National Institute for Health Research

NIHR Research for Patient Benefit (RfPB) Programme

Final Report Form

IMPORTANT

Final reports are required from all projects funded through the NIHR Research for Patient Benefit Programme. The RfPB Programme requires a final report in order to:

- ensure accountability
- aid in appropriate dissemination of project results
- encourage quality assurance of project outputs
- assess the impact of the research supported by the Programme
- demonstrate the achievements of the Programme

Please keep these aims in mind while completing your final report.

The report needs to offer:

a) a clear summary of the project for practitioners and users of research
b) a record of challenges faced and modifications made to the study
c) a description of experience with patient and public involvement that might help identify lessons for future research
d) a summary of any outputs, such as publications, from the research (which should be updated as outputs occur). Completion of this report should not pre-empt any publications that have been prepared or are in preparation detailing project results.

The views expressed in this report should reflect those of the entire research team.

Following submission and assessment of this form, the final version of the scientific and plain English summaries may be displayed on the NIHR CCF website and will be accessible to a wide range of interested parties. We will work with you to ensure that the content published on the website will not pre-empt your publication plans.

You will be required to submit a final statement of expenditure at the same time as your final report. Please note that the completed final report along with a final statement of expenditure is required prior to release of the final project payment.

For further guidance or information on completion of your final report, please contact the regional Programme Manager at NIHR CCF, using the details below:

Dr. Jennie Hejdenberg
jennie.hejdenberg@nihr.ac.uk
Telephone number: 0208 843 8055
NIHR CCF help line: 0208 843 8057

National Institute for Health Research

NIHR Research for Patient Benefit (RfPB) Programme

Final Report Form

IMPORTANT

Note the maximum field sizes shown include both printing and non-printing characters such as spaces and carriage returns.

Reference Number PB-PG-0815-20030

Region London

Date submitted

For office use only

1. Project Details

Project Title*:	Pharmacological and non-pharmacological interventions to improve symptom control and quality of life in patients with interstitial lung disease: a systematic review		
NHS Contracting Organisation*:	King's College Hospital NHS Foundation Trust		
Project Duration*: (months)	12	Grant Value:	£65,276.00
Start Date:	14 February 2017	Agreed Extension (months):	0
End Date:	13 February 2018	Revised End Date:	N/A

2. Grant Holder's Details

Title*:	Dr		
Surname*:	Bajwah	Forename*:	Sabrina
Role in Project*:	Principal Investigator, development of the protocol, management of the expert and patient advisory group, development of the literature search strategy with experienced information scientist, selection, data extraction and quality assessment of studies, drafting of the systematic reviews and final report, quality assurance, dissemination.		

Organisation*: King's College Hospital NHS Foundation Trust

Email Address*: sabrina.bajwah@kcl.ac.uk

Co-applicant 1

Title: Dr Surname: Loveman Forename: Emma

Organisation: Effective Evidence LLP

Role in project: Development of the protocol, development of the literature search strategy with experienced information scientist, selection, data extraction and quality assessment of studies, drafting of the systematic review and final report, dissemination.

Co-applicant 2

Title: Dr Surname: Colquitt Forename: Jillian

Organisation: Effective Evidence LLP

Role in project: Selection, data extraction and quality assessment of studies, drafting of the systematic review and final report, dissemination.

Co-applicant 3

Title: Professor Surname: Bausewein Forename: Claudia

Organisation: Hospital of the University of Munich

Role in project: Expert guidance on the clinical management of the condition, the evaluation and appraisal of the interventions and the interpretation of the evidence.

Co-applicant 4

Title: Professor Surname: Wells Forename: Athol

Organisation: Royal Brompton and Harefield NHS Foundation Trust

Role in project:	Expert guidance on the clinical management of the condition, the evaluation and appraisal of the interventions and the interpretation of the evidence

Co-applicant 5

Title: Mr	Surname:	Almond	Forename:	Howard

Organisation:	Action for Pulmonary Fibrosis
Role in project:	PPI advisor. Expert guidance on the management of the condition, the evaluation and appraisal of the interventions and the interpretation of the evidence.

4. Changes to the research team

Please outline any changes that have been made to the research team, including an explanation of why these changes were required.

Sadly, Mike Bray passed away before the project started. Howard Almond, also a patient with pulmonary fibrosis and from Action for Pulmonary Fibrosis, has taken his place as PPI co-applicant on this project.

5. Plain English summary*

Please provide a summary of the project, including background, findings and conclusions. It is essential that you make the content of your summary and the implications of your research evident to the public. It should avoid technical terms and should be written in an accessible style and emphasise in particular the potential for patient benefit arising from the study.
(Maximum 500 words)

Background and aims of research

Interstitial lung diseases (ILD) are serious lung diseases that generally affect people over 60 years of age. The main symptom is shortness of breath, which can have a considerable impact on a patient's life. There are numerous types of ILD. Many types respond well to treatment, but others are progressive and lung damage is irreversible. For these people effective therapies to reduce symptoms and improve quality of life (so called palliative therapies) are essential.
Important advances have been made in the last 5 years in the development of palliative therapies for ILD. We aimed to bring together the results of all recent studies examining the effectiveness of treatments to improve symptoms and quality of life. This will provide patients, carers and health professionals with a comprehensive and unbiased summary of the research. This may in turn help to improve symptoms and decrease hospital admissions.

Findings

31 studies and 1095 patients were included in the review. Pulmonary Rehabilitation was by far the most examined intervention and showed significant benefit to patients' functional ability. However, this benefit was short lived and there was no evidence of improved breathlessness or quality of life. There was some evidence for the benefit of oxygen in improving breathlessness and quality of life in patients with low oxygen levels on exertion. Opioids (eg morphine) and benzodiazepines (eg lorazepam) are now recommended for breathlessness in ILD. However, we found a lack of studies assessing effectiveness. There were 2 studies examining new interventions (PA101 and VRP700) for cough. However, the effects were inconsistent. There was no clear evidence that drugs to treat pulmonary hypertension (high lung pressure) helped improve symptoms or quality of life. Single studies showed promising results for a case conference and mindfulness. However, a Patient and Partner Empowerment Programme and a Breathlessness Support Service showed no improvement in outcomes.

Conclusions

Pulmonary Rehabilitation improves functional ability in ILD but this benefit ceases quickly after completing the course. More research in to how we maximise this benefit is needed. Oxygen helps with breathlessness and quality of life in people with low oxygen levels on exertion. More research is needed to look at whether opioids and benzodiazepines are beneficial in people with ILD.

Patient and public involvement

A patient representative from Action for Pulmonary Fibrosis is a co-applicant and has been involved in this project from the beginning. The results have been circulated to a large patient and carer group which includes those living with lung disease. Patient and public involvement has ensured that this research meets the needs of patients and carers, is more reliable and more likely to be put into practice.

Dissemination

Our review has provided clinicians and patients with updated information about therapies aimed at improving symptoms and quality of life for ILD. Our results will be shared with clinicians (through a publication and an international workshop) and patients and carers (through relevant groups such as British Lung Foundation, Action for Pulmonary Fibrosis and social media).

6. Scientific summary of research and findings*

Please provide a structured summary of the research including background, aims and objectives, methods, key findings and conclusions. Describe and explain any changes in the project since the original application was approved (if any changes have been made).
(Maximum 2,000 words)

BACKGROUND

Patients with fibrotic interstitial lung diseases (ILD) have a short disease trajectory with a high symptom burden. Improvements in symptom management may decrease patient admissions, improve the quality of life of both patient and carer and facilitate death outside of hospital. Evidenced-based palliation is seldom applied.

AIMS & OBJECTIVES

To undertake a systematic review of the effects of interventions for symptom control in people with fibrotic ILDs

METHODS

This review is a part update of two existing systematic reviews[1,2] and the Cochrane review of pulmonary rehabilitation (PR).[3] The methods are described in the research protocol (PROSPERO CRD42017065933).

We searched nine electronic databases from 2011 to November 2017 with no language restrictions, and reference lists were checked.

Inclusion criteria:

- People with a confirmed diagnosis of a fibrotic ILD. Concomitant pulmonary hypertension was eligible. People with obstructive sleep apnoea and ILD were excluded.
- Any intervention which aims to manage symptoms of ILDs, as defined by the primary outcome measure of the study. Subjective measures were included if they were assessed by validated tools. Radical interventions which aim to be disease modifying were excluded (except in concurrent pulmonary hypertension studies).
- Prospective studies of any design were eligible- Owing to the large number of studies identified we were able to justify including the best quality evidence available. We therefore excluded retrospective studies. Some studies originally identified in our bid were therefore excluded; abstracts were eligible if they contained sufficient details.

We used a two-stage process to select studies for inclusion; titles and abstracts were initially screened and full manuscripts of selected citations retrieved and assessed against the inclusion criteria by two independent reviewers. Any disagreements were resolved by consensus.

Studies were data extracted and assessed for quality by one reviewer and checked by a second. We used the Cochrane risk of bias tool for randomised controlled trials (RCTs) and controlled clinical trials (CCTs), using the risk of selection bias to establish the overall risk of bias for each study. We used tools developed by the National Institute for Health, National Heart, Lung and Blood Institute (NIH NHLBI) to assess study quality of prospective observational studies. We contacted all authors of studies reported in abstract form since 2015 and of studies with missing information.

Included studies were synthesised through a narrative review and meta-analysis where appropriate. Where possible, we updated IPF subgroup meta-analyses from the Cochrane review of PR with new data.[3] Statistical heterogeneity was assessed using the I^2 statistic. Continuous outcome data were expressed as mean difference or standardised mean difference depending on the outcomes reported.

KEY FINDINGS

Two systematic reviews[1,2] were previously undertaken by study authors with some overlap of studies. Bajwah et al[1] concluded that there is strong evidence for the use of PR to improve walking distance and moderate evidence for the use of sildenafil and PR to improve quality of life (QoL). An additional study in Loveman et al[2] provided uncertain results as to the effects of PR and an additional small RCT of thalidomide found cough, cough-related QoL and respiratory-related QoL were significantly improved compared with placebo.

Our searches identified 18,125 records after deduplication, and 221 articles were retrieved. Thirty-one studies published in 58 articles were included. Ten of the included studies assessed nine different pharmacological interventions. Pulmonary rehabilitation or exercise training was evaluated by 17 studies, and one study each evaluated a fast-track case conference, a patient and partner empowerment programme (PPEP), a mindfulness-based stress reduction program (MBSR) and a breathlessness support service (BSS).

The majority of studies included people with idiopathic pulmonary fibrosis (IPF), the most prevalent subtype of advanced ILD. In two studies, participants also had pulmonary hypertension. The severity of disease varied between studies. Sample sizes of included studies or relevant subgroups ranged from 10 to 98. Duration of the intervention and follow-up tended to be short, with only eight of the 31 studies having follow-up greater than 12 weeks and none more than 12 months. There were 12 RCTs, one CCT, 15 before and after studies, 2 cohort studies and 1 cross-sectional study. Just four of the RCTs were judged to have a low risk of selection bias; only one of the observational studies was rated as ‘good’ and ten were rated as ‘fair’.

Pharmacological interventions

One cross-over RCT[4] compared two weeks of ambulatory oxygen with two weeks without oxygen in 84 people with fibrotic ILD who desaturated on exertion. Health status was significantly improved with oxygen on most aspects. Significant improvements were also seen in shortness of breath and the St George’s Respiratory Questionnaire (SGRQ) total score.

Two studies evaluated the effects of chronic or previously administered corticosteroids.[5,6] No statistically significant differences in relevant outcomes were found between 47 ILD corticosteroid users and 51 matched steroid-naïve patients.[5] Similarly, no difference in 6-minute walk distance (6MWD) was found between people with an acute exacerbation of IPF ‘ever treated’ (n=12) and ‘never treated’ (n=12) with steroids. [6]

One before and after study[7] aimed to determine the minimum effective once-daily dose of sustained-release morphine in opioid-naïve adults. Limited data for the subgroup with ILD (n=10) were reported. Dyspnoea intensity worsened, but statistical significance was not reported. No toxicity occurred, although 40% experienced unacceptable side-effects leading to withdrawal from the next phase of the study.

One RCT[8] aimed to document the therapeutic effects of Feiwei granules, a Traditional Chinese Medicine (TCM). The control group received Jinshuibao capsules, also a TCM. Dyspnoea and SGRQ total score were statistically significantly worse in the Feiwei granules group (n=80) at baseline, and improvement was significantly greater at 6 months, compared with Jinshuibao capsules (n=20). There was no difference in change in 6MWD.

Three studies targeted cough. [9,10] [11] One crossover RCT[9] with 24 participants compared inhaled PA101 (cromolyn sodium) with placebo. After 14 days of treatment, cough frequency was significantly lower with PA101 but other outcomes were not significantly improved. One before and after study with 18 participants[10] administered either omeprazole 40 mg twice daily or lansoprazole 30 mg twice daily, plus ranitidine 300 mg at night for eight weeks. On median 24-hour cough count there was a non-significant increase from baseline to follow-up. The majority of participants had a decrease in the number of acid reflux events and an increase in the number of non-acid reflux events. One crossover RCT [11] randomised 20 IPF participants with cough to receive either a single inhaled dose of VRP700 (100mg) or placebo. The number of coughs in 4 hours following treatment with VRP700 were higher than following treatment with placebo.

Two studies assessed interventions for ILD with pulmonary hypertension. [12] [13] [14] One RCT [12,13] compared bosentan with placebo in 60 people with fibrotic ILD. No statistically significant difference was found in change in 6MWD or QoL between the two groups. However, a higher proportion of serious respiratory adverse events and deaths occurred in the placebo group. One before and after study included 23 mixed disease participants (18% with scleroderma or sarcoidosis) and pulmonary hypertension.[14] There were no significant changes in 6MWD or other relevant outcomes.

Non-pharmacological interventions

One RCT randomised participants with advanced IPF or fibrotic non-specific interstitial pneumonia to either a fast track 'Hospital2Home' case conference intervention (n=26) or a waiting list control (n=27).[15,16] At 4 weeks, there was significant improvement in the Palliative Care Outcome Scale and the SGRQ total score. One before and after study evaluated a MBSR [17] undertaken by 19 participants over 2 months. On the Profile of Mood State there was a significant change in total score at 12 months. There were no other relevant reported differences. One CCT [18,19] evaluated the effect of a short multidisciplinary PPEPP, on QoL of 13 patients with IPF and their partners, compared with a control group of seven participants. No statistically significant changes in relevant outcomes were found. One RCT [20] evaluated the effects of BSS versus usual care in a mixed population with various advanced lung diseases. Only seven participants in the ILD subgroup received the intervention. No statistically significant differences were found between groups at 6 weeks follow-up for this subgroup.

Pulmonary rehabilitation or exercise were assessed by 17 studies (5 RCTs, 1 controlled cohort study and 11 before-and-after studies) with 547 participants. Data from the included RCTs and controlled cohort study were added to the IPF subgroup meta-analyses from the Cochrane review of pulmonary rehabilitation where possible.[3]

When analysing data from the Cochrane review and new studies together, a statistically significant difference between PR and control was found for change in 6MWD immediately following the intervention (7 studies, 258 participants, MD 35.09 m, 95% CI 21.51, 48.66, I^2 25%, Fixed effects). At longer-term follow-up (3 or 6 months), there was no significant difference in change in 6MWD between groups (4 studies, 147 participants, MD 5.26 m, 95% CI -12.88, 23.40, I^2 6%) and no important statistical heterogeneity. Ten of the 11 before-after studies reported 6MWD; most studies found a tendency for improvement in 6MWD

immediately following PR, although one study found a deterioration.[21] Only two studies[22,23] reported longer (6-month) follow-up and results were contradictory.

The Cochrane review included five RCTs measuring dyspnoea and combined three of these in a meta-analysis. The current review identified four controlled trials with new data on dyspnoea, but only one of these had data that could be added to the Cochrane meta-analysis; this was considered inappropriate as a large proportion of evidence would be omitted. Overall, only four of the nine studies reporting dyspnoea immediately after the intervention found statistically significant differences, and these were inconsistent in one of the studies. [24] No significant effect of PR was found on longer follow-up. Eight before and after studies assessed dyspnoea following PR. Two studies[25,26] found a statistically significant improvement dyspnoea immediately after the intervention but they did not assess whether the effect was maintained over time. The remaining studies found no change in dyspnoea after PR. Longer follow-up (6 months) was reported by just two studies, with inconsistent results. [22 23]

Eight RCTs in the Cochrane review measured HRQoL immediately following PR, but just three of these could be pooled in a meta-analysis. Five RCTs in the current review reported new data on HRQoL. [24,27,28 29 30] Meta-analysis was considered inappropriate. Overall, results were inconsistent with most RCTs finding no statistically significant effect, and no effects of PR were found at longer follow-up where reported. HRQoL was measured by six before and after studies, again results were inconsistent.

Other outcomes assessed by the new studies included various measures of fatigue[30 34 31] and the incremental shuttle walk test; [32 33] results were generally inconsistent between the studies.

We did not identify any studies of relevance in non-invasive ventilation.

CONCLUSIONS

- Evidence for ambulatory oxygen is weak but positive with improvements in dyspnoea and QOL in patients who desaturate on exertion.
- There continues to be a paucity of studies investigating the effectiveness of opioids in ILD with one small uncontrolled study in the previous reviews and only one small before and after study identified in our review. Studies examining the efficacy and long term effects of opioids in ILD are urgently needed to support the use of opioids in this group.
- This review found one small study with inconsistent effects of PA101 on cough reduction and another on VRP700, which was found to be ineffective. There is ongoing paucity of high quality studies looking at the benefits of proton-pump inhibitors.
- There is no clear evidence that bosentan or riociguat improve symptoms, quality of life or function in those with pulmonary hypertension.
- Overall mixed results were found for non-pharmacological interventions.. This review found single studies showing promising results for a case conference and mindfulness. However, a Patient and Partner Empowerment Programme and a Breathlessness Support Service showed no improvement in outcomes.
- Pulmonary Rehabilitation was the most examined intervention with statistical improvement in 6MWD demonstrated. There was no evidence for long term benefit of pulmonary rehabilitation, however. The active ingredient within pulmonary rehabilitation and other complex interventions such as the breathlessness intervention service remains poorly understood.

1. Bajwah S, Ross JR, Peacock JL, et al. Interventions to improve symptoms and quality of life of patients with fibrotic interstitial lung disease: a systematic review of the literature. *Thorax* 2013; **68**(9): 867-79.
2. Loveman E, Copley VR, Colquitt J, et al. The clinical effectiveness and cost-effectiveness of treatments for idiopathic pulmonary fibrosis: a systematic review and economic evaluation. *Health Technology Assessment (Winchester, England)* 2015; **19**(20): i-xxiv, 1-336.
3. Dowman L, Hill CJ, Holland AE. Pulmonary rehabilitation for interstitial lung disease. *Cochrane Database of Systematic Reviews* 2014; (10): CD006322.
4. Visca D, Mori L, Tsipouri V, et al. Ambox: A Randomised Controlled, Crossover Trial Evaluating The Effects Of Ambulatory Oxygen On Health Status In Patients With Fibrotic Interstitial Lung Disease. *American Journal of Respiratory and Critical Care Medicine* 2017; **195**.
5. Hanada M, Sakamoto N, Ishimatsu Y, et al. Effect of long-term treatment with corticosteroids on skeletal muscle strength, functional exercise capacity and health status in patients with interstitial lung disease. *Respirology* 2016; **21**(6): 1088-93.
6. Papiris SA, Kagouridis K, Kolilekas L, et al. Survival in Idiopathic pulmonary fibrosis acute exacerbations: the non-steroid approach. *BMC Pulmonary Medicine* 2015; **15**: 162.
7. Currow DC, McDonald C, Oaten S, et al. Once-daily opioids for chronic dyspnea: a dose increment and pharmacovigilance study. *Journal of Pain and Symptom Management* 2011; **42**(3): 388-99.
8. Yu Y, Sun Z, Shi L, et al. Effects of Feiwei granules in the treatment of idiopathic pulmonary fibrosis: a randomized and placebo-controlled trial. *Journal of Traditional Chinese Medicine* 2016; **36**(4): 427-33.
9. Birring S, Wijsenbeek M, Al SA, Tutuncu A, Morice A. Significant improvement in refractory chronic cough with inhaled PA101 in patients with idiopathic pulmonary fibrosis: Results from phase 2 trial. *European Respiratory Journal Conference: European Respiratory Society Annual Congress* 2016; **48**(no pagination).
10. Kilduff CE, Counter MJ, Thomas GA, Harrison NK, Hope-Gill BD. Effect of acid suppression therapy on gastroesophageal reflux and cough in idiopathic pulmonary fibrosis: an intervention study. *Cough (London, England)* 2014; **10**: 4.
11. Satia I, Badri H, Dockry R, et al. A randomised, double-blind, placebocontrolled crossover study to assess the efficacy of a single dose of 100 mg of VRP700 by inhalation in reducing the frequency and severity of cough in adult patients with idiopathic pulmonary fibrosis. *Thorax* 2015; **70**: A52.
12. Corte TJ, Keir GJ, Dimopoulos K, et al. Bosentan in pulmonary hypertension associated with fibrotic idiopathic interstitial pneumonia. *American Journal of Respiratory & Critical Care Medicine* 2014; **190**(2): 208-17.
13. Keir G, Corte T, Parfitt L, et al. Bosentan in pulmonary hypertension associated with fibrotic idiopathic interstitial pneumonia: A randomized, double-blind, placebo-controlled study. *European Respiratory Journal Conference: European Respiratory Society Annual Congress* 2013; **42**(no pagination).
14. Hoeper MM, Halank M, Wilkens H, et al. Riociguat for interstitial lung disease and pulmonary hypertension: a pilot trial. *European Respiratory Journal* 2013; **41**(4): 853-60.
15. Bajwah S, Ross JR, Wells AU, et al. Palliative care for patients with advanced fibrotic lung disease: a randomised controlled phase II and feasibility trial of a community case conference intervention. *Thorax* 2015; **70**(9): 830-9.
16. Bajwah S, Higginson IJ, Wells AU, Koffman J, Ross JR, Birring SS. Developing and evaluating a hospital2home palliative care service for patients with advanced progressive idiopathic fibrotic interstitial lung disease: Phase 0-II [Abstract]. *Palliative medicine*, 2012. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/548/CN-00871548/frame.html (accessed.
17. Sgalla G, Cerri S, Ferrari R, et al. Mindfulness-based stress reduction in patients with interstitial lung diseases: a pilot, single-centre observational study on safety and efficacy. *BMJ open respiratory research* 2015; **2**(1): e000065.

18. van Manen MGJ, van 't Spiker A, Tak NC, et al. Patient and partner empowerment programme for idiopathic pulmonary fibrosis. *European Respiratory Journal* 2017; **49**: 1601596 [https://doi.org/10.1183/13993003.01596-2016].
19. Van Manen M, Van't Spijker A, Tak N, et al. Patient and partner "empowerment" program in idiopathic pulmonary fibrosis (ppepp): Improving quality of life in patients and their partners. *Qjm* 2016; **109**: S46.
20. Higginson IJ, Bausewein C, Reilly CC, et al. An integrated palliative and respiratory care service for patients with advanced disease and refractory breathlessness: a randomised controlled trial. *The Lancet Respiratory Medicine* 2014; **2**(12): 979-87.
21. Tomioka H, Kaneda T, Kida Y, Kaneko M, Fujii H. Comparison of the effect of inpatient pulmonary rehabilitation between interstitial lung disease (ILD) and chronic obstructive pulmonary diseases (COPD). *American Journal of Respiratory and Critical Care Medicine Conference: American Thoracic Society International Conference, ATS* 2011; **183**(1 MeetingAbstracts).
22. Holland AE, Hill CJ, Glaspole I, Goh N, McDonald CF. Predictors of benefit following pulmonary rehabilitation for interstitial lung disease. *Respiratory Medicine* 2012; **106**(3): 429-35.
23. Ryerson CJ, Cayou C, Topp F, et al. Pulmonary rehabilitation improves long-term outcomes in interstitial lung disease: a prospective cohort study. *Respiratory Medicine* 2014; **108**(1): 203-10.
24. Dowman LM, McDonald CF, Hill CJ, et al. The evidence of benefits of exercise training in interstitial lung disease: a randomised controlled trial. *Thorax* 2017: 17.
25. Rifaat N, Anwar E, Ali YM, Ellabban A, Hasan AA. Value of pulmonary rehabilitation in patients with idiopathic pulmonary fibrosis. *Egyptian Journal of Chest Diseases and Tuberculosis* 2014; **63**(4): 1013-7.
26. Tonelli R, Cocconcelli E, Lanini B, et al. Effectiveness of pulmonary rehabilitation in patients with interstitial lung disease of different etiology: a multicenter prospective study. *BMC Pulmonary Medicine* 2017; **17**(1): 130.
27. Koulopoulou M, Chua F, Koutoumanou E, Narayan S, Nikoletou D. Inspiratory muscle training (IMT) in interstitial lung disease (ILD) - A pilot study. *European Respiratory Journal Conference: European Respiratory Society Annual Congress* 2016; **48**(no pagination).
28. Jarosch I, Schneeberger T, Gloeckl R, et al. Effects of a 3-week pulmonary rehabilitation program in patients with idiopathic pulmonary fibrosis-a randomized, controlled trial. *European Respiratory Journal Conference: European Respiratory Society Annual Congress* 2016; **48**(no pagination).
29. Vainshelboim B, Oliveira J, Yehoshua L, et al. Exercise training-based pulmonary rehabilitation program is clinically beneficial for idiopathic pulmonary fibrosis. *Respiration* 2014; **88**(5): 378-88.
30. Gaunaurd IA, Gomez-Marin OW, Ramos CF, et al. Physical activity and quality of life improvements of patients with idiopathic pulmonary fibrosis completing a pulmonary rehabilitation program. *Respiratory Care* 2014; **59**(12): 1872-9.
31. Keyser RE, Woolstenhulme JG, Chin LM, et al. Cardiorespiratory function before and after aerobic exercise training in patients with interstitial lung disease. *Journal of Cardiopulmonary Rehabilitation & Prevention* 2015; **35**(1): 47-55.
32. Arizono S, Taniguchi H, Sakamoto K, et al. Endurance time is the most responsive exercise measurement in idiopathic pulmonary fibrosis. *Respiratory Care* 2014; **59**(7): 1108-15.
33. Lardner R, Bolton S, Hoyles R. The benefits of pulmonary rehabilitation (PR) in interstitial lung disease (ILD): Observations from oxfordshire's mixed respiratory disease, community based PR programme. *Thorax* 2014; **69**: A132-A3.

7. Patient and public involvement*

The RfPB Programme is particularly keen to learn from the experiences of research teams regarding patient and public involvement (PPI) and contribution from PPI members involved in the research is encouraged when completing this form. Please provide comment on your experiences with PPI, any changes made and lessons drawn. **(Maximum 1,500 words)**

Our research project aimed to provide up-to-date research evidence to support decision making by patients, carers and health care professionals. We aimed to ensure our research focused on treatments to improve symptoms and quality of life that are deemed to be of relevance to those with ILDs and influence policy makers. We involved patients and carers throughout the project to ensure that the research meets their needs, was more reliable and more likely to be put into practice. In addition to the representative from the patient support group 'Action for Pulmonary Fibrosis' who is a co-applicant (HA), additional representatives from patient or carers were invited to join the external project advisory group. PPI involvement in the research from the protocol development stage helped decide what the research was setting out to achieve, through to the final report and dissemination of the findings and helped understand what the research findings mean for patients and how they can be applied in the health service. This draft report has been reviewed by the patient and public group at the Cicely Saunders Institute which consists of patients and carers living with respiratory disease. In addition, this report has also been reviewed by an ILD specialist nurse and a Consultant Respiratory Physiotherapist. This has provided wider multi-disciplinary perspective.

8. Next steps to patient benefit*

Please provide comment on the likely implications for practice which may result from the outcomes of this project and the next steps to be taken to ensure patient benefit both locally and more broadly. Steps already taken and planned for the future should be included. While in funding research, RfPB emphasises a clear trajectory into practice, it is important not to 'overclaim' and care should be taken to cover the limitations of the study and any risks associated with implementation. Where the project is a feasibility study, include details of any plans for a definitive study, including the likely funder and timetable for its submission. Please give reasons if there is no plan to go forward to a trial at this stage. **(Maximum 1,000 words)**

This systematic review and meta-analyses aimed to build on the previous reviews and provide up-to-date research evidence to support decision making by patients, carers, health care professionals and policy makers. In the short term this research will guide health professionals on a daily basis on which interventions they should be using in clinical practice.

In the medium term, this research has highlighted interventions that require further investigation and symptoms that still remain poorly managed.
This review has highlighted amongst other things, the large number and variety of outcome measures which are being used to measure symptoms and quality of life in these patients. In addition, the lack of validated patient reported outcome measures assessing palliative care needs in these patients is brought to the forefront. To improve patient care in the long term, consensus on outcome measures and prioritisation of end points in ILD research is needed. Further research into the active ingredient in complex interventions such as pulmonary rehabilitation is needed.

9. Key presentations and publications*

Please list here any presentations and publications which have resulted from the work. This should include journal articles, conference proceedings, press releases and all publications in the public and scientific press, including website links to published articles if appropriate. Items that are forthcoming should also be included. **Please note you are contractually obliged to provide 28 days notification prior to any publication.**

A full report of our systematic review is available and a manuscript to be submitted to a peer review journal, which will include a full description of the evidence base from the previous systematic reviews, is currently in preparation. We aim to submit this in late March 2018 to Lancet Respiratory Medicine. On publication of this paper, we will publicise it through social media (Cicely Saunders Twitter and Facebook) and produce a policy brief to be disseminated to all appropriate policy makers and relevant organisations such as Action for Pulmonary Fibrosis, British Lung Foundation and NICE IPF quality standard committee. The policy brief and published paper will be taken and distributed at the European Association of Palliative Care Conference (Bern May 2018). In addition, an abstract of this paper has been submitted to the European Respiratory Society Conference (Paris September 2018). We have also submitted a proposal for a Professional Development Workshop at the European Respiratory Society Conference which is aimed at equipping ILD health professionals with the skills to assess and manage the symptoms of ILD patients. The results of this research will be presented at this workshop.
Results will be disseminated to patients and carers via Action for Pulmonary Fibrosis and British Lung Foundation. In addition, through the Reach and Impact committee at Cicely Saunders Institute, results will be publicised to the wider national and international population e.g through social media.

Author (s)	Title	Reference/Further Details

10. Intellectual property and innovation*

The definition of Intellectual Property (IP) includes copyright (such as new software, checklists, scales, protocols, questionnaires, toolkits, guidelines or similar) and research tools (such as data analysis techniques, assays, cell lines, biomarkers, materials or equipment and devices) patents, trademarks and designs.

Has the research generated new (or made improvements to existing) checklists, scales, protocols, questionnaires, toolkits, guidelines or software?
NO

Please indicate whether any of the following outputs have been generated during the course of the project *(Please tick all that apply)*

☐ New research tools (or improvements to existing research tools)
☐ New copyright
☐ New patent applications filed, improvements integrated into existing patent applications or pending patent applications which have now been granted
☐ New trademarks
☐ New designs, or improvements to existing designs

Please provide brief details of the material IP generated through the research.
(Maximum 250 words)

New data on the effectiveness of interventions to improve symptoms and quality of life in ILD has been generated through this research.