COPD Research Review™

Making Education Easy

Issue 77 - 2025

In this issue:

Abbreviations used in this issue:

CAT = COPD Assessment Test; **COPD** = chronic obstructive pulmonary disease; **CT** = computed tomography; **FEV_1** = forced expiratory volume in 1 s; **FVC** = forced vital capacity; **HDL** = high-density lipoprotein; **MHR** = monocyte-to-HDL cholesterol ratio; **mMRC** = modified Medical Research Council; **NHHR** = non-HDL cholesterol-to-HDL cholesterol ratio; **PR** = pulmonary rehabilitation.

Welcome to the latest issue of COPD Research Review.

In this issue, a pilot study uses spirometry to validate the "probable COPD" definition proposed by the Lancet Commission, a meta-analysis reminds us of the value of inhaler technique education, dupilumab shows promise when added to standard triple therapy in patients with COPD and eosinophilic inflammation, German and Swiss investigators assess the utility of smartphone app-based pulmonary rehabilitation, and an analysis of NHANES data provides more evidence of the importance of cardiovascular risk factors in patients with COPD.

We hope you find these and the other selected studies interesting and welcome any feedback you may have.

Kind Regards,

Associate Professor Stephen Milne
stephen.milne@researchreview.com.au

Validation of probable COPD as proposed by the Lancet Commission at a smoking cessation clinic

Authors: Yazar EE et al.

Summary: This pilot study at a smoking cessation clinic used spirometry to validate the "probable COPD" definition proposed by the Lancet Commission (presence of respiratory symptoms or exacerbation in risky people, and CAT score ≥10 points). Two hundred and twenty-four individuals aged ≥40 years (mean age 53.2 years, 49.6% female) with a smoking history of ≥15 pack-years completed a detailed case report form, including the CAT questionnaire, and underwent spirometry testing. Ninety individuals were identified as having probable COPD according to the Lancet Commission's definition. Among these individuals, 21 (23.3%) were also diagnosed with COPD based on spirometry (pre-bronchodilator FEV_1/FVC ratio). Of the 134 participants who did not meet the Lancet Commission's criteria for probable COPD, 12 (9%) were diagnosed with COPD using spirometry (p=0.003).

Comment: The Lancet Commission on COPD proposed identifying "probable COPD" in resource-limited settings where spirometry and/or CT scanning are poorly available. In this analysis, 21 out of 90 patients with probable COPD actually had spirometrically-confirmed COPD. This proportion (23%) seems low and, at face value, could be interpreted that the "probable COPD" definition has poor sensitivity for detecting true COPD. However, I would argue that it is the spirometry that has poor sensitivity. Patients with exposure (smoking) and symptoms (especially chronic cough or sputum) but normal spirometry have faster lung function decline, experience acute exacerbations, and utilise healthcare resources. For all intents and purposes, they have COPD even if their spirometric ratio does not yet reflect it. We still need strategies for how to intervene in this probable or pre-COPD group – smoking cessation at a minimum, but perhaps focusing on comorbidities and exercise too.

Reference: Respir Med. 2025;239:108004
Abstract

Clinical and prognostic differences in mild to moderate COPD with and without emphysema

Authors: Yang H et al.

Summary: This analysis of the SPIROMICS cohort investigated the clinical and prognostic characteristics of mild-to-moderate COPD with versus without emphysema. 989 patients with mild-to-moderate COPD were categorised into two groups according to whether they also had emphysema (n=428), or no emphysema (n=561) on CT scans. The annual decline in FEV_1 was –56.1 ml/year in the emphysema group and –46.9 ml/year in the no-emphysema group (p=ns). The rate of emphysema progression was significantly slower in the emphysema group, but they had a more pronounced annual increase in the St. George's Respiratory Questionnaire score and a higher rate of acute respiratory exacerbations (0.36 vs 0.25 per person-year; rate ratio 1.42, 95% CI 1.27–1.54) than the no-emphysema group.

Comment: We know that the decline in lung function is greatest in the early stages of COPD. We also know that emphysema extent is a predictor of accelerated lung function decline and poor clinical outcomes. However, we don't know much about how emphysema modifies disease trajectories in this early stage of COPD. In this study, the presence of emphysema on CT chest in mild-moderate COPD was not associated with accelerated FEV_1 decline over time, but it was associated with poorer quality of life and increased exacerbations. Assessing the extent of emphysema in mild-moderate COPD may therefore be important for risk stratification in these patients – beyond what we can predict from spirometry.

Reference: Chest 2025;167(3):724–35
Abstract

Identifying abnormal exertional breathlessness in COPD: Comparing modified Medical Research Council and COPD Assessment Test with cardiopulmonary exercise testing

Authors: Ekström M et al., for the CanCOLD Collaborative Research Group

Summary: This analysis of the CanCOLD cohort investigated the utility of the mMRC scale and CAT for detecting abnormally high exertional breathlessness on incremental cardiopulmonary cycle exercise testing (CPET) in patients with COPD. 318 patients with COPD (mean age 66.5 years, 40% female, FEV_1 79.5% predicted) were included. Twenty-four percent of patients had abnormally high exertional breathlessness on CPET despite 9% of them having an mMRC score of 0 and 11% having a CAT score of <10. An mMRC score ≥2 together with a CAT score ≥10 was most specific (95%) for detecting abnormal exertional breathlessness, but had low sensitivity (12%). Compared with patients with true-negative findings, those with abnormal exertional breathlessness but false-negative findings (low mMRC score, low CAT scores, or both) had worse physiological outcomes during CPET and were more likely to have physician-diagnosed COPD.

Comment: We know that some patients tend to under report their degree of breathlessness on exertion, and this is probably because they limit their activity to avoid the uncomfortable and often distressing symptom. This study confirms that our standard questionnaires (mMRC, CAT) do not correlate very well with 'abnormal' or excessive exertional breathlessness when measured during exercise testing. This exposes a limitation of standardised questionnaires, and reminds us that careful history taking is necessary to fully understand the impact of COPD on quality of life. For example: what activities have you stopped doing because of breathlessness? The answer could be more revealing than any symptom score.

Reference: Chest 2025;167(3):697–711
Abstract

Earn CPD

CPD Home. Subscribers can claim the time spent reading and evaluating research reviews as an Educational Activity: Professional Reading in the CPD Tracker. Please Contact Us for support.

Kindly Supported by

The Thoracic Society of Australia & New Zealand
LEADERS IN LUNG HEALTH

Peak inspiratory flow and inhaler prescription strategies in a specialized COPD clinical program

Authors: Pankovitch S et al.

Summary: This real-world observational study investigated the prevalence of suboptimal peak inspiratory flow (PIF) in patients attending a specialised COPD clinic, and their prescription inhaler strategies. Of 161 patients included in the analysis, 45 (28%) were found to have suboptimal PIF and 18 (11.2%) were using inappropriate devices for their measured PIF. Significant associations were observed between suboptimal PIF and age, female sex, height, BMI, and FEV_1. A total of 59 (36.6%) patients were using inhaler regimens with either inappropriate devices for measured PIF and/or non-single inhaler therapy (SIT)/non-similar devices.

Comment: The best inhaler is the one the patient will actually use, and use properly. There is a particular interest in the role of PIF for ensuring adequate inhalation of medications from inhalers, but most clinicians are probably not measuring this during inhaler technique checks. In this study, more than 10% of the patients studied had been prescribed an inappropriate inhaler based on their PIF; these are patients who are not getting the optimum dose of inhaled medication, regardless of their overall inhaler technique. Independent predictors of suboptimal PIF included female sex, lower FEV_1, and low BMI – in situations where time and resources are limited, perhaps a targeted strategy for measuring PIF in high-risk patients would be appropriate.

Reference: Chest 2025;167(3):736–45
Abstract

Inhalation technique-related errors after education among asthma and COPD patients using different types of inhalers – systematic review and meta-analysis

Authors: Marko M & Pawliczak R

Summary: This systematic review and meta-analysis investigated the impact of education on inhalation skills in patients with asthma or COPD using dry powder inhalers (DPIs) or pressurised metered dose inhalers (MDIs). A search of various databases identified 12 studies that were suitable for inclusion. Meta-analysis of the data showed that education reduced the number of critical errors (risk ratio [RR] 0.28, 95% CI 0.17–0.47; p<0.00001) and incorrect use events for DPIs (RR 0.38, 95% CI 0.21–0.70; p=0.002) and MDIs (RR 0.16, 95% CI 0.11–0.23; p<0.00001).

Comment: Just in case we needed more evidence that assessing and modifying inhaler technique is important, this systematic review and meta-analysis tells us that education strategies work regardless of the type of inhaler – although the benefits were greater with MDIs relative to DPIs, probably because there are greater chances of errors with MDIs in the first place. Note that there was a relatively high risk of bias in these studies, and it does not tell us exactly which educational methods are the most effective. Regardless, we should always endeavour to improve inhaler technique at any opportunity.

Reference: NPJ Prim Care Respir Med. 2025;35(1):15
Abstract

Earn CPD

Nursing and Midwifery Board of Australia (NMBA) Journal reading and watching videos (including Research Reviews') may be considered a self-directed activity set out in the NMBA Registration Standard: Continuing Professional Development. One hour of active learning will equal one hour of CPD. Details at NMBA CPD page.

Earn CPD

Royal Australasian College of Physicians (RACP) MyCPD participants can claim the time spent reading and evaluating research reviews as CPD in the online MyCPD program. Please contact MyCPD@racp.edu.au for any assistance.

RESEARCH REVIEW™
Australia's Leader in Specialist Publications

Dupilumab for chronic obstructive pulmonary disease with type 2 inflammation: A pooled analysis of two phase 3, randomised, double-blind, placebo-controlled trials

Authors: Bhatt SP et al.

Summary: This pooled analysis of the BOREAS and NOTUS trials investigated the efficacy and safety of dupilumab in patients with COPD and type 2 inflammation. A total of 1874 patients with COPD and a blood eosinophil count ≥300 cells/μL were randomised 1:1 to receive subcutaneous dupilumab 300mg or matching placebo every 2 weeks for 52 weeks, on top of established background therapy with inhaled corticosteroids, a long-acting β_2-agonist, and a long-acting muscarinic antagonist. During the 52-week treatment period, moderate or severe exacerbations were reported in 36.0% of patients in the dupilumab group and 42.1% of patients in the placebo group. The annualised rate of moderate or severe exacerbations in the dupilumab group was lower than that in the placebo group (0.794 vs 1.156; incidence rate ratio 0.687, 95% CI 0.595–0.793; p<0.0001). The time to first severe exacerbation was longer in the dupilumab group than in the placebo group, but there was no reduction in the annualised rate of severe exacerbations. Treatment-emergent adverse events did not differ significantly between groups.

Comment: This pooled analysis of the BOREAS and NOTUS trials of dupilumab in COPD with eosinophilia confirmed the findings of the primary studies, but also allowed more thorough subgroup analysis due to larger participant numbers. Interestingly, and unlike some other previous analyses, a higher peripheral blood eosinophil count did not modify the effect very much at all – participants had to have a count of >300 cells/μL to enter the study, but dupilumab was equally as effective at the lower and higher ends of the eosinophil spectrum. This probably speaks to the effects of dupilumab outside the eosinophilic pathway and modifying other elements of type 2 inflammation, as evidenced by the decrease in fractional exhaled nitric oxide (FeNO) and immunoglobulin E levels. Now that dupilumab is on its way for treating COPD, it will be interesting to see the effects outside the clinical trial setting.

Reference: Lancet Respir Med. 2025;13(3):234–43
Abstract

Short-term effects of home-based pulmonary rehabilitation during outpatient-managed exacerbations of COPD

Authors: Machado A et al.

Summary: This Portuguese study investigated the short-term impact of a home-based PR programme for patients with outpatient-managed exacerbations of COPD. Fifty patients (mean 70 years, 78% male, FEV_1 47.4% predicted) with outpatient-managed COPD exacerbations were randomised to usual care alone (controls) or in conjunction with home-based PR for 3 weeks commencing within 48h of diagnosis. When assessed after 3 weeks, the PR group had significantly greater improvements in CAT scores compared with controls (p=0.002), and also in 12 of 13 secondary outcome measures.

Comment: We already know that early commencement of PR after an acute hospitalised exacerbation of COPD is safe and effective, but this study examined a less-well-studied group: the milder, outpatient-managed exacerbations. The improvements compared to standard of care (medications alone) were quite impressive: physical attributes such as grip strength improved as we would expect following an exercise intervention, but other aspects such as cough symptoms also improved quite dramatically. Overall this suggests that PR following an outpatient COPD exacerbation is associated with faster recovery in both symptoms and functional status. The challenge remains how to identify these patients in primary care and provide a pathway to PR.

Reference: Thorax 2025;80(4):218–26
Abstract

Smartphone application-based pulmonary rehabilitation in COPD

Authors: Gloeckl R et al.

Summary: This multicentre randomised controlled trial investigated the utility of smartphone app-based PR in patients with COPD. At 18 sites in Germany and Switzerland, 278 patients with COPD (median age 65 years, FEV_1 48% predicted) were randomised to use a mobile PR app (Kaia COPD®) or enhanced standard-of-care (control group) for 12 weeks. Quality of life was measured by CAT, and exercise capacity was assessed by 1-min-sit-to-stand-test (1MSTST). At week 12, CAT score had improved from baseline by a median −4 points in the intervention group and −3 points in the control group (p=ns), and 1MSTST had improved by 1 versus 2 repetitions in the respective groups (p=ns). When the intervention group was divided according to adherence (≥3 days/week for ≥75% of the weeks), adherent users (40.4%) improved 1MSTST versus non-adherent users by a median 2 repetitions (p=0.006). There were no safety concerns.

Comment: The use of smartphone apps to improve PR access and uptake is very welcome. The lack of superiority of the app-based intervention compared to conventional face-to-face PR should not be discouraging, since it suggests that an app-based programme may be a feasible and equivalent alternative that produces similar outcomes. However, this study once again showed that adherence to PR is critical to improving clinical outcomes. In this group, the 40% of participants who adhered to the app-based programme ≥3 days/week for ≥75% of the weeks significantly improved their functional exercise status. So while we are focusing on developing alternative PR programmes using remote technology, efforts to incorporate adherence measures may be critical to the success of the programme.

Reference: Thorax 2025;80:209–17
Abstract

Independent commentary by Associate Professor Stephen Milne

Stephen is an Associate Professor in Medicine at Sydney Medical School, The University of Sydney, and a Staff Specialist (Ludwig Engel Fellow) respiratory physician at Westmead Hospital. His current research programme focuses on the discovery of novel biomarkers in COPD.

MHR as a promising predictor for coronary artery disease in COPD patients: Insights from a retrospective nomogram study

Authors: Sun F et al.

Summary: This retrospective case-control study evaluated risk factors for coronary artery disease (CAD) in patients with COPD. Four hundred and six patients with COPD who underwent coronary artery CT angiography (CCTA) were categorised into co-CAD and non-CAD groups based on CCTA findings. Demographic and laboratory data were used to determine independent risk factors for CAD. The co-CAD group was significantly older than the non-CAD group, and had a higher prevalence of males and individuals with hypertension, diabetes, cardiovascular/cerebrovascular diseases, and lower FEV_1 values. The co-CAD group also had higher levels of glycated haemoglobin, interleukin-6, monocyte count, and monocyte-to-HDL cholesterol ratio (MHR). Multivariate logistic regression showed that age, hypertension, and MHR were independent predictors of CAD in patients with COPD. A nomogram incorporating these predictors showed robust predictive accuracy with an area under the receiver-operating characteristic curve of 0.758.

Comment: We know that cardiovascular comorbidities are highly prevalent in COPD, but this study asks if there are ways we can better predict exactly which patients are likely to have CAD within this already high-risk group. MHR is a relatively new marker used to assess cardiovascular risk. In theory, the ratio of monocytes to HDL cholesterol describes the balance of proinflammatory and antioxidant factors in circulation. An independent association between MHR and CAD in this group is interesting, but how it would fit into our current cardiovascular risk stratification algorithms would need further study. After all, the presence of COPD itself is considered a strong risk factor for CAD – the cardiologists know this better than we do!

Reference: Respir Med. 2025;239:107993
Abstract

Association between the non-high-density lipoprotein cholesterol-to-high-density lipoprotein cholesterol ratio (NHHR) and mortality in patients with COPD: Evidence from the NHANES 1999-2018

Authors: Zhong Y et al.

Summary: NHHR is a new composite blood lipid index. This study used NHANES 1999–2018 data to investigate the association between NHHR and mortality in patients with COPD. After adjusting for confounding factors, weighted multivariate Cox proportional hazards regression models showed that higher NHHR was not significantly associated with all-cause mortality, cardiovascular disease mortality, or chronic lower respiratory disease-related mortality. However, restricted cubic splines revealed a U-shaped association between NHHR and all-cause mortality, and Kaplan-Meier survival analysis revealed a significantly lower survival rate for patients in the high-NHHR group.

Comment: This analysis from the NHANES cohort provides even more evidence for the importance of cardiovascular risk factors in people with COPD. The U-shaped relationship with mortality was interesting – the models were adjusted for BMI, but it does make you wonder whether (mal)nutrition leading to an abnormally low NHHR was a mediating factor in this relationship. Unlike some other prognostic indicators in COPD, this is one we can actually modify through diet and/or medications. However, we still don't know to what extent targeting this risk factor works in COPD patients. Until we have large studies in COPD patients, we instead have to extrapolate the findings of studies performed in the non-COPD population. This should not stop us from assessing and aggressively modifying cardiovascular risk factors in our COPD patients!

Reference: Int J Chron Obstruct Pulmon Dis. 2025;20:857–68
Abstract

