

# Supported self-management for patients with moderate to severe chronic obstructive pulmonary disease (COPD): an evidence synthesis and economic analysis

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## Scientific summary

### Supported self-management for patients with COPD

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# Scientific summary

## Background

Systematic reviews have shown that self-management (SM) interventions can lead to improved health-related quality of life (HRQoL) and reduced hospital admissions. However, the content and delivery of SM support varies considerably. There are unanswered questions about whether or not SM support would be effective and cost-effective if started immediately after a hospital admission for an exacerbation, and what is the most effective content and method of delivery of SM programmes.

## Objectives

- To undertake a systematic review of the evidence for the effectiveness of SM interventions commencing within 6 weeks of hospital discharge for an exacerbation of chronic obstructive pulmonary disease (COPD) (review 1).
- To undertake a systematic review of the qualitative evidence about patient satisfaction, acceptance and barriers to SM interventions (review 2).
- To undertake a systematic review of the cost-effectiveness of SM support within 6 weeks of hospital discharge for an exacerbation of COPD (review 3).
- To undertake a cost-effectiveness analysis and economic model of post-exacerbation SM support compared with usual care (UC) (economic model).
- To undertake a wider systematic review of the evidence of the effectiveness of SM support including interventions [such as pulmonary rehabilitation (PR)] where there are significant components of SM, to identify which components are the most important in reducing exacerbations, hospital admissions and improving quality of life (review 4).

## Methods

### Systematic reviews

A comprehensive search strategy of the effectiveness of SM interventions was carried out. The following electronic databases were searched from inception to May 2012, with no language restriction: MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), and Science Citation Index [Institute of Scientific Information (ISI)]. Subject-specific databases were also searched: PEDro physiotherapy evidence database, PsycINFO and the Cochrane Airways Group Register of Trials. Ongoing studies were sourced through the *metaRegister* of Current Controlled Trials, International Standard Randomised Controlled Trial Number database, World Health Organization, International Clinical Trials Registry Platform Portal and ClinicalTrials.gov. Specialist abstract and conference proceedings were sourced through ISI's Conference Proceedings Citation Index and British Library's Electronic Table of Contents (Zetoc). Hand-searching through European Respiratory Society, the American Thoracic Society and British Thoracic Society conference proceedings from 2010 to 2012 was also undertaken, and selected websites were also examined.

Study selection was undertaken by two independent reviewers using predefined criteria. Full-text manuscripts were obtained of all abstracts that were likely to meet these criteria.

For review 1, randomised controlled trials (RCTs) and relevant outcomes were included. For review 2, only qualitative studies were included. For review 3, any cost-effectiveness study design was accepted. For the

wider exploratory review (review 4), only RCTs were included and the primary outcomes were pre-specified as HRQoL, hospital admissions and exacerbations.

Studies in which  $\approx 90\%$  of patients had COPD, and where the majority of the patients were moderately/severely affected, were included. For reviews 1–3, patients must have been discharged from hospital with acute exacerbation of their COPD within the previous 6 weeks. For review 4, there were no restrictions around time period.

Self-management was defined as including disease education, medication management, smoking cessation advice, action planning, breathing management, bronchial hygiene techniques, respiratory muscle training (RMT), exercise, correct inhaler technique, advice about nutrition, stress management, relaxation and attendance at patient support groups.

Risk of bias of the selected RCTs was assessed using the Cochrane Risk of Bias tool. The quality of the qualitative study was assessed using the Critical Appraisal Skills Programme tool for qualitative evidence, and the Drummond checklist was used to assess the cost-effectiveness study.

The results of each review were presented descriptively and in forest plots where appropriate. When meta-analysis was undertaken, continuous outcome data were pooled using mean difference with 95% confidence intervals (CIs), and hazard ratios (HRs) with 95% CI for dichotomous events. Owing to the expectation of high levels of heterogeneity, random-effects models were used throughout. The  $I^2$ -statistic was used to assess statistical heterogeneity between trials. To explore sources of heterogeneity, subgroup analyses were undertaken. Prediction intervals were calculated to describe the range in which 95% of the distribution of the effects lie. HRQoL measured by the St George's Respiratory Questionnaire (SGRQ) were reversed so that a positive result favoured the intervention group.

### ***Economic model of cost-utility of post-discharge self-management support***

A Markov model was developed to consider short-term risks of readmission and mortality, and long-term natural history of COPD. The model compared a SM intervention immediately after a hospital admission for an acute exacerbation with UC. Clinical effectiveness parameters for SM were derived from the clinical effectiveness review, specifically the risk reduction in admissions. The model was speculative; thus, although the clinical review was not conclusive, the model could assess the potential effect and the uncertainty around this assumption. Resource use and costs associated with SM and usual treatment for COPD were taken from a mixture of published and unpublished sources, and expert clinical advice. A clinical cohort of 1000 patients of mixed age, sex, smoking status and disease severity was modelled for a 30-year horizon. Incremental costs and quality-adjusted life-years (QALYs) were calculated. Extensive sensitivity analyses were carried out.

## **Results**

### ***Review of self-management post-discharge (review 1)***

The search identified 13,355 citations, of which 836 full-text papers were assessed and 12 were included, reporting 10 RCTs. The interventions included were very heterogeneous, ranging from an exercise-only intervention to intensive integrated care at home. Studies generally had small sample sizes, frequently high risk of bias with poor reporting, high loss to follow-up (particularly for the HRQoL outcomes) and inappropriate analyses in some studies.

Meta-analysis identified no evidence of benefit of early SM support on admissions (HR 0.78, 95% CI 0.52 to 1.17;  $I^2 = 70.9\%$ ), mortality (HR 1.07, 95% CI 0.74 to 1.54;  $I^2 = 0\%$ ) and most other health outcomes. A modest improvement in HRQoL was identified, but this was possibly biased owing to high loss to follow-up in studies. However, the direction of effect for many outcomes (including admissions) favoured the SM intervention.

### **Review of qualitative studies reporting patient experience of self-management post discharge (review 2)**

Only one paper from Australia with a small qualitative component was included. Patients found that the SM programme improved their communication with health-care professionals and access to resources.

### **Review of cost-effectiveness and costing studies post-discharge (review 3)**

Only one trial from Spain met the criteria and was a hospital-at-home intervention with a substantial SM component.

The cost analysis [using 2000 price data in euros (€)] found that the home hospitalisation intervention was significantly less costly than conventional care (average cost per patient: €1255.12 vs. €2033.51;  $p = 0.003$ ).

### **Economic model of self-management support post discharge**

Owing to considerable uncertainty around the impact on readmissions and heterogeneity of the trial results, the model-based analysis should be viewed as speculative and, therefore, only providing estimates of the potential impact of a SM programme delivered in the post-exacerbation period.

The main drivers of the model were the effect on hospital readmissions, duration of the effect, and the cost of a SM programme. The base-case analysis showed that, compared with UC, SM support (delivered within 6 weeks of hospital discharge) was more costly but resulted in better outcomes, with a £683 cost difference and a gain of 0.0831 QALYs. To be cost-effective, a SM programme, post admission for an acute exacerbation, would need to cost no more than £2200 if the relative reduction in admissions was consistent with a HR of 0.82. The sensitivity analysis suggested that SM support had a probability of 68% of being cost-effective at a threshold incremental cost-effectiveness ratio of £20,000 per QALY, demonstrating the uncertainty around the impact of SM on readmissions.

### **Review of effectiveness of different models and components of self-management (review 4)**

A total of 194 papers reporting 174 RCTs reported one of the three primary outcomes. The majority of populations had moderate or severe COPD and recruited participants from secondary care. Trials were generally small (47% had < 50 participants) and had short follow-up (45% up to 3 months). Most trials (163, 96.6%) reported HRQoL, 42 (24.1%) reported hospital readmissions and only 20 (11.5%) reported exacerbations. In the intervention groups, exercise was the most commonly reported component (76.9%), followed by breathing techniques and management of dyspnoea (64.2%), and general education about COPD and its management (47.2%). Seventy-three (31.9%) of the intervention arms had six or more components; 38 (16.6%) were single components, with the vast majority of these being exercise-only interventions.

Sequence generation and allocation concealment were adequate in 66 (37.9%) and 27 (15.5%) studies, respectively. Owing to lack of blinding of participants of their allocation, HRQoL results were considered at high risk of bias, except in trials with an active intervention or sham comparator. A frequent and significant risk of bias was the reporting of the characteristics of only those who completed the study, rather than those randomised.

Studies assessing the effect of individual components were few, but only exercise significantly improved patient outcomes compared with UC, which was restricted to HRQoL in the short term (SGRQ at 3-months' follow-up 4.87, 95% CI 3.96 to 5.79;  $P = 0\%$ ). This is above the minimally clinically important difference of four points for the SGRQ. Multicomponent (at least three individual components) SM interventions were likely to be more effective than UC: at 9–12 months' follow-up, SGRQ = 2.40 (95% CI 0.75 to 4.04;  $P = 57.9\%$ ), hospital admissions HR = 0.79 (95% CI 0.60 to 1.05;  $P = 62.6\%$ ). However, the degree of heterogeneity suggests that there are important features of these interventions that need to be established. Compared with UC, multicomponent SM interventions with supervised exercise (as in a PR

programme) or structured unsupervised exercise (as in a home rehabilitation programme) appear effective. SM programmes that provide an enhanced level of care and support (where there is proactive involvement of health-care professionals) may reduce hospital admissions in the medium term (at 6 months: HR 0.78, 95% CI 0.62 to 0.99;  $I^2 = 55.1\%$ ) and improve HRQoL (SGRQ at 6 months = 4.05, 95% CI 2.23 to 5.87;  $I^2 = 8.4\%$ ). The number of studies included in a range of other analyses which investigated modality of exercise, RMT, duration of programme and person delivering the programme were too limited to provide sufficient evidence to determine their effectiveness. No conclusive findings emerged from direct comparisons between different SM interventions. Notably, there was no evidence that action plans were effective by themselves.

## Conclusions

This report provides a thorough evaluation of the available evidence from which to design future research in this area. The reviews of the effectiveness of SM interventions immediately post admission for an exacerbation revealed modest potential benefits to HRQoL, with no other statistically significant effects, but with most other outcomes (excluding mortality) favouring the SM arm. There were no good qualitative papers reporting patient experience of these early SM interventions and only one cost-effectiveness study. A speculative economic model describes the assumptions required for such an intervention to be cost-effective.

The wider exploratory review of SM interventions revealed that although some components of SM interventions were associated with positive effects of HRQoL, such as structured exercise (either within a supervised group or home based) enhanced care and multicomponent interventions, it was not possible to establish the relative roles of individual components in reducing hospital admissions and improving HRQoL.

### *Implications for health care*

The evidence is not consistent with recommending SM support be provided post discharge from hospital after an acute exacerbation of COPD. However, the risk of readmission is so high that further research is needed to establish whether or not some aspects of SM for some patients might be an effective approach.

It is difficult to recommend specific components that should be included in SM support interventions in general. The evidence is most consistent with exercise being an important and effective component, particularly in a supervised or structured unsupervised format. However, the evidence is insufficient to establish the relative importance of other aspects.

### *Recommendations for research*

1. Current interventions to support patient SM delivered post discharge cannot currently be recommended because interventions are heterogeneous and methodology problematic, and, despite there being potential benefit in terms of HRQoL, there is not enough good evidence to be sure that clinical outcomes could be improved. Therefore:
  - i. High-quality studies should be undertaken among patients with COPD post discharge.
  - ii. This should include qualitative work to explore barriers and facilitators to SM when patients have recently had an exacerbation, exploration of novel approaches to affect behaviour change and exploration of approaches tailored to the individual and their circumstances.
  - iii. New approaches should be evaluated by properly designed and conducted trials, with special attention to reducing loss to follow-up.

2. Owing to the heterogeneity and complexity of interventions, it was not possible to unpick the most important components of SM interventions in general, or to confirm whether they improve clinical outcomes. It is clear that action plans alone do not seem to work in their present form, but that structured exercise and more heavily supported interventions (which may not usually be defined as SM) might work better. Therefore:
  - i. Further in-depth work using individual participant data (e.g. an individual participant data meta-analysis) should be carried out to try to identify which are the most effective components of interventions and identify patient-specific factors that may modify this. This work is ongoing by other researchers.
  - ii. Future studies might try to identify the characteristics of patients who are more likely to be able to self-manage and consider a more targeted approach.
  - iii. Further qualitative work is needed to explore patients' barriers and facilitators to SM interventions.
  - iv. Novel approaches to influence behaviour change and to help patients manage or prevent exacerbations should be explored, first using qualitative studies and then properly designed and conducted RCTs.
  - v. Most trials include a mixture of components; more trials teasing out the individual elements either as lone interventions, or with the addition of one component, would be useful.
  
3. Recommendations for the design and conduct of future RCTs of interventions to support patient SM:
  - i. In general new trials should adhere to modern standards of design, conduct and reporting in order to reduce risks of bias, for example, blinding of outcome assessment, attempts to maximise follow-up or methods to impute this, reporting of the characteristics of all randomised patients.
  - ii. The behaviour change theories and strategies that underpin COPD SM interventions need to be better characterised and described.
  - iii. A clear framework for describing and classifying SM interventions and their comparators is required.
  - iv. Trials need to be adequately powered to detect a clinically relevant difference and long enough to assess changing effects over time. There should be clear reporting of outcomes to include self-efficacy, behaviour change and clinical outcomes, such as hospital admissions and exacerbations.
  - v. Given the wide range of HRQoL outcomes available, it would be useful to standardise their use within COPD research and ensure that they are reported accurately within publications.
  - vi. Statistical analysis methods should be improved, in particular (1) analysis of HRQoL outcomes should routinely adjust for baseline values to overcome baseline imbalance, account for correlation between final score and baseline score, and increase statistical power; and (2) time-to-event outcomes should be analysed using suitable analyses that allow for differential patient follow-up and summarised using HRs (rather than odds ratios).

## Study registration

This study is registered as PROSPERO CRD42011001588.

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