



# Pulmonary rehabilitation for patients with COPD during and after an exacerbation-related hospitalisation: back to the future?

*To the Editor:*


The European Respiratory Society (ERS) and American Thoracic Society (ATS) guideline on management of chronic obstructive pulmonary disease (COPD) exacerbations was published in the March 2017 issue of the *European Respiratory Journal* [1]. Based on evidence syntheses, including meta-analyses, relevant evidence up to September 2015 was summarised and clinical recommendations for treatment of COPD exacerbations were formulated. These guidelines were endorsed by the ERS Executive Committee and approved by the ATS Board of Directors in December 2016.

These guidelines should provide the basis for rational decisions in the treatment of COPD exacerbations. Unexpectedly, however, this ERS/ATS Task Force made a conditional recommendation against the initiation of pulmonary rehabilitation during hospitalisation and a conditional recommendation in favour of starting pulmonary rehabilitation  $\leq 3$  weeks after hospital discharge. Moreover, the Task Force rated the quality of evidence for both conditional recommendations to be very low. We take the liberty to challenge these conditional recommendations as well as the assessment of the evidence relating to them. Indeed, there are multiple arguments to recommend the initiation of pulmonary rehabilitation during and (especially) directly after hospitalisation.

Patients with COPD report a broad spectrum of symptoms during exacerbations, including dyspnoea, depression and fatigue [2], which seem to be the basis of the extreme declines in physical activity during hospitalisations [3]. Additionally, comorbidities may flare up [4], and significant losses in quadriceps muscle strength [5], exercise tolerance [6] and health status occur during hospitalisation [7], which only partially recover with usual care after discharge [3, 5, 8]. In addition, it has been shown that patients with anxiety and depression have a doubled risk of short-term hospital re-admission [9]. Therefore, we strongly believe that there is a clear rationale to start early rehabilitative interventions during exacerbation-related hospitalisation of patients with COPD and to continue this after discharge. Importantly, the content of the integrated peri-exacerbation pulmonary rehabilitation programme (which is much more than physiotherapy alone) needs to be tailored to the patient's physical and psychological status [10].

Recent randomised controlled trials (RCTs) have shown that rehabilitative interventions initiated during patients' hospital stay prevent a decline in lower-limb muscle function, balance and exercise performance, and facilitates recovery afterwards [11–15]. These RCTs did not report serious adverse events. Starting early rehabilitation in the hospital setting is clearly also in line with international developments to encourage early rehabilitative interventions, which are safe and effective for patients with a spectrum of illnesses, even in mechanically ventilated, critically ill patients [16–19].

The current ERS/ATS Task Force concluded that pulmonary rehabilitation initiated during hospitalisation increased mortality [1]. This conclusion seems based solely on the study by GREENING *et al.* [20], who reported a significant difference in mortality at 12 months between the rehabilitative group (starting with a median of three rehabilitative sessions during a median 5-day hospital stay, followed by a 6-week unsupervised home-based programme supported by telephone consultations) and the usual care control group (who did receive daily physiotherapy during hospitalisation as per standard UK practice). As argued

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previously [21], the difference in mortality began >5 months after the completion of the intervention. While of concern, the difference does not clearly relate to the early rehabilitation intervention. Indeed, the per protocol analysis did not show a difference in mortality, suggesting that those who actually received the intervention were not those who came to harm [20]. Thus, it is questionable to base a conditional recommendation against the initiation of pulmonary rehabilitation during hospitalisation on a single trial and not on the entirety of evidence. Also, it is not entirely clear how the quality of the evidence relating to this recommendation was rated by the ERS/ATS Task Force [1], which led to very different conclusions on the quality of the evidence compared to the recently updated Cochrane review [22].

A conditional recommendation indicates that well-informed patients may make different choices regarding whether or not to have the intervention [1]. While such preference-sensitive decision making is most welcome, it should be noted that, unfortunately, patients with COPD are mostly unaware of the value of (peri-exacerbation) pulmonary rehabilitation programmes for their health outcomes [23]. Moreover, our anecdotal clinical experience shows that healthcare professionals who are uneducated in pulmonary rehabilitation are already using this ERS/ATS conditional recommendation to withhold an early rehabilitative intervention in the peri-exacerbation period from patients. Indeed, during the ERS School Course on Pulmonary Rehabilitation (April 2017 in Athens, Greece), multiple concerns were expressed by participants that their local physicians read the ERS/ATS guideline on management of COPD exacerbations and, in turn, did not refer for early pulmonary rehabilitation.

On December 8, 2016, PUHAN *et al.* [22] published an update of their Cochrane review entitled “Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease”, including 20 studies, and concluded that “Quality of life and exercise capacity were improved by rehabilitation, that the effect was substantially larger than the minimal important difference, and the quality of evidence according to GRADE was high. Results for hospital readmissions and mortality were diverse, with some studies showing that pulmonary rehabilitation reduced hospital admissions and mortality compared with usual community care (no rehabilitation), and other studies not showing such effects”. Based on the existing literature, we believe that the ERS/ATS Task Force should have made a strong recommendation in favour of starting pulmonary rehabilitation in the first weeks after hospital discharge, without the conditional reservation.

To conclude, pulmonary rehabilitation ambassadors around the world have promoted pulmonary rehabilitation in patients with COPD during and shortly after an exacerbation-related hospitalisation [10, 24], as this results in clinically relevant improvements in exercise performance, lower-limb muscle function, balance and quality of life compared to usual care [22]. Presently, >75% of current pulmonary rehabilitation programmes include those patients [25]. Obviously, we recognise the heterogeneity of effects on mortality and hospital re-admission, which should be monitored closely. As always, the specific content of the rehabilitation intervention in the peri-exacerbation period must be tailored carefully to the patient’s condition and needs. Nevertheless, given the current evidence, the basis for the ERS/ATS conditional recommendation against the initiation of pulmonary rehabilitation during hospitalisation is not clear. This recommendation is therefore likely to have adverse impact on the quality of care, and in turn, the physical and emotional function and quality of life of these patients. We believe this recommendation is potentially harmful for the further broadening of the scope of pulmonary rehabilitation and sets pulmonary rehabilitation back 15 years. Therefore, we would like to encourage healthcare professionals to educate their patients and recommend pulmonary rehabilitation in the peri-exacerbation period, as only 5–15% of hospitalised COPD patients are currently referred for early pulmonary rehabilitation [26]. The ERS and ATS should commit to undertake actions that will improve access to and pulmonary rehabilitation services for suitable patients, including those with an exacerbation-related hospitalisation [24].

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*From the authors:*

We thank M.A. Spruit and colleagues for their questions about our decisions regarding initiating pulmonary rehabilitation in patients with chronic obstructive pulmonary disease (COPD) exacerbations. Their main objection is the recommendation against initiating pulmonary rehabilitation during the patient's hospitalisation. We agree that the recommendation was based primarily on the finding of increased mortality (6-min walking test had statistically significant improvement and hospital readmission had non-statistically significant improvement) and that the trial led by GREENING *et al.* [1] contributed 389 out of 415 patients. We further agree that there is uncertainty about whether or not inpatient-initiated pulmonary rehabilitation is associated with increased mortality, particularly since the mortality difference emerged more than 5 months after hospital discharge in the study by GREENING *et al.* [1] and that the per protocol analysis in this study found no difference in mortality among those who actually received pulmonary rehabilitation *versus* the control group.

However, we believe the guideline panel's judgment is justified. Faced with the decision about whether to recommend for or against an intervention for which the only major clinical trial found increased mortality and no reduction in the re-exacerbation rate, and only a few subsequent analyses raised doubt about the finding, we elected to minimise the potential for harm by recommending against the intervention until further evidence becomes available to revisit the decision. When combined with a recommendation in favour of pulmonary rehabilitation within 3 weeks of discharge, the net effect of the recommendations is a mere delay of days to weeks in the interest patient safety.

M.A. Spruit and colleagues cite the results of a 2016 Cochrane systematic review and meta-analysis to support their concerns [2]. However, they fail to acknowledge that the Cochrane report also found substantial evidence of heterogeneity of treatment effects on hospital readmissions and mortality, and that the "reasons for diverse effects ... are not fully clear. Further studies should explore whether the extent of the rehabilitation program and the organization of such programs within specific healthcare systems (*e.g.* within the rehabilitation setting *versus* embedded in the continuum of care from hospital to home to outpatient care) determines the effects of rehabilitation after COPD exacerbations."

We agree with these conclusions in the Cochrane report and, in the European Respiratory Society/American Thoracic Society guideline [3], we advocated for further research: patients, clinicians and other decision-makers need adequately powered, well-designed randomised clinical trials to more clearly delineate the role of pulmonary rehabilitation in the peri-exacerbation period.

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**Guideline recommendation against the initiation of pulmonary rehabilitation during hospitalisation was justified** <http://ow.ly/ve2L30hiqop>

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