui Huang](#)⁴

Affiliations expand

- PMID: 36208788
- DOI: [10.1016/j.envres.2022.114489](https://doi.org/10.1016/j.envres.2022.114489)

Abstract

Background: There is rapidly growing evidence indicating that extreme temperature is a crucial trigger and potential activator of asthma; however, the effects of extreme temperature on asthma are inconsistently reported and the its potential mechanisms remain undefined.

Objectives: This review aims to estimate the impacts of extreme heat, extreme cold, and temperature variations on asthma by systematically summarizing the existing studies from epidemiological evidence to biological plausibility.

Methods: We conducted a systematic search in PubMed, Embase, and Web of Science from inception to June 30, 2022, and we retrieved articles of epidemiology and biological studies which assessed associations between extreme temperatures and asthma. This protocol was registered with PROSPERO (CRD42021273613).

Results: From 12,435 identified records, 111 eligible studies were included in the qualitative synthesis, and 37 articles were included in the meta-analysis (20 for extreme heat, 16 for extreme cold, and 15 for temperature variations). For epidemiological evidence, we found that the synergistic effects of extreme temperatures, indoor/outdoor environments, and individual vulnerabilities are important triggers for asthma attacks, especially when there is extreme heat or cold. Meta-analysis further confirmed the associations, and the pooled relative risks for asthma attacks in extreme heat and extreme cold were 1.05 (95%CI: 1.01-1.09) and 1.18 (95%CI: 1.10-1.26), respectively. Additionally,

this review discussed the potential inflammatory mechanisms behind the associations between extreme temperatures and asthma exacerbation, and highlighted the regulatory role of immunological pathways and transient receptor potential ion channels in asthma triggered by extreme temperatures.

Conclusions: We concluded that both extreme heat and cold could significantly increase the risk of asthma. Additionally, we proposed a potential mechanistic framework, which is important for understanding the disease pathogenesis that uncovers the complex mechanisms of asthma triggered by extreme temperatures and protects the sensitive individuals from impacts of extreme weather events and climate change.

Keywords: Asthma; Epidemiology; Extreme temperature; Mechanism; Review.

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Conflict of interest statement

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

SUPPLEMENTARY INFO

Publication typesexpand

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Allergy

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. 2022 Oct 7.

doi: 10.1111/all.15543. Online ahead of print.

Dual Activation of Estrogen Receptor Alpha and Glucocorticoid Receptor

Upregulate CRTh2-Mediated Type 2 Inflammation; Mechanism Driving Asthma Severity in Women?

[Meerah Vijeyakumaran¹](#), [MohdWessam Al Jawhri^{#1}](#), [Jenna Fortunato^{#1}](#), [Lauren Solomon¹](#), [Nami Shrestha Palikhe²](#), [Harissios Vliagoftis²](#), [Lisa Cameron¹](#)

Affiliations expand

- PMID: 36207765
- DOI: [10.1111/all.15543](https://doi.org/10.1111/all.15543)

Abstract

Background: Type 2-high asthma is characterized by elevated levels of circulating Th2 cells and eosinophils, cells that express chemoattractant-homologous receptor expressed on Th2 cells (CRTh2). Severe asthma is more common in women than men; however, the underlying mechanism(s) remain elusive. Here we examined whether the relationship between severe asthma and type 2 inflammation differs by sex and if estrogen influences Th2 cell response to glucocorticoid (GC).

Methods: Type 2 inflammation and the proportion of blood Th2 cells (CD4⁺ CRTh2⁺) were assessed in whole blood from subjects with asthma (n = 66). The effects of GC and estrogen receptor alpha (ER α) agonist on in vitro differentiated Th2 cells were examined. Expression of CRTh2, type 2 cytokines and degree of apoptosis (Annexin V⁺, 7-AAD) were determined by flow cytometry, qRT-PCR, western blot and ELISA.

Results: In severe asthma, the proportion of circulating Th2 cells and hospitalizations were higher in women than men. Women with severe asthma also had more Th2 cells and serum IL-13 than women with mild/moderate asthma. Th2 cells, eosinophils and CRTh2 mRNA correlated with clinical characteristics associated with asthma control in women but not men. In vitro, GC and ER α agonist treated Th2 cells exhibited less apoptosis, more CRTh2 as well as IL-5 and IL-13 following CRTh2 activation than Th2 cells treated with GC alone.

Conclusion: Women with severe asthma had higher levels of circulating Th2 cells than men, which may be due to estrogen modifying the effects of GC, enhancing Th2 cell survival and type 2 cytokine production.

Keywords: Asthma; Th2 cells; estrogen; glucocorticoid; sex differences.

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PLoS One

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. 2022 Oct 7;17(10):e0275864.

doi: 10.1371/journal.pone.0275864. eCollection 2022.

Severe, but not moderate asthmatics share blood transcriptomic changes with post-traumatic stress disorder and depression

[Sandor Haas-Neil](#)¹, [Anna Dvorkin-Gheva](#)², [Paul Forsythe](#)³

Affiliations expand

- PMID: 36206293
- PMCID: [PMC9543640](#)
- DOI: [10.1371/journal.pone.0275864](#)

Abstract

Asthma, an inflammatory disorder of the airways, is one of the most common chronic illnesses worldwide and is associated with significant morbidity. There is growing recognition of an association between asthma and mood disorders including post-traumatic stress disorder (PTSD) and major depressive disorder (MDD). Although there are

several hypotheses regarding the relationship between asthma and mental health, there is little understanding of underlying mechanisms and causality. In the current study we utilized publicly available datasets of human blood mRNA collected from patients with severe and moderate asthma, MDD, and PTSD. We performed differential expression (DE) analysis and Gene Set Enrichment Analysis (GSEA) on diseased subjects against the healthy subjects from their respective datasets, compared the results between diseases, and validated DE genes and gene sets with 4 more independent datasets. Our analysis revealed that commonalities in blood transcriptomic changes were only found between the severe form of asthma and mood disorders. Gene expression commonly regulated in PTSD and severe asthma, included ORMDL3 a gene known to be associated with asthma risk and STX8, which is involved in TrkA signaling. We also identified several pathways commonly regulated to both MDD and severe asthma. This study reveals gene and pathway regulation that potentially drives the comorbidity between severe asthma, PTSD, and MDD and may serve as foci for future research aimed at gaining a better understanding of both the relationship between asthma and PTSD, and the pathophysiology of the individual disorders.

Conflict of interest statement

The authors have declared that no competing interests exist.

- [113 references](#)
- [5 figures](#)

SUPPLEMENTARY INFO

Grant support[expand](#)

[Proceed to details](#)

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PLoS One

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. 2022 Oct 6;17(10):e0274951.

doi: 10.1371/journal.pone.0274951. eCollection 2022.

GSDM gene polymorphisms regulate the IgE level in asthmatic patients

[Amer Imraish¹](#), [Tuqa Abu-Thiab¹](#), [Tareq Alhindi¹](#), [Malek Zihlif²](#)

Affiliations expand

- PMID: 36201519
- PMCID: [PMC9536611](#)
- DOI: [10.1371/journal.pone.0274951](#)

Free PMC article

Abstract

Background: Gasdermin A (GSDMA) and gasdermin B (GSDMB) have been associated with childhood and adult asthma in many populations including the Jordanian population. It is also known that IgE plays a crucial role in various allergic disorders, such as elevated levels of total serum IgE were detected in asthma and allergic rhinitis. IgE immunoglobulin is responsible for the release of numerous inflammatory mediators, such as histamine and prostaglandins, from mast cells in asthmatic patients.

Objective: In this study, single nucleotide polymorphisms of GSDMA (rs7212938, T/G) and GSDMB (rs7216389, T/C) in Jordanian population were investigated for their association with total IgE levels in serum of asthmatic children and adult subjects.

Methods: The genetic polymorphism analysis for SNPs was performed using the polymerase chain reaction (PCR)/restriction fragment length polymorphism method (RFLP). Three analysis models were applied to the genotype data: co-dominant, dominant and recessive.

Results: Our data demonstrate a significant correlation between GSDMB genetic SNP (rs7216389) and the total IgE serum level. Where one minor allele in the GSDMB gene is sufficient to induce significant changes in the IgE serum levels and plays a role in the pathogenesis of asthma in asthmatic children of the Jordanian population. Suggesting that this polymorphism might have a protective effect against asthma risk. While the presence of the GSDMB polymorphism alone might not be sufficient to associate with the high risk of developing asthma or responding to it in adults in Jordanian population.

Conclusion: In conclusion, the current study confirms the significant association of GSDMB genetic SNP (rs7216389) with IgE levels in asthma patients in Jordanian population, while no significant correlation of GSDMA and IgE level was found in both child and adult asthmatic patients.

Conflict of interest statement

The authors have declared that no competing interests exist.

- [22 references](#)

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JAMA Netw Open

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. 2022 Oct 3;5(10):e2234714.

doi: 10.1001/jamanetworkopen.2022.34714.

Development of a Symptom-Based Tool for Screening of Children at High Risk of Preschool Asthma

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[Mandhane](#)⁹, [Stuart E Turvey](#)¹⁰, [Graham L Hall](#)^{3,4}, [Theo J Moraes](#)¹, [Malcolm R Sears](#)⁶, [Padmaja Subbarao](#)¹²

Affiliations expand

- PMID: 36201211
- DOI: [10.1001/jamanetworkopen.2022.34714](https://doi.org/10.1001/jamanetworkopen.2022.34714)

Free article

Abstract

Importance: Despite advances in asthma therapeutics, the burden remains highest in preschool children; therefore, it is critical to identify primary care tools that distinguish preschool children at high risk for burdensome disease for further evaluation. Current asthma prediction tools, such as the modified Asthma Predictive Index (mAPI), require invasive tests, limiting their applicability in primary care and low-resource settings.

Objective: To develop and evaluate the use of a symptom-based screening tool to detect children at high risk of asthma, persistent wheeze symptoms, and health care burden.

Design, setting, and participants: The cohort for this diagnostic study included participants from the CHILd Study (n = 2511) from January 1, 2008, to December 31, 2012, the Raine Study from January 1, 1989, to December 31, 2012 (n = 2185), and the Canadian Asthma Primary Prevention Study (CAPPS) from January 1, 1989, to December 31, 1995 (n = 349), with active follow-up to date. Data analysis was performed from November 1, 2019, to May 31, 2022.

Exposures: The CHILdhood Asthma Risk Tool (CHART) identified factors associated with asthma in patients at 3 years of age (timing and number of wheeze or cough episodes, use of asthma medications, and emergency department visits or hospitalizations for asthma or wheeze) to identify children with asthma or persistent symptoms at 5 years of age.

Main outcomes and measures: Within the CHILd Study cohort, CHART was evaluated against specialist clinician diagnosis and the mAPI. External validation was performed in both a general population cohort (Raine Study [Australia]) and a high-risk cohort (CAPPS [Canada]). Predictive accuracy was measured by sensitivity, specificity, area under the receiver operating characteristic curve (AUROC), and positive and negative predicted values.

Results: Among 2511 children (mean [SD] age at 3-year clinic visit, 3.08 [0.17] years; 1324 [52.7%] male; 1608 of 2476 [64.9%] White) with sufficient questionnaire data to apply CHART at 3 years of age, 2354 (93.7%) had available outcome data at 5 years of age.

CHART applied in the CHILD Study at 3 years of age outperformed physician assessments and the mAPI in predicting persistent wheeze (AUROC, 0.94; 95% CI, 0.90-0.97), asthma diagnosis (AUROC, 0.73; 95% CI, 0.69-0.77), and health care use (emergency department visits or hospitalization for wheeze or asthma) (AUROC, 0.70; 95% CI, 0.61-0.78). CHART had a similar predictive performance for persistent wheeze in the Raine Study (N = 2185) in children at 5 years of age (AUROC, 0.82; 95% CI, 0.79-0.86) and CAPPS (N = 349) at 7 years of age (AUROC, 0.87; 95% CI, 0.80-0.94).

Conclusions and relevance: In this diagnostic study, CHART was able to identify children at high risk of asthma at as early as 3 years of age. CHART could be easily incorporated as a routine screening tool in primary care to identify children who need monitoring, timely symptom control, and introduction of preventive therapies.

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J Investig Allergol Clin Immunol

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. 2022 Oct 6;0.

doi: 10.18176/jiaci.0865. Online ahead of print.

[The influence of BMI in asthma. Which traits are due to obesity and which to asthma and obesity phenotype?](#)

[I Esteban-Gorgojo](#)¹, [M P Gorgojo](#)², [J Sastre](#)^{3 4 5}, [F García-Río](#)^{4 5 6}, [S Quirce](#)^{4 5 7}

Affiliations expand

- PMID: 36200980

- DOI: [10.18176/jiaci.0865](https://doi.org/10.18176/jiaci.0865)

Abstract

Background and objectives: Characteristics of the asthma and obesity phenotype have been described by cluster studies, but they have not been subsequently confirmed. Specific characteristics of this phenotype have not been differentiated from those inherent to the patient's body mass index (BMI). This study aims to assess the effect of BMI on asthma. This will allow to identify which traits could define the asthma and obesity phenotype, and which are inherent to the patient's BMI.

Methods: A real-life retrospective observational study was conducted with a 2,514 patients database. Data was collected on the first visit to the Allergy clinic of all patients who underwent a correct spirometry maneuver due to suspected asthma between November 2014 and November 2017. All BMI, sex and age groups were represented.

Results: BMI influence over asthma differed in different age groups and genders. All spirometric results and FeNO were influenced by BMI. Concerning asthma characteristics only a later asthma onset with higher BMI values was observed. No other differences were found between different BMI groups.

Conclusions: The effect of BMI on asthma is age dependent, so it should be corrected for age. The most important variations are on FeNO and spirometric results. The specific characteristics of the asthma and obesity phenotype are a greater perception of symptoms with fewer alterations in respiratory function tests and a lower prevalence of atopy, rhinitis and allergy, including allergic asthma. Other characteristics of this phenotype, such as a higher women prevalence or being late-onset or non-eosinophilic asthma, are non-specific for this phenotype.

Keywords: Asthma; Asthma and obesity; BMI; Obesity; Phenotype; Severe asthma.

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ERJ Open Res

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. 2022 Oct 4;8(4):00238-2022.

doi: 10.1183/23120541.00238-2022. eCollection 2022 Oct.

Complete response to anti-interleukin-5 biologics in a real-life setting: results from the nationwide Danish Severe Asthma Register

[Marianne Baastrup Soendergaard](#)¹, [Susanne Hansen](#)^{1,2}, [Anne-Sofie Bjerrum](#)³, [Ole Hilberg](#)⁴, [Sofie Lock-Johansson](#)⁵, [Kjell Erik Julius Håkansson](#)⁶, [Truls Sylvan Ingebrigtsen](#)⁷, [Claus Rikard Johnsen](#)⁸, [Linda Makowska Rasmussen](#)⁸, [Anna von Bülow](#)¹, [Karin Dahl Assing](#)⁹, [Johannes Martin Schmid](#)³, [Charlotte Suppli Ulrik](#)⁶, [Celeste Porsbjerg](#)^{1,10}

Affiliations expand

- PMID: 36199589
- PMCID: [PMC9530888](#)
- DOI: [10.1183/23120541.00238-2022](#)

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Abstract

Background: Phase III regulatory trials show that anti-interleukin (IL)-5 biologics efficiently reduce exacerbations and the use of maintenance oral corticosteroids (mOCS) in patients with severe eosinophilic asthma. However, patients eligible for these trials differ significantly compared with real-life severe asthma populations. Therefore, our aim was to explore efficacy in a real-life setting. The Danish Severe Asthma Register (DSAR) is a complete, nationwide register that comprises all Danish patients on biological therapy for severe asthma.

Methods: This prospective study identified patients in the DSAR who were complete responders to anti-IL-5 biologics after 1 year of treatment. A complete response was defined as resolution of the parameter setting the indication, *i.e.* recurrent exacerbations and/or use of mOCS.

Results: A total of 289 out of 502 (58%) patients were complete responders to anti-IL-5 biologics after 12 months. Complete responders had greater improvements in forced expiratory volume in 1 s and Asthma Control Questionnaire (ACQ) score compared with noncomplete responders (Δ 210 *versus* 30 mL; $p < 0.0001$ and Δ -1.04 *versus* -0.68; $p = 0.016$, respectively). A complete response was predicted by age at onset, less severe disease at baseline (*i.e.* no mOCS and lower ACQ score) and higher blood eosinophils.

Conclusions: More than half of Danish patients treated with anti-IL-5 biologics for severe asthma achieve a complete response to treatment, thereby becoming free from asthma exacerbations and the need for mOCS. Complete responders also achieved superior effects on lung function and symptoms compared with noncomplete responders.

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Conflict of interest statement

Conflict of interest: M.B. Soendergaard has received lecture fees from GlaxoSmithKline, outside the submitted work. Conflict of interest: S. Hansen has nothing to disclose. Conflict of interest: A.S. Bjerrum has received lecture fees from AstraZeneca and GlaxoSmithKline, outside the submitted work. Conflict of interest: O. Hilberg has nothing to disclose. Conflict of interest: S. Lock-Johansson has nothing to disclose. Conflict of interest: K.E.J. Håkansson has received unrestricted research grants, paid to his institution, from AstraZeneca and Sanofi Genzyme, outside the submitted work; and payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from AstraZeneca, Teva, GlaxoSmithKline and Sanofi Genzyme, outside the submitted work. Conflict of interest: T.S. Ingebrigtsen has nothing to disclose. Conflict of interest: C.R. Johnsen has nothing to disclose. Conflict of interest: L.M. Rasmussen has received payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from AstraZeneca, GlaxoSmithKline, Teva and ALK, outside the submitted work; support for attending meetings and/or travel received from AstraZeneca and Chiesi, outside the submitted work; and participation on data safety monitoring or advisory boards for AstraZeneca, GlaxoSmithKline, Teva and Sanofi, outside the submitted work. Conflict of interest: A. von Bülow has done consultancy work for Novartis DK, outside the submitted work; lectures and speakers fees received from AstraZeneca, Novartis and GlaxoSmithKline, outside the submitted work; and advisory boards for AstraZeneca and Novartis, outside the submitted work. Conflict of interest: K.D. Assing has nothing to disclose. Conflict of interest: J.M. Schmid has nothing to disclose. Conflict of interest: C.S. Ulrik received payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from AstraZeneca, GlaxoSmithKline, Teva, Sanofi, Orion Pharma, Novartis and Chiesi, outside the submitted work. Conflict of interest: C. Porsbjerg has received grants or contracts from AstraZeneca, GlaxoSmithKline, Novartis, Teva, Sanofi, Chiesi and ALK, outside the submitted work; consulting fees from AstraZeneca, GlaxoSmithKline, Novartis, Teva, Sanofi, Chiesi and ALK, outside the submitted work; payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events, received from AstraZeneca, GlaxoSmithKline,

Novartis, Teva, Sanofi, Chiesi and ALK, outside the submitted work; and participation on data safety monitoring or advisory boards for AstraZeneca, Novartis, Teva, Sanofi and ALK, outside the submitted work.

- [44 references](#)
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J Asthma

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. 2022 Oct 5;1-21.

doi: 10.1080/02770903.2022.2132957. Online ahead of print.

Effectiveness and Quality of life in asthmatic patients treated with budesonide/formoterol via Elpenhaler® device in primary care. The "SKIRON" real world study

[Paschalis Steiropoulos¹](#), [Konstantinos Exarchos²](#), [Maria Bertoli³](#), [Foteini Karakontaki⁴](#), [Georgios Antonogiannakis⁵](#), [Vlassios Polychronopoulos⁴](#), [Athena Gogali²](#), [Konstantinos Kostikas²](#)

Affiliations expand

- PMID: 36199217
- DOI: [10.1080/02770903.2022.2132957](https://doi.org/10.1080/02770903.2022.2132957)

Abstract

Aim Inhaled corticosteroid (ICS)/long-acting β_2 agonist (LABA) combination therapy is used for the effective control of asthma. Aim of this study was to collect data on the effectiveness, safety, quality of life, and patient satisfaction from a fixed dose combination of budesonide/formoterol administered with the Elpenhaler® device following 3-months' treatment. **Methods** A 3-month real-life, multicentre, one-arm, prospective observational study (SKIRON study-[NCT03055793](#)) was conducted, using the following questionnaires: Asthma Control Questionnaire (ACQ-6) for asthma control assessment, MiniAQLQ questionnaire for QoL assessment, and Feeling of Satisfaction with Inhaler questionnaire (FSI-10) for patients' satisfaction with the inhaler device. Comorbidities and safety data were also recorded during the study. **Results** We enrolled 1,174 asthmatic patients following standard clinical practice in primary care from 126 sites in urban and rural areas of Greece. The majority of patients (71.5%) had at least one comorbidity. A statistically significant improvement in the ACQ-6 score was noted at 3 months compared to the baseline evaluation (mean \pm SD 2.19 ± 0.97 at baseline vs. 0.55 ± 0.56 at 3 months; mean change -1.64 (95%CI $-1.69, -1.57$), $p < 0.0001$). MiniAQLQ score was statistically and clinically significantly improved, compared to baseline, (4.55 ± 1.04 at baseline vs. 6.37 ± 0.64 at 3 months; mean change 1.82 (95%CI $1.75, 1.87$), $p < 0.0001$). The mean FSI-10 score of 44.2 ± 5.4 indicated patient satisfaction and ease-of-use of the Elpenhaler® device. **Conclusions** In this large real-world study of inadequately-controlled asthma patients in primary care settings, the treatment with budesonide/formoterol FDC with the Elpenhaler® device was associated with significant improvement in patients' asthma control and quality of life.

Keywords: Asthma; Asthma Control; Dry Powder Inhaler; Elpenhaler® device; Feeling of Satisfaction with Inhaler; Fixed-dose budesonide/formoterol; Observational; Primary Care; Quality of life.

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ACS Sens

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. 2022 Oct 4.

doi: 10.1021/acssensors.2c01628. Online ahead of print.

Biodegradable Smart Face Masks for Machine Learning-Assisted Chronic Respiratory Disease Diagnosis

[Kaijun Zhang](#)¹, [Zhaoyang Li](#)¹, [Jianfeng Zhang](#)^{1,2}, [Dazhe Zhao](#)¹, [Yucong Pi](#)¹, [Yujun Shi](#)¹, [Renkun Wang](#)¹, [Peisheng Chen](#)³, [Chaojie Li](#)³, [Gangjin Chen](#)², [Iek Man Lei](#)¹, [Junwen Zhong](#)¹

Affiliations expand

- PMID: 36196484
- DOI: [10.1021/acssensors.2c01628](https://doi.org/10.1021/acssensors.2c01628)

Abstract

Utilizing smart face masks to monitor and analyze respiratory signals is a convenient and effective method to give an early warning for chronic respiratory diseases. In this work, a smart face mask is proposed with an air-permeable and biodegradable self-powered breath sensor as the key component. This smart face mask is easily fabricated, comfortable to use, eco-friendly, and has sensitive and stable output performances in real wearable conditions. To verify the practicability, we use smart face masks to record respiratory signals of patients with chronic respiratory diseases when the patients do not have obvious symptoms. With the assistance of the machine learning algorithm of the bagged decision tree, the accuracy for distinguishing the healthy group and three groups of chronic respiratory diseases (asthma, bronchitis, and chronic obstructive pulmonary disease) is up to 95.5%. These results indicate that the strategy of this work is feasible and may promote the development of wearable health monitoring systems.

Keywords: biodegradable; chronic respiratory disease diagnosis; machine learning; self-powered sensors; smart face mask.

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Am J Respir Crit Care Med

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. 2022 Oct 4.

doi: 10.1164/rccm.202205-0855LE. Online ahead of print.

Circulating Biomarkers in Young Individuals With Low Peak FEV₁

[Nuria Olvera](#)¹, [Sandra Casas](#)², [Judith M Vonk](#)³, [Tamara Garcia](#)⁴, [H Marike Boezen](#)^{5,6}, [Maarten van den Berge](#)^{7,8}, [Alvar Agusti](#)⁹, [Rosa Faner](#)¹⁰

Affiliations expand

- PMID: 36194601
- DOI: [10.1164/rccm.202205-0855LE](https://doi.org/10.1164/rccm.202205-0855LE)

No abstract available

Keywords: Chronic bronchitis, Emphysema, Smoking, Lung function, Trajectory.

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Am J Respir Crit Care Med

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. 2022 Oct 4.

Skeletal Muscle Adiposity and Lung Function Trajectory in the Severe Asthma Research Program (SARP)

[Matthew C Tattersall](#)¹, [Kristine E Lee](#)², [Nanae Tsuchiya](#)³, [Fauzia Osman](#)⁴, [Claudia E Korcarz](#)⁵, [Kristin M Hansen](#)¹, [Michael C Peters](#)⁶, [John V Fahy](#)⁷, [Colin A Longhurst](#)⁸, [Eleanor Dunican](#)⁹, [Sally E Wentzel](#)^{10,11}, [Joseph K Leader](#)¹², [Elliot Israel](#)¹³, [Bruce D Levy](#)¹³, [Mario Castro](#)¹⁴, [Serpil C Erzurum](#)¹⁵, [Jason Lempel](#)¹⁶, [Wendy Moore](#)¹⁷, [Eugene Bleeker](#)¹⁸, [Brenda R Phillips](#)¹⁹, [David T Mauger](#)²⁰, [Eric A Hoffman](#)²¹, [Sean B Fain](#)²², [Scott B Reeder](#)¹, [Ron L Sorkness](#)²³, [Nizar N Jarjour](#)²⁴, [Loren C Denlinger](#)²⁵, [Mark L Schiebler](#)²⁶

Affiliations expand

- PMID: 36194556
- DOI: [10.1164/rccm.202203-0597OC](https://doi.org/10.1164/rccm.202203-0597OC)

Abstract

Rationale: Extra-pulmonary manifestations of asthma, including fatty infiltration in tissues, may reflect systemic inflammation and influence lung function and disease severity.

Objectives: To determine if skeletal muscle adiposity predicts lung function trajectory in asthma.

Methods: Adult Severe Asthma Research Program-3 participants with baseline computed tomography imaging and longitudinal post-bronchodilator FEV1%-predicted (median follow-up 5 years [1132 person-years]) were evaluated. The mean (Hounsfield unit [HU]) of the left and right paraspinal muscle density (PSMD) at the 12th thoracic vertebral body was calculated. A lower PSMD reflects higher muscle adiposity. We derived PSMD reference ranges from healthy, non-asthma controls. A linear multivariable mixed-effects model evaluated associations of baseline PSMD, and lung function trajectory stratified by sex.

Measurements and main results: Participants included 219 with asthma (67% female, mean (SD) BMI of 32.3 [8.8] kg/m²); and 37 controls (51% female, mean [SD] BMI of 26.3 (4.7) kg/m²). Asthmatic participants had lower adjusted PSMD than controls (42.2 vs. 55.8 HU, $p < 0.001$). In adjusted models, PSMD predicted lung function trajectory in asthmatic females, [$\beta = -0.47$ Δ -slope per 10 HU decrease), $p = 0.03$], but not males [$\beta = 0.11$ Δ -slope per 10 HU decrease), $p = 0.77$]. The highest PSMD tertile predicted a 2.9% improvement

while the lowest tertile predicted a 1.8% decline in FEV1%-predicted among asthmatic females over 5 years.

Conclusions: Asthmatic participants have lower PSMD, reflecting greater muscle fat infiltration. Baseline PSMD predicted lung function decline among females with asthma, but not males. These data support an important role of metabolic dysfunction in lung function decline.

Keywords: Adult Asthma, Computed Tomography. Muscle Density, Lung function loss.

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[Published Erratum](#)

Nat Commun

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. 2022 Oct 3;13(1):5806.

doi: 10.1038/s41467-022-33097-z.

[Author Correction: Nasal airway transcriptome-wide association study of asthma reveals genetically driven mucus pathobiology](#)

[Satria P Sajuthi](#)¹, [Jamie L Everman](#)¹, [Nathan D Jackson](#)¹, [Benjamin Saef](#)¹, [Cydney L Rios](#)¹, [Camille M Moore](#)^{1 2 3}, [Angel C Y Mak](#)⁴, [Celeste Eng](#)⁴, [Ana Fairbanks-Mahnke](#)¹, [Sandra Salazar](#)⁴, [Jennifer Elhawary](#)⁴, [Scott Huntsman](#)⁴, [Vivian Medina](#)⁵, [Deborah A Nickerson](#)⁶, [Soren Germer](#)⁷, [Michael C Zody](#)⁷, [Gonçalo Abecasis](#)⁸, [Hyun Min Kang](#)⁸, [Kenneth M Rice](#)⁹, [Rajesh Kumar](#)¹⁰, [Noah A](#)

[Zaitlen](#)¹¹, [Sam Oh](#)⁴, [NHLBI Trans-Omics for Precision Medicine \(TOPMed\) Consortium](#); [José Rodríguez-Santana](#)⁵, [Esteban G Burchard](#)^{4 12}, [Max A Seibold](#)^{13 14 15}

Affiliations expand

- PMID: 36192399
- PMCID: [PMC9530212](#)
- DOI: [10.1038/s41467-022-33097-z](#)

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Erratum for

- [Nasal airway transcriptome-wide association study of asthma reveals genetically driven mucus pathobiology.](#)
Sajuthi SP, Everman JL, Jackson ND, Saef B, Rios CL, Moore CM, Mak ACY, Eng C, Fairbanks-Mahnke A, Salazar S, Elhawary J, Huntsman S, Medina V, Nickerson DA, Germer S, Zody MC, Abecasis G, Kang HM, Rice KM, Kumar R, Zaitlen NA, Oh S; NHLBI Trans-Omics for Precision Medicine (TOPMed) Consortium, Rodríguez-Santana J, Burchard EG, Seibold MA. *Nat Commun.* 2022 Mar 28;13(1):1632. doi: [10.1038/s41467-022-28973-7](#). PMID: 35347136 **Free PMC article.**
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Predicting asthma attacks using connected mobile devices and machine learning: the AAMOS-00 observational study protocol

[Kevin Cheuk Him Tsang](#)^{1,2}, [Hilary Pinnock](#)³, [Andrew M Wilson](#)^{3,4,5}, [Dario Salvi](#)⁶, [Syed Ahmar Shah](#)^{3,2}

Affiliations expand

- PMID: 36192103
- PMCID: [PMC9535155](#)
- DOI: [10.1136/bmjopen-2022-064166](#)

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Abstract

Introduction: Supported self-management empowering people with asthma to detect early deterioration and take timely action reduces the risk of asthma attacks. Smartphones and smart monitoring devices coupled with machine learning could enhance self-management by predicting asthma attacks and providing tailored feedback. We aim to develop and assess the feasibility of an asthma attack predictor system based on data collected from a range of smart devices.

Methods and analysis: A two-phase, 7-month observational study to collect data about asthma status using three smart monitoring devices, and daily symptom questionnaires. We will recruit up to 100 people via social media and from a severe asthma clinic, who are at risk of attacks and who use a pressurised metered dose relief inhaler (that fits the smart inhaler device). Following a preliminary month of daily symptom questionnaires, 30

participants able to comply with regular monitoring will complete 6 months of using smart devices (smart peak flow meter, smart inhaler and smartwatch) and daily questionnaires to monitor asthma status. The feasibility of this monitoring will be measured by the percentage of task completion. The occurrence of asthma attacks (definition: American Thoracic Society/European Respiratory Society Task Force 2009) will be detected by self-reported use (or increased use) of oral corticosteroids. Monitoring data will be analysed to identify predictors of asthma attacks. At the end of the monitoring, we will assess users' perspectives on acceptability and utility of the system with an exit questionnaire.

Ethics and dissemination: Ethics approval was provided by the East of England - Cambridge Central Research Ethics Committee. IRAS project ID: 285 505 with governance approval from ACCORD (Academic and Clinical Central Office for Research and Development), project number: AC20145. The study sponsor is ACCORD, the University of Edinburgh. Results will be reported through peer-reviewed publications, abstracts and conference posters. Public dissemination will be centred around blogs and social media from the Asthma UK network and shared with study participants.

Keywords: Asthma; Health informatics; Information technology; World Wide Web technology.

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Conflict of interest statement

Competing interests: None declared.

- [47 references](#)
- [8 figures](#)

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. 2022 Oct 2;18(1):89.

doi: 10.1186/s13223-022-00727-6.

Two cases of dupilumab-associated conjunctivitis with high expression of IL-8 mRNA on the ocular surface: a case report

[Rumi Adachi](#)¹, [Jun Shoji](#)¹, [Akira Hirota](#)¹, [Akiko Tomioka](#)¹, [Yukiko Tonoizuka](#)¹, [Noriko Inada](#)¹, [Satoru Yamagami](#)²

Affiliations expand

- PMID: 36184619
- PMCID: [PMC9526929](#)
- DOI: [10.1186/s13223-022-00727-6](#)

Free PMC article

Abstract

Background: Dupilumab-induced ocular surface disease (DIOSD) has been reported in patients with atopic dermatitis treated with dupilumab, and has been recognized as an adverse event of dupilumab. Our objective was to describe two cases of DIOSD with alterations in eotaxin-2 and interleukin (IL)-8 messenger ribonucleic acid (mRNA) expression on the ocular surface.

Case presentation: In the ocular surface test, specimens were collected from the patient's ocular surface, and eotaxin-2 and IL-8 mRNA levels in the specimens were measured using real-time polymerase chain reaction. The clinical score of ocular surface findings was quantified using a 5-5-5 exacerbation grading scale for allergic conjunctivitis. The first case was of a 27-year-old man who developed DIOSD 3 months after starting treatment with

dupilumab injection for atopic dermatitis. After 5 weeks of topical instillation of tacrolimus ophthalmic suspension, the clinical score of ocular surface findings improved and IL-8 and eotaxin-2 mRNA expression levels gradually decreased. The second patient was a 55-year-old man who developed DIOSD 11 weeks after the start of treatment with dupilumab injection for atopic dermatitis. Four weeks after starting ophthalmological treatment with tacrolimus ophthalmic suspension, his clinical scores on ocular surface findings improved and IL-8 mRNA expression levels decreased. The ocular surface test in this case revealed increased expression levels of IL-8 mRNA on the ocular surface at the onset of DIOSD, which decreased with the improvement of objective findings.

Conclusions: DIOSD, which has been successfully treated with tacrolimus ophthalmic suspension, may involve IL-8-related inflammation in addition to type 2 inflammation.

Keywords: Conjunctivitis; Dupilumab; Eotaxin-2; Interleukin-8.

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Conflict of interest statement

J.S. received honoraria from Santen Pharmaceutical Co., Ltd. and Senju Pharmaceutical Co., Ltd. The authors declare that they have no conflicts of interest.

- [23 references](#)
- [4 figures](#)

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J Asthma

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. 2022 Oct 6;1-12.

doi: 10.1080/02770903.2022.2128372. Online ahead of print.

Identification of key modules and hub genes for eosinophilic asthma by weighted gene co-expression network analysis

[Fanmin Li](#)^{1,2}, [Min Li](#)³, [Lijia Hu](#)⁴, [Wenye Zhu](#)⁵, [Deyun Cheng](#)¹

Affiliations expand

- PMID: 36165511
- DOI: [10.1080/02770903.2022.2128372](https://doi.org/10.1080/02770903.2022.2128372)

Abstract

Objective: Eosinophilic asthma (EA) is one of the most important asthma phenotypes with distinct features. However, its genetic characteristics are not fully understood. This study aimed to investigate the transcriptome features and to identify hub genes of EA.

Methods: Differentially expressed genes (DEGs) analysis, weighted gene coexpression network analysis (WGCNA) and protein-protein interaction (PPI) network analysis were performed to construct gene networks and to identify hub genes. Enrichment analyses were performed to investigate the biological processes, pathways and immune status of EA. The hub genes were validated in another dataset. The diagnostic value of the identified hub genes was assessed by receiver operator characteristic curve (ROC) analysis.

Results: Compared with NEA, EA had a different gene expression pattern, in which 81 genes were differentially expressed. WGCNA identified two gene modules significantly associated with EA. Intersections of the DEGs and the genes in the modules associated with EA were mainly enriched in chemotaxis and signal transduction by GO and KEGG enrichment analyses. Single-sample gene set enrichment analysis (ssGSEA) indicated that EA had different immune infiltration and functions compared with NEA. Seven hub genes of EA were identified and validated, including *CCL17*, *CCL26*, *CD1C*, *CXCL11*, *CXCL10*, *CCL22*, and *CCR7*, all of which have diagnostic values for distinguishing EA from NEA (All AUC > 0.7).

Conclusions: This study demonstrated the distinct gene expression patterns, biological processes, and immune status of EA. Hub genes of EA were identified and validated. Our study could provide a framework of co-expression gene modules and potential therapeutic targets for EA.

Keywords: Eosinophilic asthma; WGCNA; gene expression; hub genes.

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. 2022 Oct 6;60(4):2200257.

doi: 10.1183/13993003.00257-2022. Print 2022 Oct.

Pre-pubertal smoke exposure of fathers and increased risk of offspring asthma: a possible transgenerational effect

[Jiacheng Liu](#)¹, [Gayan Bowatte](#)^{1,2}, [Jonathan Pham](#)^{1,3}, [Jennifer L Perret](#)^{1,4}, [John W Holloway](#)^{5,6}, [Adrian J Lowe](#)^{1,7}, [John A Burgess](#)¹, [Cecilie Svanes](#)^{8,9}, [Paul Thomas](#)¹⁰, [Melissa A Russell](#)¹, [Bircan Erbas](#)¹¹, [Caroline J Lodge](#)¹, [David Martino](#)¹², [Gita D Mishra](#)¹³, [Michael J Abramson](#)¹⁴, [Eugene H Walters](#)^{1,15}, [Shyamali C Dharmage](#)^{16,7,17}, [Dinh S Bui](#)^{1,17}

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- PMID: 36104290
- DOI: [10.1183/13993003.00257-2022](https://doi.org/10.1183/13993003.00257-2022)

No abstract available

Conflict of interest statement

Conflicts of interest: M.J. Abramson holds investigator initiated grants from Pfizer, Boehringer Ingelheim, Sanofi and GSK for unrelated research; has undertaken an unrelated consultancy and received assistance with conference attendance from Sanofi; and has also received a speaker's fee from GSK. J.L. Perret, A.J. Lowe, C.J. Lodge and S.C. Dharmage declare they have received research funds from GSK's competitively awarded Investigator Sponsored Studies program for unrelated research. A.J. Lowe also declares he has received donations of interventional product (EpiCeram) from Primus Pharmaceuticals for unrelated research. The rest of the authors declare that they have no conflicts of interest.

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. 2022 Oct 6;60(4):2102395.

doi: 10.1183/13993003.02395-2021. Print 2022 Oct.

Early-life respiratory tract infections and the risk of school-age lower lung function and asthma: a meta-analysis of 150 000 European children

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[Duchen](#)²⁰, [Merete Eggesbø](#)²¹, [Cornelis van der Ent](#)²², [Maria Fantini](#)²³, [Claudia Flexeder](#)²⁴, [Urs Frey](#)²⁵, [Francesco Forastiere](#)²⁶, [Ulrike Gehring](#)²⁷, [Davide Gori](#)²³, [Raquel Granell](#)²⁸, [Lucy J Griffiths](#)²⁹, [Hazel Inskip](#)^{9 30}, [Joanna Jerzynska](#)³¹, [Anne M Karvonen](#)³², [Thomas Keil](#)^{33 34 35}, [Cecily Kelleher](#)³⁶, [Manolis Kogevinas](#)^{13 14 37 38}, [Gudrun Koppen](#)³⁹, [Claudia E Kuehni](#)^{40 41}, [Nathalie Lambrechts](#)³⁹, [Susanne Lau](#)⁴², [Irina Lehmann](#)⁴³, [Johnny Ludvigsson](#)²⁰, [Maria Christine Magnus](#)^{28 44}, [Erik Mélen](#)⁴⁵, [John Mehegan](#)³⁶, [Monique Mommers](#)⁴⁶, [Anne-Marie Nybo Andersen](#)⁴⁷, [Wenche Nystad](#)⁴⁸, [Eva S L Pedersen](#)⁴⁰, [Juha Pekkanen](#)^{32 49}, [Ville Peltola](#)⁵⁰, [Katharine C Pike](#)⁵¹, [Angela Pinot de Moira](#)⁴⁹, [Costanza Pizzi](#)⁵², [Kinga Polanska](#)³¹, [Maja Popovic](#)⁵², [Daniela Porta](#)²⁶, [Graham Roberts](#)^{7 8 9}, [Ana Cristina Santos](#)¹⁰, [Erica S Schultz](#)⁴⁵, [Marie Standl](#)^{24 53}, [Jordi Sunyer](#)^{13 14 15 38}, [Carel Thijs](#)⁴⁶, [Laura Toivonen](#)⁵⁰, [Eleonora Uphoff](#)⁵⁴, [Jakob Usemann](#)²⁵, [Marina Vafeidi](#)⁵⁵, [John Wright](#)⁵⁴, [Johan C de Jongste](#)², [Vincent W V Jaddoe](#)^{1 3 56}, [Liesbeth Duijts](#)^{57 58}

Affiliations expand

- PMID: 35487537
- PMCID: [PMC9535116](#)
- DOI: [10.1183/13993003.02395-2021](#)

Free PMC article

Abstract

Background: Early-life respiratory tract infections might affect chronic obstructive respiratory diseases, but conclusive studies from general populations are lacking. Our objective was to examine if children with early-life respiratory tract infections had increased risks of lower lung function and asthma at school age.

Methods: We used individual participant data of 150 090 children primarily from the EU Child Cohort Network to examine the associations of upper and lower respiratory tract infections from age 6 months to 5 years with forced expiratory volume in 1 s (FEV₁), forced vital capacity (FVC), FEV₁/FVC, forced expiratory flow at 75% of FVC (FEF_{75%}) and asthma at a median (range) age of 7 (4-15) years.

Results: Children with early-life lower, not upper, respiratory tract infections had a lower school-age FEV₁, FEV₁/FVC and FEF_{75%} (z-score range: -0.09 (95% CI -0.14- -0.04) to -0.30 (95% CI -0.36- -0.24)). Children with early-life lower respiratory tract infections had a higher increased risk of school-age asthma than those with upper respiratory tract infections (OR range: 2.10 (95% CI 1.98-2.22) to 6.30 (95% CI 5.64-7.04) and 1.25 (95% CI 1.18-1.32) to 1.55 (95% CI 1.47-1.65), respectively). Adjustment for preceding respiratory tract infections slightly decreased the strength of the effects. Observed associations were similar for those with and without early-life wheezing as a proxy for early-life asthma.

Conclusions: Our findings suggest that early-life respiratory tract infections affect development of chronic obstructive respiratory diseases in later life, with the strongest effects for lower respiratory tract infections.

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Conflict of interest statement

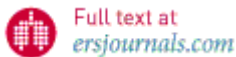
Conflict of interest: T.S. Ahluwalia received funding for the current manuscript from the Novo Nordisk Foundation (NNF180C0052457). I. Annesi-Maesano is member of the ATS Environment Health Policy Committee, the ERS Ethics and Integrity Committee, and the French IRD Ethics Committee. S.H. Arshad received funding for the manuscript from Asthma UK (364) and National Institutes of Health USA (R01HL082925). H. Bisgaard received funding for the current manuscript from the Lundbeck Foundation (R16-A1694), Ministry of Health (903516), Danish Council for Strategic Research (0603-00280B) and Capital Region Research Foundation. M. Eggesbø received paid honorarium for making small videos relating to allergy and asthma, by the Norwegian LHL organisation. U. Frey received funding for the manuscript from the Swiss National Science Foundation (320030_204717/1), and is chair of the National Steering Board, Swiss Personalized Health Network (SPHN). H. Inskip received funding for the manuscript from the UK Medical Research Council and the European Union, and was President for the Society for Social Medicine and Population Health. J. Jerzynska received funding for the current manuscript from the National Science Centre, Poland (DEC-2014/15/B/N27/00998). A.M. Karvonen received funding for the present manuscript from the Academy of Finland (139021, 287675, 296814, 296817, 308254), Juho Vainio Foundation, EVO/VTR funding, Pavivikki and Sakari Sohlberg Foundation, Farmers' Social Insurance Institution (Mela), Finnish Cultural Foundation, Foundation for Pediatric Research, and the European Union (QLK4-CT-2001-0250). M. Mommers received grants from the Research Council of Norway (262700) and European Research Council (947684). A. Pinot de Moira received a Lundbeck Foundation fellowship (R264-2017-3099). V. Peltola received funding for the present manuscript from the Academy of Finland and Foundation for Pediatric Research Finland. K.C. Pike received consulting fees from Novartis and Spiriva, payment or honoraria for lectures from Novartis, and is participating on a data safety monitoring board or advisory board for Adherium. K. Polanska received funding for the current manuscript from the National Science Centre, Poland (DEC-2014/15/B/N27/00998), grant PRNF-218-AI-1/07 from Norway through the Norwegian Financial Mechanisms within the Polish–Norwegian Research Fund, and the Ministry of Science and Higher Education, Poland (PBZ-MEiN-/8/2//2006). G. Roberts is president of the BSACI. A.C. Santos received funding for the current manuscript from FCT Investigators contracts (IF/01060/2015). J. Sunyer received a grant from the European Research Council (Prenatal exposure to urban AIR pollution and pre- and postNatal Brain development (AIR-NB), 785994). J. Usemann received grants from the Palatin Foundation, University of Basel Switzerland, Swiss Cancer League and Swiss Lung Foundation, and payments or honoraria for lectures from Vertex and Zurich Lung Foundation. V.W.V. Jaddoe received a grant from the European Research Council (ERC-2014-CoG-648916). L. Duijts received funding from cofunded ERA-Net on Biomarkers for Nutrition and Health

(ERA HDHL), Horizon 2020 (696295; 2017), the Netherlands Organisation for Health Research and Development (ZonMw; 529051014; 2017), Science Foundation Ireland (SFI/16/ERA-HDHL/3360), and the European Union (ALPHABET project). All other authors declare no conflict of interest.

Comment in

- [The lower respiratory tract: the hot spot for chronic fixed airflow limitation.](#) Polverino F, Marin JM. *Eur Respir J*. 2022 Oct 6;60(4):2201214. doi: 10.1183/13993003.01214-2022. Print 2022 Oct. PMID: 36202404 No abstract available.
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. 2022 Oct 6;60(4):2102446.

doi: 10.1183/13993003.02446-2021. Print 2022 Oct.

[Impact of former smoking exposure on airway eosinophilic activation and autoimmunity in patients with severe asthma](#)

[Ditte K Klein](#)^{1,2}, [Alexander Silberbrandt](#)^{1,2}, [Laurits Frøssing](#)¹, [Morten Hvidtfeldt](#)¹, [Anna von Bülow](#)¹, [Parameswaran Nair](#)³, [Manali Mukherjee](#)³, [Celeste Porsbjerg](#)⁴

Affiliations expand

- PMID: 35236724
- DOI: [10.1183/13993003.02446-2021](https://doi.org/10.1183/13993003.02446-2021)

Abstract

Introduction: Severe eosinophilic asthma is characterised by frequent exacerbations and a relative insensitivity to steroids. Experimentally, smoking may induce eosinophilic airway inflammation, but the impact in patients with severe asthma is not clear.

Objective: To investigate the association between smoking exposure in patients with severe asthma, and eosinophilic inflammation and activation, as well as airway autoimmunity and steroid responsiveness.

Methods: Patients with severe asthma according to European Respiratory Society/American Thoracic Society criteria were assessed with sputum samples, analysed by cell differential count, and for the presence of free eosinophil granules (FEGs), autoantibodies against eosinophil peroxidase (EPX) and macrophage receptor with collagenous structure (MARCO). A subgroup of patients with eosinophilic airway inflammation was re-assessed after a 2-week course of prednisolone.

Results: 132 severe asthmatics were included in the study. 39 (29.5%) patients had ≥ 10 pack-years of smoking history: 36 (27.3%) were former smokers and three (2.3%) current smokers; and 93 (70.5%) had < 10 pack-years exposure. Eosinophilic airway inflammation was more prevalent among patients with ≥ 10 pack-years (66.7%), compared to patients with < 10 pack-years (38.7%, $p=0.03$), as was the level of FEGs ($p=0.001$) and both anti-EPX and anti-MARCO ($p<0.05$ and $p<0.0001$, respectively). Omitting current smokers did not affect these associations. Furthermore, prednisolone reduced, but did not normalise, sputum eosinophils in patients with a ≥ 10 pack-year smoking history.

Conclusion: In patients with severe asthma, a former smoking history is associated with eosinophilic airway inflammation and activation and relative insensitivity to steroids, as well as airway autoimmunity.

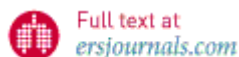
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Conflict of interest statement

Conflict of interest: D.K. Klein declares no competing interests. A. Silberbrandt declares no competing interests. L. Frøssing declares payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from GlaxoSmithKline, in the 36 months prior to manuscript submission. M. Hvidtfeldt declares no competing interests. A. von Bülow declares grants from Novartis Healthcare, Denmark; payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from AstraZeneca, GlaxoSmithKline and Novartis; and participation on a data safety monitoring board or advisory board for Novartis, all in the 36 months prior to manuscript submission. P. Nair reports grants and personal fees from AstraZeneca, grants from Novartis, grants and personal fees from Teva, grants from Sanofi, grants and personal fees from Roche, personal fees from Novartis, personal fees from Merck, personal fees from Equillium, grants from Foresee, outside the submitted work. M. Mukherjee reports grants from Canadian Institutes of Health Research, grants from Methapharm Specialty Pharmaceuticals, personal fees from AstraZeneca, personal fees from GlaxoSmithKline, outside the submitted work. C. Porsbjerg declares grants, consulting fees and payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from AstraZeneca, GlaxoSmithKline, Novartis, Teva, Sanofi, Chiesi and ALK, all in the 36 months prior to manuscript submission.

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RHINITIS

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. 2022 Oct 6;2200943.

doi: 10.1183/13993003.00943-2022. Online ahead of print.

Rhinitis phenotypes and multimorbidities in the general population Constances cohort

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Affiliations expand

- PMID: 36202419
- DOI: [10.1183/13993003.00943-2022](https://doi.org/10.1183/13993003.00943-2022)

Abstract

Background: Scarce epidemiological studies have characterised allergic rhinitis (AR) and non-allergic rhinitis (NAR) in adults.

Aims: In a population-based cohort, to (1) describe rhinitis, AR and NAR, and (2) explore how asthma and conjunctivitis may lead to the identification of novel rhinitis phenotypes.

Methods: In this cross-sectional analysis, current rhinitis was defined in the last 12 months using questionnaire from the French Constances cohort. Participants with current rhinitis reporting nasal allergies were considered as AR, otherwise as NAR. We described AR and NAR phenotypes, and their phenotypes including co-occurrence with ever-asthma and ever-conjunctivitis.

Results: Among the 20 772 participants included in this analysis (55.2% women, mean age: 53±13 years), crude prevalences of AR and NAR were 28.0% and 10.9%. AR participants reported more frequently persistent rhinitis (31.6% *versus* 25.1%), and moderate to severe rhinitis (40.1% *versus* 24.2%) than NAR participants. Among AR or NAR participants, those with ever-asthma reported more moderate-severe rhinitis. Participants with AR, ever-asthma, and ever-conjunctivitis had an earlier age of rhinitis onset, more severe rhinitis, and higher eosinophil counts than participants in other groups. Results were replicated in another cohort.

Conclusions: In this large population-based cohort, 40% reported current rhinitis, with a lower prevalence of moderate-severe rhinitis than in clinical practice. For the first time in a general adult population, we showed that AR and NAR alone or in combination with asthma or in combination with asthma and conjunctivitis are different phenotypes. These results provide new insights on how best to manage rhinitis and its multimorbidities.

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PLoS One



. 2022 Oct 6;17(10):e0274951.

doi: [10.1371/journal.pone.0274951](https://doi.org/10.1371/journal.pone.0274951). eCollection 2022.

[GSDM gene polymorphisms regulate the IgE level in asthmatic patients](#)

[Amer Imraish](#)¹, [Tuqa Abu-Thiab](#)¹, [Tareq Alhindi](#)¹, [Malek Zihlif](#)²

Affiliations [expand](#)

- PMID: 36201519
- PMCID: [PMC9536611](#)
- DOI: [10.1371/journal.pone.0274951](https://doi.org/10.1371/journal.pone.0274951)

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Abstract

Background: Gasdermin A (GSDMA) and gasdermin B (GSDMB) have been associated with childhood and adult asthma in many populations including the Jordanian population. It is also known that IgE plays a crucial role in various allergic disorders, such as elevated levels of total serum IgE were detected in asthma and allergic rhinitis. IgE immunoglobulin is responsible for the release of numerous inflammatory mediators, such as histamine and prostaglandins, from mast cells in asthmatic patients.

Objective: In this study, single nucleotide polymorphisms of GSDMA (rs7212938, T/G) and GSDMB (rs7216389, T/C) in Jordanian population were investigated for their association with total IgE levels in serum of asthmatic children and adult subjects.

Methods: The genetic polymorphism analysis for SNPs was performed using the polymerase chain reaction (PCR)/restriction fragment length polymorphism method (RFLP). Three analysis models were applied to the genotype data: co-dominant, dominant and recessive.

Results: Our data demonstrate a significant correlation between GSDMB genetic SNP (rs7216389) and the total IgE serum level. Where one minor allele in the GSDMB gene is sufficient to induce significant changes in the IgE serum levels and plays a role in the pathogenesis of asthma in asthmatic children of the Jordanian population. Suggesting that this polymorphism might have a protective effect against asthma risk. While the presence of the GSDMB polymorphism alone might not be sufficient to associate with the high risk of developing asthma or responding to it in adults in Jordanian population.

Conclusion: In conclusion, the current study confirms the significant association of GSDMB genetic SNP (rs7216389) with IgE levels in asthma patients in Jordanian population, while no significant correlation of GSDMA and IgE level was found in both child and adult asthmatic patients.

Conflict of interest statement

The authors have declared that no competing interests exist.

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J Investig Allergol Clin Immunol

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. 2022 Oct 6;0.

doi: 10.18176/jiaci.0865. Online ahead of print.

The influence of BMI in asthma. Which traits are due to obesity and which to asthma and obesity phenotype?

[I Esteban-Gorgojo](#)¹, [M P Gorgojo](#)², [J Sastre](#)^{3,4,5}, [F García-Río](#)^{4,5,6}, [S Quirce](#)^{4,5,7}

Affiliations expand

- PMID: 36200980
- DOI: [10.18176/jiaci.0865](https://doi.org/10.18176/jiaci.0865)

Abstract

Background and objectives: Characteristics of the asthma and obesity phenotype have been described by cluster studies, but they have not been subsequently confirmed. Specific characteristics of this phenotype have not been differentiated from those inherent to the patient's body mass index (BMI). This study aims to assess the effect of BMI on asthma. This will allow to identify which traits could define the asthma and obesity phenotype, and which are inherent to the patient's BMI.

Methods: A real-life retrospective observational study was conducted with a 2,514 patients database. Data was collected on the first visit to the Allergy clinic of all patients who underwent a correct spirometry maneuver due to suspected asthma between November 2014 and November 2017. All BMI, sex and age groups were represented.

Results: BMI influence over asthma differed in different age groups and genders. All spirometric results and FeNO were influenced by BMI. Concerning asthma characteristics

only a later asthma onset with higher BMI values was observed. No other differences were found between different BMI groups.

Conclusions: The effect of BMI on asthma is age dependent, so it should be corrected for age. The most important variations are on FeNO and spirometric results. The specific characteristics of the asthma and obesity phenotype are a greater perception of symptoms with fewer alterations in respiratory function tests and a lower prevalence of atopy, rhinitis and allergy, including allergic asthma. Other characteristics of this phenotype, such as a higher women prevalence or being late-onset or non-eosinophilic asthma, are non-specific for this phenotype.

Keywords: Asthma; Asthma and obesity; BMI; Obesity; Phenotype; Severe asthma.

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BMC Med Res Methodol

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. 2022 Oct 5;22(1):262.

doi: 10.1186/s12874-022-01730-6.

[Reporting of the safety from allergic rhinitis trials registered on ClinicalTrials.gov and in publications: An observational study](#)

[Ivan Paladin](#)¹, [Shelly Melissa Pranić](#)²

Affiliations [expand](#)

- PMID: 36199040

- PMCID: [PMC9533497](#)

- DOI: [10.1186/s12874-022-01730-6](https://doi.org/10.1186/s12874-022-01730-6)

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Abstract

Background: Incomplete and inconsistent reporting of adverse events (AEs) through multiple sources can distort impressions of the overall safety of the medical interventions examined as well as the benefit-risk relationship. We aimed to assess completed allergic rhinitis (AR) trials registered in ClinicalTrials.gov for completeness and consistency of AEs reporting comparing ClinicalTrials.gov and corresponding publications.

Methods: We retrospectively examined completed randomised controlled trials on AR registered in ClinicalTrials.gov on or after 9/27/2009 to trials updated with results on or before 12/31/2021 along with any corresponding publications. Complete reporting of AEs in ClinicalTrials.gov were summarised in tables describing AE information, and complete reporting in publications was an explicit statement of serious AE, death or other AE. Difference in completeness, number, or description of AEs between ClinicalTrials.gov and publication was classified as inconsistent reporting of AEs.

Results: There were 99 registered trials with 45 (45.5%) available publications. All published trials completely reported AEs in ClinicalTrials.gov, and 21 (46.7%) in publications ($P < .001$). In 43 (95.6%) publications, there was at least one inconsistency in the reporting of AEs ($P < .001$). 8 (17.8%) publications had different number of serious AEs ($P = .003$), 36 (80.0%) of other AEs ($P < .001$) while deaths reporting was inconsistent in 8 (57.1%) publications ($P = .127$).

Conclusion: The reporting of AEs from AR trials is complete in ClinicalTrials.gov and incomplete and inconsistent in corresponding publications. There is a need to improve the reporting of AEs from AR trials in corresponding publications, and thus to improve patient safety.

Keywords: Adverse events; Allergic rhinitis; ClinicalTrials.gov; Completeness; Randomised controlled trial; Safety.

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- 1 figure

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Environ Health

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. 2022 Oct 3;21(1):90.

doi: 10.1186/s12940-022-00902-7.

Does early life exposure to exogenous sources of reactive oxygen species (ROS) increase the risk of respiratory and allergic diseases in children? A longitudinal cohort study

[Teresa To](#)^{1,2,3}, [Emilie Terebessy](#)⁴, [Jingqin Zhu](#)^{4,5}, [Kimball Zhang](#)^{4,5}, [Pascale Sj Lakey](#)⁶, [Manabu Shiraiwa](#)⁶, [Marianne Hatzopoulou](#)⁷, [Laura Minet](#)⁸, [Scott Weichenthal](#)^{9,10}, [Sharon Dell](#)^{11,12}, [Dave Stieb](#)¹³

Affiliations [expand](#)

- PMID: 36184638
- PMCID: [PMC9528154](#)
- DOI: [10.1186/s12940-022-00902-7](#)

Free PMC article

Abstract

Background: Excess reactive oxygen species (ROS) can cause oxidative stress damaging cells and tissues, leading to adverse health effects in the respiratory tract. Yet, few human epidemiological studies have quantified the adverse effect of early life exposure to ROS on child health. Thus, this study aimed to examine the association of levels of ROS exposure at birth and the subsequent risk of developing common respiratory and allergic diseases in children.

Methods: 1,284 Toronto Child Health Evaluation Questionnaire (T-CHEQ) participants were followed from birth (born between 1996 and 2000) until outcome, March 31, 2016 or loss-to-follow-up. Using ROS data from air monitoring campaigns and land use data in Toronto, ROS concentrations generated in the human respiratory tract in response to inhaled pollutants were estimated using a kinetic multi-layer model. These ROS values were assigned to participants' postal codes at birth. Cox proportional hazards regression models, adjusted for confounders, were then used to estimate hazard ratios (HR) with 95% confidence intervals (CI) per unit increase in interquartile range (IQR).

Results: After adjusting for confounders, iron (Fe) and copper (Cu) were not significantly associated with the risk of asthma, allergic rhinitis, nor eczema. However, ROS, a measure of the combined impacts of Fe and Cu in PM_{2.5}, was associated with an increased risk of asthma (HR = 1.11, 95% CI: 1.02-1.21, $p < 0.02$) per IQR. There were no statistically significant associations of ROS with allergic rhinitis (HR = 0.96, 95% CI: 0.88-1.04, $p = 0.35$) and eczema (HR = 1.03, 95% CI: 0.98-1.09, $p = 0.24$).

Conclusion: These findings showed that ROS exposure in early life significantly increased the childhood risk of asthma, but not allergic rhinitis and eczema.

Keywords: Air pollution; Allergic rhinitis; Asthma; Early life exposures; Eczema; Reactive oxygen species.

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Conflict of interest statement

The authors declare that they have no competing interests.

- [21 references](#)
- [1 figure](#)

SUPPLEMENTARY INFO

MeSH terms, Substances, Grant support[expand](#)

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CHRONIC COUGH

1

Review

Lancet Respir Med

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. 2022 Oct 4;S2213-2600(22)00228-4.

doi: 10.1016/S2213-2600(22)00228-4. Online ahead of print.

Home monitoring in interstitial lung diseases

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- PMID: 36206780
- DOI: [10.1016/S2213-2600\(22\)00228-4](https://doi.org/10.1016/S2213-2600(22)00228-4)

Abstract

The widespread use of smartphones and the internet has enabled self-monitoring and more hybrid-care models. The COVID-19 pandemic has further accelerated remote monitoring, including in the heterogeneous and often vulnerable group of patients with interstitial lung diseases (ILDs). Home monitoring in ILD has the potential to improve access to specialist care, reduce the burden on health-care systems, improve quality of life for patients, identify acute and chronic disease worsening, guide treatment decisions, and simplify clinical trials. Home spirometry has been used in ILD for several years and studies with other devices (such as pulse oximeters, activity trackers, and cough monitors) have emerged. At the same time, challenges have surfaced, including technical, analytical, and implementational issues. In this Series paper, we provide an overview of experiences with

home monitoring in ILD, address the challenges and limitations for both care and research, and provide future perspectives. VIDEO ABSTRACT.

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Conflict of interest statement

Declaration of interests MSW reports grants from Boehringer Ingelheim, Hoffman la Roche, The Netherlands Organisation for Health Research and Development, The Dutch Lung Foundation, and The Dutch Pulmonary Fibrosis Foundation; consulting fees from Boehringer Ingelheim, Hoffman la Roche, Galapagos, Bristol Myers Squibb (BMS), Galecto, Respivant, Nerretherapeutics, PureTech Health, Kinevant Sciences, Molecure, Horizontherapeutics, and CSL Behring; speaker fees from Boehringer Ingelheim, Hoffman la Roche, and Novartis; support for attending meetings from Boehringer Ingelheim, Hoffman la Roche, and Galapagos; and DSMB fees from Savara and Galapagos. All grant and fees were paid to her institution. CCM reports grants from Boehringer Ingelheim and AstraZeneca; and speakers fees from Boehringer Ingelheim and Hoffman-la Roche. All grants and fees were paid to her institution. KAJ reports grants from Three Lakes Foundation, Chest Foundation, University of Calgary, and University Hospital Foundation; consulting fees from Boehringer Ingelheim, Hoffman-La Roche, Pliant, and Three Lakes Foundation; and speaker fees from Boehringer Ingelheim and Hoffman-La Roche. PDJ reports grants from the Pulmonary Foundation Scholar Award, Chest/ATS Foundation COVID19 diversity grant, VCU DOIM Pilot award, and NIH Fogarty Fellowship; and speaker fees from the Virginia Association of Community Psychiatric Nurses. YHK reports grants from the National Health and Medical Research Council Investigator Grant, Centre of Research Excellence in Pulmonary Fibrosis PACT Grant-in-Aid and CREATE Grant-in-Aid, Austin Medical Research Foundation Research Grant, Royal Australasian College of Physicians Research Establishment Fellowship and Robert and Elizabeth Albert Travel Grant, and Lung Foundation Australia-Lizotte Family Award for Idiopathic Pulmonary Fibrosis Research. YK reports speaker fees from Asahi Kasei Pharma, Shionogi, Boehringer Ingelheim, AstraZeneca, Eisai, KYORIN Pharmaceutical, Mitsubishi Tanabe Pharma, and Novartis Pharma; and advisory board fees from Shionogi, Boehringer Ingelheim, Taiho Pharmaceutical, Chugai Pharmaceutical, Janssen Pharmaceutical, and Healios. GCT reports consulting fees from Boehringer Ingelheim and Knight pharmaceuticals; and speaker fees from Boehringer Ingelheim, Tutear, Raffo, AstraZeneca and Knight pharmaceuticals. BEV reports travel support from Boehringer Ingelheim, Raffo, Roche, Bago, and Tutear; and advisory board fees from Boehringer Ingelheim, and Tutear. RNvZ-S reports consulting fees from Aspen/GlaxoSmithKline (GSK), Novartis, and Boehringer Ingelheim; speaker fees from Novartis, Pfizer, Johnson & Johnson, MSD, AstraZeneca, Hoffman la Roche, Philips, and Cipla. MK reports grants from Boehringer Ingelheim and Hoffman-La Roche; consulting fees from Boehringer Ingelheim, Hoffman-La Roche, and Galapagos; and speaker fees from Boehringer Ingelheim and Hoffman-La Roche. TMM reports consulting fees from Boehringer Ingelheim, Roche/Genentech, AstraZeneca, Bayer, Blade Therapeutics, BMS, Galapagos, Galecto, GSK, IQVIA, Pliant, Respivant, Theravance, and

Veracyte; and speaker fees from Boehringer Ingelheim and Roche/Genentech. SKR and PvdW declare no competing interests.

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. 2022 Oct 6.

doi: 10.1007/s10388-022-00953-2. Online ahead of print.

Efficacy of laparoscopic fundoplication in patients with chronic cough and gastro-oesophageal reflux

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- PMID: 36201134
- DOI: [10.1007/s10388-022-00953-2](https://doi.org/10.1007/s10388-022-00953-2)

Abstract

Background: The outcome of anti-reflux surgery in patients with suspected gastro-oesophageal reflux-induced cough is frequently uncertain. The aims of this study were to assess the efficacy of laparoscopic fundoplication for controlling cough in patients with chronic cough without asthma, who have pathologic gastro-oesophageal reflux, and to identify predictors of response.

Methods: From a prospective database of 1598 patients who have undergone laparoscopic fundoplication, 66 (4%) with proven gastro-oesophageal reflux disease (GORD) and chronic cough without asthma were studied. All patients underwent gastroscopy and 24-h pH monitoring before operation. Heartburn and regurgitation were assessed using a modified DeMeester score. Severity of cough before and after surgery was self-assessed by the patient using a visual analog scale at a minimum of 12 months post-operatively (median 43 mo; range: 14-104 mo). Patients were considered to have responded to fundoplication if they had no cough or the cough had improved by 50% or more after operation.

Results: Cough and heartburn/regurgitation were relieved in 61% (40/66) and 90% (44/49) of the patients, respectively. The presence of typical GORD symptoms or oesophagitis, and pH study variables did not predict the response of the cough to fundoplication.

Conclusion: Refinement in the aetiological diagnosis of chronic cough due to GORD is necessary for improved outcome. Patients diagnosed with GORD-related chronic cough need to be counseled regarding their expectations from anti-reflux surgery.

Keywords: Cough; Fundoplication; Gastroesophageal reflux; Laparoscopy.

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