



## JOURNAL CLUB

APRIL 2018 | KEY PAPER SUMMARIES

#### Do patients and carers agree on symptom burden in advanced COPD?

Emma Mi, Ella Mi, Gail Ewing, et al. (on behalf of the Living with Breathlessness Study Team)

Intl J COPD 2018;13:969—77

doi.org/10.2147/COPD.S147892

Patients with advanced chronic obstructive pulmonary disease (COPD) exhibit a range of symptoms. Informal carers capable of accurately assessing these symptoms can enhance their ability to judge the appropriate level of support required by a patient in their home. However, inaccurate assessment could lead to overtreatment or inadequate symptom control. The extent of agreement between patients and carers has been extensively studied in cancer, but few studies have been undertaken in COPD or in population-based settings.

In this prospective, cross-sectional analysis of 119 patients living with advanced COPD, alongside their carers, the Living with Breathlessness Study Team reports on agreement between patients and carers on symptoms and factors associated with disagreement. Six symptoms representing physical and psychological aspects were considered: breathlessness, fatigue, anxiety, depression, constipation and diarrhoea.

The study reported fair-to-moderate agreement between patients and carers, but poorer agreement for less observable, more subjective symptoms. Carers who estimated a greater burden of symptoms for patients had less patient-centred contact, more symptoms of anxiety and depression themselves, and had a range of unmet carer support needs. The study identified the need for a more open dialogue between patients and their carers. It also suggests a need to screen for and address psychological morbidities in patients with advanced COPD and in their carers, and to address unmet support needs in carers.

## Long-term oxygen therapy in COPD patients: population-based cohort study on mortality

Nikolay Pavlov, Alan Gary Haynes, Armin Stucki, et al. Intl J COPD 2018;13:979–88 doi.org/10.2147/COPD.S154749

Mortality from COPD is projected to become the world's third leading cause of mortality by 2030. Current treatment guidelines recommend the use of long-term oxygen therapy (LTOT) in COPD patients with severe chronic hypoxaemia. However, despite LTOT, survival of these patients remains poor, as severe hypoxaemia is a symptom of end-stage COPD. Few studies have addressed mortality in this subgroup of patients.

The aim of this population-based prospective cohort study by Nikolay Pavlov and colleagues was to gain a better understanding of the natural course of COPD at its end stage, and to identify those risk factors that might be modified, so as to improve patient management and give insight into novel care strategies for patients with COPD on LTOT.

The study was conducted over two years with all COPD patients receiving LTOT in Bern, Switzerland (n=771). The two-year mortality rate of COPD patients on incident LTOT was found to be somewhat lower in this study than in older cohorts, but remained high compared with the general population (especially in younger patients receiving LTOT for less than six months). The recommendation from this observation was that patients on LTOT should receive a closer follow-up in the first months, which looks at compliance, indication for oxygen therapy and dose adjustment according to blood gas analysis. Close attention should be given to type 2 respiratory

failure, which was associated with mortality, while non-invasive ventilation should be considered early.

### Support needs of patients with COPD: a systematic literature search and narrative review

A Carole Gardener, Gail Ewing, Isla Kuhn and Morag Farquhar *Intl J COPD* 2018;13: 1021–35 doi.org/10.2147/COPD.S155622

Patients living with advanced stage COPD experience loss of functionality and high levels of psycho-social distress. Understanding how they regard their support needs is key to providing holistic, person-centred care. Existing reviews have focused on patient difficulties (e.g. breathlessness), requirements for specific aspects of supportive input (e.g. nursing care), support in understanding COPD, and managing personal care and practical tasks. However, none of these reviews has comprehensively outlined the full range of underlying support needs people can experience.

Morag Farquhar and colleagues have undertaken a systematic review of the relevant literature to assess the full range of support needs of people with advanced-stage COPD. The aim of the review was to develop an evidence-based tool to help the team identify and talk to healthcare professionals about their needs. The inclusion criteria for the systematic review stipulated that all papers be primary research published in peer-reviewed journals in English, that some or all of the participants (aged 18 years+) be patients with COPD, and that the support needs be identified by those patients.

The findings from this review enable clinicians to enhance patient support and researchers to develop evidence-based interventions. It highlights commonalities and differences in the support needs of patients living with COPD compared with those living with other life-threatening conditions, thereby adding to the thinking that goes into end-of-life care, which fully integrates long-term conditions.

### The impact of aging on outpatients with asthma in a real-world setting

Giorgio Ciprandi, Irene Schiavetti and Fabio LM Ricciardolo *Resp Med* 2018; 136:58-64. doi.org/10.1016/j.rmed.2018.01.018

Biomechanical factors cause a decline in lung function in older patients. However, less is known about the clinical and functional impacts of ageing on patients with asthma. Giorgio Ciprandi and colleagues from Genoa and Turin, Italy, sought to evaluate how several clinical parameters differed between asthmatic patients in different age groups.

A total of 391 adult patients presenting at a specialist asthma clinic were enrolled, of whom elderly asthmatics (aged >65 years) made up approximately 25%. The study findings confirmed the association between age and decreased lung function, with significant differences observed for older patients in most of the clinical and functional variables analysed. FEV<sub>1</sub> as a percentage of predicted was significantly lower in elderly patients compared with both adult (41-64 years) and young adult (18-40 years) groups. This pattern of decreasing values with increasing age was also true for FVC as a percentage of predicted and for the FEV<sub>1</sub>/FVC ratio. Asthma control (defined by the Asthma Control Test) was also generally worse in older patients, while BMI and average doses of inhaled corticosteroids (ICS) were higher.

Conversely, the opposite effect was seen for allergy and rhinitis. Across the whole population, approximately 80% of patients had at least one allergy, and 89.8% had rhinitis as a comorbidity. However, adult patients were three times more likely to have allergies than the elderly group, and young adults were eight times more likely. The paper therefore concluded that older patients with asthma are more likely to have reduced lung function, higher BMI and higher ICS doses, but less likely to have comorbid allergy or rhinitis, than their younger counterparts.

#### Association of inhaled corticosteroids and longacting beta-agonists as controller and quick relief therapy with exacerbations and symptom control in persistent asthma: a systematic review and meta-analysis

Diana M Sobieraj, Erin R Weeda, Elaine Nguyen, et al. JAMA 2018; 319(14):1485-96. doi.org/10.1001/jama.2018.2769

Recently, interest has grown in the use of single maintenance and reliever therapy (SMART), in which as-needed short-acting beta-agonists (SABA) are replaced with a combined ICS and long-acting beta-agonist (LABA) inhaler to relieve acute symptoms in patients with asthma. Diana Sobieraj and colleagues from the University of Connecticut School of Pharmacy conducted a systematic review of the evidence base for this therapeutic strategy. Sixteen randomised controlled trials were included, evaluating patients aged five years or older with persistent asthma. Most studies (14) compared SMART with ICS/LABA controller therapy, while four compared SMART with ICS maintenance alone.

In patients aged 12 years or older SMART was associated with a decreased risk of asthma exacerbations compared with the same dose of ICS monotherapy and compared with a higher comparative dose of ICS. SMART was also associated with improved FEV<sub>1</sub> and decreased need for rescue medication compared with the same dose of ICS alone. No difference was seen in mortality. Additionally, in patients aged 4-11 years, SMART was associated with a reduced risk of asthma exacerbations compared with the same dose of ICS alone.

In comparison with ICS/LABA controller therapy, similar results were seen among patients aged 12 years or over. SMART was associated with a lower risk of asthma exacerbations compared with both the same dose of ICS/LABA controller and a higher dose of ICS/LABA. SMART was not associated with any changes in asthma symptom control, mortality, quality of life or lung function.

Overall, the pooled evidence base supports the use of SMART as an alternative to the use of a daily controller therapy and as-needed SABA, in patients aged 12 years and over. Evidence also suggests similar benefits in patients aged 4-11 years, but this is limited.

#### Association of inhaled corticosteroids and longacting muscarinic antagonists with asthma control in patients with uncontrolled, persistent asthma: a systematic review and meta-analysis

Diana M. Sobieraj, William L. Baker, Elaine Nguyen, et al. JAMA 2018;319(14):1473-84 doi.org/10.1001/jama.2018.2757

Guidelines recommend the stepwise escalation of corticosteroid therapy when asthma severity increases, risking patient exposure to systemic effects of drugs and increasing the risk of adverse effects. Diana Sobieraj and colleagues explored the role of long-acting anti-muscarinic (LAMA) as an adjunct therapy to ICS to aid the management of patients with persistent asthma. Data from 15 randomised clinical trials, covering 7,122 patients, was analysed, comparing the effect of add-on LAMA therapy on the risk of exacerbation with either a placebo or other controllers – e.g. LABAs. Researchers also compared the effectiveness of triple therapy (LAMA, ICS and LABA) with IC and LABA.

Results showed the addition of LAMA to ICS significantly reduced the risk of exacerbation when compared with placebo. However, when compared with other controllers (e.g. LABA), no significant improvement in asthma exacerbation risk was found. Triple therapy demonstrated some improved outcomes, but association with improved exacerbations was not demonstrated when compared with ICS and LABA therapy. Conclusions stated that, although use of LAMA does reduce the risk of exacerbation when compared with placebo, similar improvements were not noted when compared with other controllers or triple therapy. The researchers concluded that the association of LAMA with benefits to persistent asthma management may not be greater than that associated with LABA.

# Tiotropium and olodaterol in the prevention of chronic obstructive pulmonary disease exacerbations (DYNAGITO): a double-blind, randomised, parallel-group, active-controlled trial

Peter M A Calverley, Antonio R Anzueto, Kerstine Carter, et al. Lancet Respir Med 2018; online ahead of print doi.org/10.1016/S2213-2600(18)30102-4

For patients with COPD requiring combination bronchodilator therapy, the combination of a long-acting LABA and a LAMA is considered the preferred option. This double-blind randomised controlled trial from Peter Calverley and colleagues explored whether the combination of the LABA tiotropium and the LAMA olodaterol was effective in reducing the rate of COPD exacerbations in the study population, compared with tiotropium alone.

A total of 9,009 patients from 51 countries were screened, of whom 7,880 were treated. Patients were aged 40 years or older with a diagnosis of COPD, a smoking history of more than 10 pack-years, stable airflow obstruction, and a history of at least one moderate or severe exacerbation in the preceding year.

To the surprise of the authors, the combination treatment did not perform as well as expected. There was no significant difference between combination and tiotropium alone in the rate of moderate and severe exacerbations. The time to first exacerbation was also not significantly different.

Some benefits were seen in post-hoc analyses: the rate of exacerbations treated with corticosteroids (with or without antibiotics) was lower in the combination group, and among patients who had been receiving ICS as maintenance treatment at baseline, the risk of exacerbations was lower with combination therapy than tiotropium alone.

The authors suggested a few reasons why the combination therapy did not demonstrate the expected benefit. The variance in the study population was higher than expected, and there was differential study withdrawal between treatment arms, both of which may have had an impact on the treatment effect size.

This study was funded by Boehringer Inhelheim International GmbH; some of the paper authors are employees of Boehringer Ingelheim.





These are synopses of articles as they appeared at the time of writing.

Articles are always subject to change post-publication; please ensure you check the latest version of the article before referencing any of this information.

The Primary Care Respiratory Academy has been developed and is produced by Cogora, the publisher of Healthcare Leader, Management in Practice, Nursing in Practice and Pulse working in partnership with PCRS-UK. All educational content for the website and workshops has been initiated and produced by PCRS-UK/Cogora. The Clinical Platform is funded by Circassia Limited, ClaxoSmithKline and Mylan Pharmaceuticals.





