Evidence-based management of symptoms in serious respiratory illness: what's in our toolbox?

Journal:	*European Respiratory Review*
Manuscript ID	ERR-0205-2024.R1
Manuscript Type:	Editorial
Date Submitted by the Author:	n/a
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Keyword:	breathlessness, cough, symptom management, fatigue, non-pharmacological treatments

Evidence-based management of symptoms in serious respiratory illness: what's in our toolbox?

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Living with a respiratory illness requires patients to manage a wide range of symptoms, many of which will worsen as disease progresses. Breathlessness is a hallmark feature of respiratory conditions, occurring in almost all individuals with chronic obstructive pulmonary disease (COPD) and interstitial lung disease (ILD) [1, 2]. Cough is present in 78% of people with ILD and is frequently distressing, with physical, social and emotional impacts [1, 3]. Fatigue is common across a range of respiratory conditions including COPD, asthma, ILD and pulmonary hypertension [4-7], but is under-recognised and infrequently raised by health professionals [8]. Greater symptom burden is associated with lower health-related quality of life, worse mood, less physical activity, poor sleep, more frequent exacerbations and worse prognosis [9]. Treatments recommended in clinical practice guidelines do not always relieve symptoms (e.g. anti-fibrotic therapy for progressive fibrotic ILD) and many guidelines do not address symptom relief in any detail [10, 11], despite this being the reason for which many patients seek care. Research investigating new treatments to relieve symptoms is a patient priority [12].

This series of systematic reviews addresses six treatments for symptomatic relief in people with chronic respiratory disease – multicomponent services, graded exercise therapy, increased airflow, oxygen therapy, opioids and breathing exercises [13-18]. These ~~systematic~~ reviews were conducted to underpin evidence synthesis for the European Respiratory Society (ERS) Clinical Practice Guideline on symptom management for adults with serious respiratory illness [19]. The interventions and outcomes addressed by the Clinical Practice Guideline and the systematic reviews were chosen with consumer consultation, and the guideline panel included consumer members (people with ILD and COPD). Eligible participants had ‘serious respiratory illness’, defined across all reviews as ‘a respiratory condition that carries a high risk of mortality, negatively impacts quality of life and daily function, and/or is burdensome in symptoms, treatments, or caregiver stress’ [20]. The six systematic reviews included a total of 214 randomised controlled trials with 12868 participants. The majority of participants had moderate to severe lung disease, with COPD the most common

diagnosis, and smaller numbers with asthma, interstitial lung disease, bronchiectasis or pulmonary hypertension.

~~This series of~~Collectively, these reviews provide~~s~~ evidence that simple non-pharmacological treatments such as breathing exercises and increased airflow can relieve breathlessness across a range of respiratory conditions, albeit with a modest effect size (Figure 1) and low certainty of evidence. Pursed lip breathing, diaphragmatic breathing and Yoga breathing showed particular promise and are worthy of further investigation. Multicomponent services, defined as delivering a package of care that includes at least one non-pharmacological treatment (including those evaluated in other systematic reviews of this series) also reduced breathlessness, with a moderate effect size (Figure 1). However not all the examined treatments showed benefits; perhaps the most surprising finding was the lack of impact of opioids on breathlessness in daily life[17], reflecting recent clinical trials which have reported no reduction in breathlessness, alongside significant numbers of adverse events [21]. Oxygen therapy similarly did not relieve breathlessness in daily life when administered for symptom relief rather than treatment of hypoxaemia [16]. Graded exercise therapy was the only treatment with evidence for reduction in fatigue [14].

The results ~~of these~~reported in this series ~~systematic reviews~~ reinforce the importance of non-pharmacological treatments to reduce symptoms, and provide assurance of their benefits. Some of these treatments (e.g. breathing exercises, increased airflow) are relatively inexpensive, quick and simple to deliver, which enhances their applicability across a wide range of settings. Others are more complex (e.g. multicomponent services) and may be restricted to higher income settings and where a wider range of health professionals are available. Graded exercise therapy is already available to patients in many settings in the context of pulmonary rehabilitation, albeit with ongoing and well-documented challenges related to access and uptake [22]. The evidence for efficacy of non-pharmacological techniques in relieving symptoms highlights the importance of a multidisciplinary

team in the care of those living with serious respiratory illness. For many of these interventions, individuals with serious respiratory illness need to be active participants in treatment, and with this comes the potential to gain a sense of personal control over symptoms. The ERS Clinical Practice Guideline on symptom management for adults with serious respiratory illness provides guidance on how these treatments might be considered and sequenced for individual patients [19].

~~This series of systematic reviews has highlighted~~There are a number of gaps in knowledge regarding symptom management that should be addressed by future research. Firstly, the majority of studies across all six reviews included people with COPD, so more research evaluating symptom management interventions for patients with other respiratory diagnoses is needed. There was very little evidence that any of the studied interventions improved the important symptom of cough. A recent crossover trial suggests that opioids may reduce cough frequency over 14 days in people with idiopathic pulmonary fibrosis [23], although longer studies are needed, and concerns regarding side effects are likely to remain. Similarly, graded exercise therapy was the only intervention to address the important but often overlooked symptom of fatigue [14], however this intervention may not be suitable for or acceptable to all patients, particularly those with severe fatigue or post exertional malaise. None of the systematic reviews included evidence specific to people with serious respiratory illness who were close to the very end of life, a time when symptom management is very important and particularly challenging.

Methodological challenges for clinical trials of symptom management techniques were evident across all six reviews. Trials of symptom management interventions delivered in the laboratory during formal exercise testing showed much larger effect sizes than when the same interventions were delivered in daily life (Figure 1), reinforcing the importance of testing such treatments in a real world setting. The quality of evidence was generally low across all reviews. Many trials did not blind outcome assessors, which substantially increases the risk of bias for patient-reported outcomes such

as breathlessness and fatigue. The close monitoring attention provided to clinical trial participants may also influence these outcomes, although this concern is offset by including only studies that had a control group. Incomplete outcome data with lack of intention to treat analysis was also common. The review authors could not exclude the possibility of selective reporting for many trials, usually due to a lack of prospective protocol registration. These methodological issues should be addressed as a priority for future trials of symptom management interventions, in order to increase our confidence in the effects of these important treatments.

In conclusion, this series of systematic reviews highlights some effective treatments for symptom management for patients with serious respiratory illness, including graded exercise therapy, breathing exercises, increased airflow and multicomponent services. There remains an urgent need to address the gaps in our symptom management toolbox, particularly for relief of cough.

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Figure 1. Effect size for primary outcome of systematic reviews in this series.

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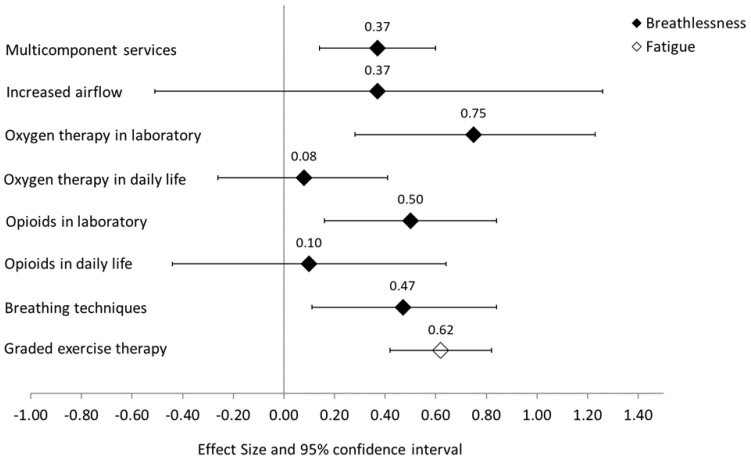

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