Suppl 1: Summary of previous reviews

Author, year, EN#	Bajwah et al, 2012[1]
Study population	People with progressive idiopathic fibrotic interstitial lung diseases (IPF, NSIP, cryptogenic fibrosing alveolitis (CFA) and idiopathic interstitial pneumonia (IIP))
Intervention(s)	Any single or combined interventions for the treatment of progressive idiopathic fibrotic ILDs, excluding lung transplantation (relevant to the present review: sildenafil, pulmonary rehabilitation, disease management programme, oxygen, diamorphine, thalidomide)
Included studies, N Reference details	Total 35. Relevant to present review: 13 (in 12 publications) *Sildenafil: (4 studies in 3 publications)* Zisman 2010, N Engl J Med; 363:620–8. Collard 2007, Chest; 131: 897-900 Jackson 2010, Lung; 188: 115-23 *Pulmonary Rehabilitation:* Nishiyama 2008, Respirology;13:394–9. Holland 2008, Thorax;63: 549–54. Ozalevli 2010, Multidisciplinary Respir Med;5: 31–7. Rammaert 2009, Rev Mal Respir; 26: 275–82. Kozu 2011, Respiration; 81: 196–205. Swigris 2011, Respir Care; 56: 783–9. *Disease management programme:* Lindell 2010, Heart Lung;39:304–13. *Diamorphine:* Allen 2005, Palliat Med; 19: 128–30. *Thalidomide*: Horton 2008, Thorax;63:749
Results (relevant outcomes)	*Sildenafil:* on 6MWD one study found a significant improvement, but a meta-analysis of two RCTs did not (5.25 (95% CI −8.90 to 19.40)). For dyspnoea there was no overall benefit from meta-analysis. Quality of life remained stable / was better preserved in the sildenafil arm of one study than in the placebo arm but this was not seen during longer follow-up. *Pulmonary Rehabilitation:* Meta-analysis showed an overall significant benefit of PR on 6MWD (2 studies, mean difference 27.4, 95% CI 4.1 to 50.7) which was supported in the non-randomised studies. Effects on dyspnoea and other symptoms were mixed with a few studies finding significant effects on dyspnoea. Four studies found significant effects on QOL, the remaining 2 studies did not. *Disease management programme:* There was mixed evidence of benefit for symptoms and QOL in the one study. *Diamorphine:* in one study there was a significant decline in dyspnoea (weak evidence). *Thalidomide*: cough and quality of life were improved (weak evidence).
Review conclusions	There is strong evidence for the use of pulmonary rehabilitation to improve 6MWD and moderate evidence for the use of sildenafil and pulmonary rehabilitation to improve QoL.

Author, year, EN#	Loveman 2015[2]
Study population	People with a confirmed diagnosis of IPF
Intervention(s)	Any available and currently used (in the NHS) interventions which aim to manage symptoms or modify IPF (relevant to the present review: thalidomide, sildenafil, disease management programme, PR)
Included studies, N Reference details	Total 14. Relevant to present review: 5. *Thalidomide*: Horton 2012, Ann Intern Med;157:398–406, Am J Respir Crit Care Med 2012;185:A3635. *Sildenafil:* Zisman 2010, N Engl J Med;363:620–8. *Disease management programme:* Lindell 2010, Heart Lung;39:304–13. *PR:* Jastrzebski 2008, Pneumonologia i Alergologia Polska 2008;76:131–41. Nishiyama 2008, Respirology 2008;13:394–9.
Results (relevant outcomes)	*Thalidomide*: One randomised crossover trial (low risk of bias) found cough, cough-related QoL and respiratory-related QoL were significantly improved with thalidomide compared with placebo. Adverse events were experienced with thalidomide. Caution is required given the small sample size. *Sildenafil:* One RCT (unclear risk of bias) found no significant difference between sildenalfil and placebo in the proportion with a 20% improvement on 6MWT (primary outcome). Dyspnoea may be improved (depending on the measure used and test conditions). QoL was better in those treated with sildenafil when measured using the SGRQ, but not when using the SF-36 or the EQ-5D. Adverse events were similar between groups. *Disease management programme:* One pilot RCT (unclear risk of bias) found no significant differences in dyspnoea compared to usual care. QoL appeared to be adversely affected on measures of physical health but not on measures of mental health. The study was unlikely to be sufficiently powered. *PR:* One RCT (unclear risk of bias) and one CCT (high risk of bias) provided uncertain results as to the effects of these types of intervention, and there were baseline differences between groups on many key outcomes.
Review conclusions	Few interventions have any statistically significant effect on IPF and a lack of studies on palliative care approaches was identified. Research is required into the effects of symptom control interventions, in particular pulmonary rehabilitation and thalidomide.

Author, year, EN#	Dowman et al 2014[3]
Study population	People with ILD of any origin (includes sarcoidosis)
Intervention(s)	Pulmonary rehabilitation (any prescribed exercise training, with or without education, supervised or unsupervised, combined with another intervention permitted)
Included studies, N Reference details	9 RCTs (6 published as abstracts only), up to 5 included in meta-analysis. (Note: RCTs with sarcoidosis not in meta-analyses) Baradzina 2005 (abstract) Holland 2008 Jackson 2014 (ahead of print) Mejia 2000 (abstract) Menon 2011 (abstract) Nishiyama 2008 Perez Bogerd 2011 (abstract) Vainshelboim 2013 (abstract) Wewel 2005 (abstract)
Results (relevant outcomes)	In 8 trials (n=365) PR significantly improved functional exercise capacity immediately following the programme, no significant change on 6MWD in the other 1 study. Pooled analysis of change in 6MWD from 5 RCTs (168 participants) was MD 44.34 metres (95%CI 26.04, 66.64), I^2 14%. favouring PR. GRADE[a]: moderate quality. No significant effect of PR evident on 6MWD in 2 studies reporting longer-term follow-up (3 and 6 months respectively). In 5 trials (n=281) 3 reported reduced dyspnoea following PR; 2 reported no change in dyspnoea. Pooled analysis of 3 studies (113 participants) SMD for change in dyspnoea was -0.66 (95% CI -1.05, -0.28), I^2 49%, in favour of PR. GRADE[a]: low quality. No significant effect of PR evident on dyspnoea in 1 study reporting a 6-month follow-up. In 8 trials measured HRQoL and 3 found significant differences immediately following PR (2 others non-significant improvements, remaining 3 unclear). Pooled analysis of 3 studies (106 participants) SMD 0.59 (95% CI 0.20, 0.98) I^2 0%. in favour of PR. GRADE[a]: low quality. No significant effect of PR evident on HRQoL in 2 studies reporting longer-term follow-up (3 and 6 months respectively). Subgroup analyses by subtype of ILD reported, not extracted. No adverse events in two studies that reported it.
Review conclusions	PR seems to be safe for people with ILD. Improvements in functional exercise capacity, dyspnoea and quality of life are seen immediately following pulmonary rehabilitation, with benefits also evident in IPF. Because of inadequate reporting of methods and small numbers of included participants, the quality of evidence was low to moderate. Little evidence was available regarding longer-term effects of pulmonary rehabilitation.

Appendix B: Search strategy

Medline search

Ovid MEDLINE(R) ALL 1946 to January 14, 2019
1. idiopathic pulmonary fibrosis.tw.
2. interstitial lung disease*.tw.
3. non-specific interstitial pneumonia*.tw.
4. idiopathic interstitial pneumonia*.tw.
5. cryptogenic organi* pneumonia*.tw.
6. (IPF or ILD or IIP or NSIP).m_titl.
7. Idiopathic Pulmonary Fibrosis/dt, pc, rh, su [Drug Therapy, Prevention & Control, Rehabilitation, Surgery]

8. Lung Diseases, Interstitial/dt, pc, rh, su [Drug Therapy, Prevention & Control, Rehabilitation, Surgery]
9. Idiopathic Interstitial Pneumonias/dt, pc, th [Drug Therapy, Prevention & Control, Therapy]
10. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. (comment or letter or editorial).pt.
12. 10 not 11
13. limit 12 to yr="2011 -Current"
14. animals/
15. Humans/
16. 14 not (14 and 15)
17. 13 not 16

Ovid Embase 1974 to 2019 January 14
1. *interstitial lung disease/dm, dr, dt, rh, su, th [Disease Management, Drug Resistance, Drug Therapy, Rehabilitation, Surgery, Therapy]
2. *interstitial pneumonia/dt, rh [Drug Therapy, Rehabilitation]
3. idiopathic pulmonary fibrosis.tw.
4. interstitial lung disease*.tw.
5. non-specific interstitial pneumonia*.tw.
6. idiopathic interstitial pneumonia*.tw.
7. cryptogenic organi* pneumonia*.tw.
8. (IPF or ILD or IIP or NSIP).m_titl.
9. (letter or editorial).pt.
10. conference.pt.
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
12. 11 not 9
13. limit 12 to yr="2011 -Current"
14. 10 and 13
15. 13 not 14

Web of Science Core Collection
TOPIC: (idiopathic pulmonary fibrosis) OR TOPIC: (interstitial lung disease*) OR TOPIC: (idiopathic interstitial pneumonia*) OR TOPIC: (non-specific interstitial pneumonia*)
Refined by: DOCUMENT TYPES: (ARTICLE OR REVIEW OR MEETING ABSTRACT
Timespan: 2011-2019. Indexes: SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI.

Cochrane Library: Cochrane Database of Systematic Reviews (Issue 1 of 12 January 2019) and Cochrane Central Register of Controlled Trials (Issue 1 of 12, January 2019)
Search: 'idiopathic pulmonary fibrosis OR interstitial lung disease* OR idiopathic interstitial pneumonia* OR non-specific interstitial pneumonia* or cryptogenic organ* pneumonia OR IPF or ILD or IIP or NSIP in Title, Abstract, Keywords, Publication Year from 2011 to 2019.

CRD databases https://www.crd.york.ac.uk/CRDWeb/
Search: 'idiopathic pulmonary fibrosis OR interstitial lung disease* OR idiopathic interstitial pneumonia* OR non-specific interstitial pneumonia* or cryptogenic organ* pneumonia OR IPF or ILD or IIP or NSIP: 2011 to 2019.

Ongoing studies

- NIH ClinicalTrials.gov (http://www.clinicaltrials.gov/
- WHO International Clinical Trials Registry Platform (ICTRP) http://www.who.int/ictrp/en/
- UK Clinical Trials Gateway. https://www.ukctg.nihr.ac.uk
- PROSPERO – Ongoing reviews

Searched using keywords:
idiopathic pulmonary fibrosis OR interstitial lung disease OR non-specific interstitial pneumonia OR idiopathic interstitial pneumonia* OR cryptogenic organizing pneumonia

Auto-alerts
Set up to run weekly in Medline and Embase from Feb 2nd to November 2017. Searches were then updated from November 2017 to January 2019.

1. Bajwah S, Ross JR, Peacock JL, Higginson IJ, Wells AU, Patel AS, Koffman J, Riley J. 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): 867-879.
2. Loveman E, Copley VR, Colquitt J, Scott DA, Clegg A, Jones J, O'Reilly KM, Singh S, Bausewein C, Wells A. 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.