Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Objective: A meta-analysis of randomized controlled trials (RCTs) was conducted to determine the effect of pulmonary rehabilitation on functional capacity and quality of life in interstitial lung diseases, including those caused by coronaviruses.

Data Sources: MEDLINE, EMBASE, SPORTDiscus, Cochrane Library, Web of Science, and MedRxiv from inception to November 2020 were searched to identify documents.

Study Selection: Publications investigating the effect of pulmonary rehabilitation on lung function (forced vital capacity [FVC]), exercise capacity (6-minute walk distance [6MWD]), health-related quality of life (HRQOL), and dyspnea were searched.

Data Extraction: The data were extracted into predesigned data extraction tables. Risk of bias was evaluated with the Cochrane Risk of Bias tool (RoB 2.0).

Data Synthesis: A total of 11 RCTs with 637 interstitial lung disease patients were eligible for analyses. The pooled effect sizes of the association for pulmonary rehabilitation were 0.37 (95% confidence interval [CI], 0.02-0.71) for FVC, 44.55 (95% CI, 32.46-56.64) for 6MWD, 0.52 (95% CI, 0.22-0.82) for HRQOL, and 0.39 (95% CI, −0.08 to 0.87) for dyspnea. After translating these findings considering clinical improvements, pulmonary rehabilitation intervention increased predicted FVC by 5.5%, the 6MWD test improved by 44.55 m, and HRQOL improved by 3.9 points compared with baseline values. Results remained similar in sensitivity analyses.

Conclusions: Although specific evidence for pulmonary rehabilitation of coronavirus disease 2019 patients has emerged, our data support that interstitial lung disease rehabilitation could be considered as an effective therapeutic strategy to improve the functional capacity and quality of life in this group of patients.

Interstitial lung diseases (ILDs), also known as diffuse parenchymal lung diseases, are a set of chronic lung conditions characterized by exercise limitation and dyspnea. Pathologic features dominated by diffuse alveolar damage have also been reported in severe acute respiratory syndrome (SARS) and coronavirus disease 2019 (COVID-19), both diseases result from infection by viruses in the coronavirus (CoV) family. CoVs are a family of enveloped, single-stranded–RNA viruses responsible for the 2 large epidemics in the past 2 decades, SARS and the Middle East Respiratory Syndrome. Toward the end of 2019, COVID-19 was identified as the cause of a severe respiratory illness, which was declared a global pandemic and is still spreading across the world with a growing number of confirmed cases.

Although most individuals with COVID-19 develop mild or asymptomatic disease, approximately 14% experience severe disease and 6% become critically ill. In the acute phase, severely affected patients may develop pneumonia characterized by
bilateral interstitial infiltrate, acute respiratory distress syndrome,\textsuperscript{10} and related pulmonary fibrosis that is even susceptible to lung transplantation.\textsuperscript{15} Moreover, an increased risk of encephalopathy has been described in hospitalized patients with acute respiratory symptoms.\textsuperscript{12,13} The evolution of COVID-19 in the medium and long-term is still uncertain; however, it appears to be similar to SARS regarding its clinical features.\textsuperscript{14} Epidemic data of previous CoV infections show that pulmonary fibrosis may develop early in patients with SARS,\textsuperscript{15} which has shown a functional disability associated with the degree of lung function impairment that might be related to residual lung fibrosis, muscle weakness, and systemic effects of the viral illness.\textsuperscript{4,16} Additionally, research has shown an important decrease in lung function, physical fitness, and health related quality of life (HRQOL) among patients recovering from CoV infections.\textsuperscript{17,18}

Recent clinical guidelines recommend pulmonary rehabilitation for the management of the long-term effects of critical illness associated with severe acute respiratory syndrome coronavirus 2 infection.\textsuperscript{19} Pulmonary rehabilitation is an evidence-based standard of care designed to improve the physical and psychological condition for patients with lung disease that include but are not limited to exercise training, education, and behavior change.\textsuperscript{20} Previous research reports have shown the effectiveness of pulmonary rehabilitation in improving health and HRQOL in patients with CoV or diseases with similar respiratory consequences.\textsuperscript{21,22}

As COVID-19 is a new disease, there is a lack of data in the literature about the recovery pathway on sequelae of severely affected patients, and an optimal treatment is extremely urgent. Pulmonary rehabilitation might have an important role in improving functional capacity and the quality of life of survivors of this disease. Thus, the aim of this systematic review and meta-analysis was to synthesize the evidence about the effectiveness of pulmonary rehabilitation in health outcomes of ILDs, including those caused by CoVs.

\section*{Methods}

This systematic review and meta-analysis followed the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions.\textsuperscript{23} The Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines were used as a reporting structure for this systematic review.\textsuperscript{24} This meta-analysis was registered in the International Prospective Register of Systematic Reviews (PROSPERO registration no.: CRD42020178937).

\textbf{List of abbreviations:}

\begin{itemize}
  \item 6MWD 6-minute walk distance
  \item CI confidence interval
  \item CoV coronavirus
  \item COVID-19 coronavirus disease 2019
  \item ES effect size
  \item FVC forced vital capacity
  \item HRQOL health-related quality of life
  \item ILD interstitial lung disease
  \item RCT randomized controlled trial
  \item SARS severe acute respiratory syndrome
\end{itemize}

\section*{Search strategy}

Two reviewers (S.R.-G, S.N.A.-A.) independently searched the MEDLINE (via PubMed), EMBASE (via Scopus), SPORTDiscus, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Web of Science, and MedRxiv databases from inception to November 2020. Disagreements were solved by consensus or involving a third researcher (V.M.-V.). The search strategy used was: (covid OR coronavirus OR “Middle East Respiratory Syndrome Coronavirus” OR “Severe Acute Respiratory Syndrome” OR SARS-CoV OR “Acute Respiratory Distress Syndrome” OR ARDS OR “acute hypoxemic respiratory failure” OR “pulmonary fibrosis” OR “lung fibrosis” OR “interstitial lung disease” OR “interstitial pneumonia”) AND (“physical therapy” OR “respiratory muscle training” OR “respiratory rehabilitation” OR “pulmonary rehabilitation” OR exercise OR exercises). The reference lists of the articles included in this review, as well as the list of references of studies included in previous systematic reviews and meta-analyses, were reviewed for any additional relevant studies.

\section*{Study selection}

Studies concerning the effectiveness of different pulmonary rehabilitation programs in ILD or patients with CoV were included in this systematic review. Inclusion criteria were: (1) randomized controlled trials (RCT); (2) participants who had ILD (including pulmonary fibrosis) or postacute CoV; (3) physical exercise or pulmonary rehabilitation as the intervention; (4) comparison with controls undergoing usual care or activities without physical demand; and (5) outcomes of lung function, exercise capacity, HRQOL, and dyspnea.

The exclusion criteria were: (1) patients with mild-moderate severity of COVID-19 as they were not at risk of developing pulmonary fibrosis\textsuperscript{25}; (2) studies comparing the same modality of exercise with different doses of time, frequency, or duration; (3) conference abstracts without a full published article; (4) studies with inconsistencies or that did not provide enough data to calculate the effect size (ES); and (5) studies published in languages other than English or Spanish.

When more than 1 report provided data from the same sample, only the publication with the most detailed results or providing data for the largest sample size was included. Regarding HRQOL, only studies reporting a total score of a HRQOL scale were selected.

\section*{Search and data extraction}

The main characteristics of the selected studies were summarized in an ad hoc table including information about (1) study characteristics such as year of publication, country, and sample size; (2) population characteristics such as type of respiratory disease, mean age, and time from diagnosis; (3) intervention characteristics such as duration, frequency, type, and exercise regime training; and (4) outcomes such as lung function, exercise capacity, HRQOL, and dyspnea. Disagreements in data collection were settled by consensus.

\section*{Classification of the outcome}

Pulmonary rehabilitation program outcomes were classified according to 4 main areas: lung function, measured using forced
vital capacity (FVC); exercise capacity measured using the 6-minute walk distance (6MWD); HRQOL, measured using a quality of life scale; and dyspnea measured at baseline using a dyspnea scale.

**Risk of bias assessment**

The quality of RCTs was assessed using Cochrane Collaboration’s tool for assessing risk of bias. This tool evaluates the risk of bias according to 5 domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Overall bias was considered as “low risk of bias” if the study was classified as low risk in all domains, “some concerns” if there was at least 1 domain rated as having some concerns, and “high risk of bias” if there was at least 1 domain rated as high risk or several domains rated as having some concerns that could affect the validity of the results.

Data extraction and quality assessment were independently performed by 2 reviewers (S.N.A.-A., S.R.-G.), and inconsistencies were solved by consensus or involving a third researcher (V.M.-V.).

**Statistical analysis**

We calculated a pooled ES of the mean differences for 6MWD using a random effects model based on the DerSimonian and Laird method. A pooled ES of the standardized mean differences was necessary to use for FVC, HRQOL, and dyspnea outcomes because different measures or scales were reported by studies. A combined estimate was calculated when studies applied more than 1 questionnaire for reporting the dyspnea grade. Additionally, statistical heterogeneity was analyzed using the $I^2$ statistic. Heterogeneity was considered as not important ($I^2$, 0%-40%), moderate ($I^2$, 30%-60%), substantial ($I^2$, 50%-90%), or considerable ($I^2$, 75%-100%); the corresponding $P$ values were also considered.

Following the Cochrane Handbook recommendations, when data on the SD of change on outcomes from baseline were lacking, the estimates relied on standard errors, 95% confidence intervals (CI), and $P$ values to calculate the SD. Finally, when studies were scaled inversely (ie, lower values indicated worse outcomes), the mean in each group was multiplied by $\frac{1}{C_0}$. Random effects metaregression analyses were conducted to assess whether baseline age influenced the association of pulmonary rehabilitation and outcome related variables. Sensitivity analyses were performed by removing studies one by one to assess the robustness of the summary estimates and to detect whether any particular study accounted for a large proportion of heterogeneity among pulmonary rehabilitation ES pooled estimates.

Finally, we used Egger’s regression asymmetry test to assess publication bias. A level of <0.10 was used to determine whether publication bias might be present. Statistical analyses were performed using Stata Statistical software, version 16.0.

**Results**

The literature search retrieved 12,214 articles, which were reviewed based on the title and abstract after discarding duplicates. Finally, 11 RCTs met the inclusion criteria and were selected for this systematic review and meta-analysis (fig 1), including a total sample of 637 participants. Excluded studies with reasons for exclusion are available in supplementary table S1 (available online only at http://www.archives-pmr.org/).

**Risk of bias**

As evaluated by Cochrane Collaboration’s tool for RCTs, 18.2% of the studies showed a high risk of bias, 72.7% showed some concerns, and 9.1% had a low risk of bias. When studies were analyzed by individual domains, 91% had shortcomings in the selection of the reported results domain (supplementary fig S1, available online only at http://www.archives-pmr.org).
| Study Characteristics | Population Characteristics | Intervention | Study Country |
|-----------------------|---------------------------|--------------|---------------|
| Study                 | Respiratory Disease       | Time From Diagnosis | Age (y) | Frequency (Times/wk) | Weeks | Experimental Group | Control Group | Outcomes |
| Dowman et al²⁰       | ILD                       | NR           | EG: 69±11 | NR | 2 | 8 | 30 min of aerobic exercise (cycling and walking) Upper and lower limb resistance training (10-12 RM) Weekly telephone support | Control Group | 6MWD, SGRQ-I, UCSD SGRQ, mMRC |
| Gaunaud et al³¹       | Idiopathic pulmonary fibrosis | EG: 71±6 | NR | 90 | 2 | 12 | 10 educational lectures, 30 min of endurance training, 20 min of flexibility exercises (3 sets/30s), 25 min of strength training (2-3 sets/10-15 repetitions) Handouts about the educational lectures | Control Group | SGRQ-I |
| Holland et al³²       | ILD                       | NR           | EG: 70±8 | NR | 2 | 8 | 30 min of endurance training (cycling and walking) Upper limb endurance training Functional strength for lower limbs Weekly telephone support | Control Group | 6MWD, mMRC |
| Jackson et al³³       | Idiopathic pulmonary fibrosis | EG: 71±6 | 3-48 mo before screening | 120 | 2 | 12 | 15 min of educational lectures, 30 min of endurance training (cycling and walking), 15 min of flexibility exercises (3 sets/30s), 15-30 min of strength training (3 sets/15 repetitions) Normal activities | Control Group | 6MWD, Borg Dyspnea Index |
| Jarosh et al³⁴        | Idiopathic pulmonary fibrosis | EG: 68±9 | NR | 5-6 | 3 | Medical care, psychological support, breathing therapy, education. Endurance or interval cycle training (60% or 100% peak work rate) Resistance training for major muscle groups (3 sets/10-15 repetitions maximum) Usual care | Control Group | 6MWD, CRDQ |
| Lau et al³⁵           | Recovering from SARS      | EG: 35.9±9.3 | NR | 60-90 | 4-5 | 6 | 30-65 min of endurance training (limbs ergometer, stepper, or treadmill) Upper and lower limbs resistance training (3 sets/10-15 repetitions at maximum load) Educational session about exercise rehabilitation | Control Group | 6MWD |
| Liu et al³⁶           | COVID-19                  | EG: 69.4±8.0 | NR | 10 | 2 | 6 | Respiratory muscle training (3 sets/10 breaths/60% MEP) and diaphragm muscle (30 contractions, placing a weight on the anterior abdominal wall) Stretching and cough exercise Home exercise (pursed-lip breathing and coughing training) Usual care | Control Group | FVC, 6MWD |
| Nishiyama et al³⁶     | Idiopathic pulmonary fibrosis | EG: 68.1±8.9 | >3 mo | NR | 2 | 10 | Educational lectures Treadmill 20 min of strength training for the limbs Endurance training (cycling, treadmill, arm cranking and stair climbing) and peripheral muscle training (3 sets/8 repetitions) 30 min of multidisciplinary treatment Medical care and medical follow-upUsual care | Control Group | FVC, 6MWD, SGRQ, BDI |
| Perez-Bogerd et al³⁷ | ILD                       | NR           | EG: 64±13 | 90 | 3-2 | 12-12 | Medical care and identical medical follow-up as EG | Control Group | 6MWD, SGRQ |
| Vainshelbom et al³⁸  | Idiopathic pulmonary fibrosis | EG: 68.8±6 | EG: 3±3.7 | 60 | 2 | 12 | Regular medical care and exercise training: calisthenic and deep breathing exercises, 30 min of aerobic training (treadmill walking, leg cycling, step climbing) Resistance training (1-2 sets/12-15 repetitions) Regular medical care | Control Group | FVC, 6MWD, SGRQ, mMRC |

(continued on next page)
Heterogeneity among studies was rated as not important for 6MWD ($I^2$, 0.0%), moderate for HRQOL ($I^2$, 50.1%), and substantial for dyspnea ($I^2$, 71.3%) (figs 2-4). FVC data were available in 3 studies, which showed a significant effect of treatment (ES, 0.37; 95% CI, 0.02-0.71) (not shown).

The random effects metaregression models indicated that age ($=-0.3499$, $P=0.489$ for FVC; $=-0.4345$, $P=0.499$ for 6MWD; $=0.0913$, $P=0.413$ for HRQOL; and $=0.4196$, $P=0.117$ for dyspnea) was not related to the association between the intervention and outcome-related variables (supplementary table S2, available online only at http://www.archives-pmr.org/).

**Sensitivity analysis**

The pooled ES estimates for the association between pulmonary rehabilitation and all outcome related variables were not significantly modified in magnitude or direction when individual study data were removed from the analysis one at a time. Extra sensitivity analysis was performed excluding the 2 CoV studies showing a pooled ES estimate of 42.00 (95% CI, 27.08-56.92) for 6MWD.

**Publication bias**

Egger’s test revealed no significant publication bias for any pooled analyses. Funnel plots are shown in supplementary figures S2-S4 (available online only at http://www.archives-pmr.org/).

**Discussion**

This systematic review and meta-analysis provides a synthesis of evidence supporting the effectiveness of pulmonary rehabilitation to improve lung function (measured by FVC), exercise capacity (measured by 6MWD), and HRQOL in patients with ILD, including patients with CoV. Meta-regression analysis did not find an association between the magnitude of the effect and the age of patients in the studies.

Among nonpharmacologic interventions to treat these clinical entities, regular exercise is known to be a low-cost solution to improve health, wellbeing, and economic productivity of patients with chronic lung disease, especially for those with ILD, in whom conventional pharmacologic treatment has shown a limited response.

Previous Cochrane reviews support positive effects and no adverse events of pulmonary rehabilitation in patients with ILD, showing improvements of 38.61-44.34 m for 6MWD, 0.58-0.59 for HRQOL, or $-0.47$ to $-0.68$ for dyspnea. Our meta-analysis, in line with the results of previous studies, confirms consistent clinical benefits for exercise capacity (6MWD), HRQOL, and dyspnea in patients with ILD, adding beneficial effects respect to lung function (FCV). Also, our data were similar with regard to the magnitude of change in 6MWD in patients post-CoV, probably because similar respiratory improvements have been reported in both patients with ILD and those post-CoV who are severely respiratory affected because they have interstitial pneumonia, fibrosis, or diffuse alveolar damage in common.

Translating our research effect estimates to clinical improvements by using methods endorsed by the Cochrane Collaboration, a pulmonary rehabilitation intervention increased the predicted FVC by 5.47%, and HRQOL improved 3.9 points with respect to baseline values. The 6MWD test improved by 44.55 m compared with baseline values.
Functional status is extremely important for people with diffuse parenchymal lung disease, and the 6MWD test is widely recognized as a valid and reliable measuring tool. Additionally, the distance achieved for these patients is closely related with disease severity and mortality risk. Recent studies have reported severe disability in postacute patients with COVID-19 with poor results in this test because walk distances are below those expected for their age. In patients with diffuse parenchymal lung disease, Holland et al concluded that changes between 29-34 m may be clinically significant; thus, an increase of 44.55 m is significant for improving functional capacity in this population. Previous studies have reported similar clinical changes compared with our data, with results ranging between 38.38-48.6 m. Regarding FVC, the other major clinical outcome for pulmonary rehabilitation, differences between 2%-6% are suggested to be clinically relevant. Our pooled ES (5.47%) falls within this range of improvement.

The HRQOL scales used in our study are considered an instrument whose validity, reliability, and responsiveness is sufficiently proven. Additionally, they are considered appropriate to measure HRQOL that may have a predictive value for mortality in patients with ILD. Although a 3.9-point improvement vs baseline assessment resulted in a moderate ES, this change remains under the recognized minimal clinical important difference for this value, which is in line with previous findings. Our data also show a positive, but not statistically significant, effect of pulmonary rehabilitation on dyspnea. In this sense, the direction of the association was not homogeneous between studies, probably owing to the different tools used to assess this outcome.

**Fig 2** Mean difference (95% CI) of effect of pulmonary rehabilitation vs usual care on exercise capacity (measured by 6MWD) immediately after intervention (n= 616).

**Fig 3** Standardized mean difference (95% CI) of effect of pulmonary rehabilitation vs usual care on health related quality of life immediately after intervention (n= 354).
and the lack of responsiveness of some of the dyspnea measurement tools.\textsuperscript{57,58}

### Study limitations

This study has some limitations that should be acknowledged. First, our study focused on rehabilitation of pulmonary involvement in patients with COVID-19. However, because this is a systemic disease,\textsuperscript{59} along with the lung damage, other comorbidities such as myopathy of femoral head necrosis\textsuperscript{60} might have an important effect in the functional capacity of these patients. Thus, the rehabilitation treatment plan should be carried out according to the framework of the International Classification of Functioning, Disability and Health.\textsuperscript{61} Second, because of the scarcity of studies, it was not possible to conduct a subgroup analysis separating those interventions that uniquely included an exercise modality from those that included a modality combining 2. Additionally, it was not possible to examine the pulmonary rehabilitation regime (intensity, duration, frequency of the exercise) because information was lacking or was presented in a heterogeneous manner across studies. Nevertheless, most studies showed the same exercise training modality, which may help the generalizability of our findings. Also, although the overall methodological quality of included trials was satisfactory, most trials lacked information regarding the selection of the reported results domain from the Cochrane Collaboration’s tool for assessing risk of bias and the risk of bias was rated as “some concerns” in most. Third, the pooled estimates of this meta-analysis were calculated from studies that, in addition to pulmonary fibrosis, included other ILD-related entities, which might have influenced our findings. In this sense, disease severity may have influenced the effect of the intervention, but it was not available in most studies. Nevertheless, with respect to participants with CoV, all were hospitalized with lung lesions, and participants with mild-moderate severity symptoms were excluded. Fourth, to assess the effect of pulmonary rehabilitation on patients’ HRQOL, we only analyzed studies that provided a total score of the scale used. However, physical or mental domains provided by other scales may potentially act as confounders or mediators in this association. To overcome some of these limitations, we conducted several sensitivity analyses to provide evidence regarding the robustness of the results.

### Conclusions

This meta-analysis revealed a positive association between pulmonary rehabilitation and lung function, exercise capacity, and quality of life in patients with ILD, including severely affected patients with CoV. We are aware that further studies are necessary to confirm the role of pulmonary rehabilitation in the management of respiratory disabilities caused by COVID-19; however, although specific evidence of the effect of pulmonary rehabilitation in patients who have survived the severe acute respiratory syndrome coronavirus 2 infection appears contradictory, our data support that this intervention improves their functional capacity and their quality of life.

### Suppliers

a RoB 2: a revised tool for assessing risk of bias in randomised trials; Cochrane Collaboration
b Stata statistical software, version 16.0; Stata Corp.

### Keywords

Coronavirus; COVID-19; Pulmonary fibrosis; Rehabilitation; SARS virus

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| Reference (Author and Year) | Reason for Exclusion                      |
|----------------------------|------------------------------------------|
| Barbier et al, 2014        | Conference abstract                      |
| Bogerd et al, 2011         | Conference abstract                      |
| Cohen et al, 2013          | Conference abstract                      |
| De Las Heras et al, 2019   | Conference abstract                      |
| Dowman et al, 2015         | Conference abstract                      |
| Gaunaurd et al, 2011       | Conference abstract                      |
| Gaunaurd et al, 2013       | Conference abstract                      |
| Gaunaurd et al, 2014       | Conference abstract                      |
| Gomez et al, 2012          | Conference abstract                      |
| Gomez et al, 2013          | Conference abstract                      |
| Jackson et al, 2012        | Conference abstract                      |
| Jackson et al, 2014        | Conference abstract                      |
| Jarosch et al, 2016        | Conference abstract                      |
| Jastrzebski et al, 2017    | Conference abstract                      |
| Koulopoulou et al, 2016    | Conference abstract                      |
| Kramer et al, 2013         | Conference abstract                      |
| Lanza et al, 2019          | Conference abstract                      |
| Menon et al, 2011          | Conference abstract                      |
| Nykvist et al, 2016        | Conference abstract                      |
| Schneeberger et al, 2016   | Conference abstract                      |
| Shen et al, 2016           | Conference abstract                      |
| Stessel et al, 2015        | Conference abstract                      |
| Vainshelboim et al, 2013   | Conference abstract                      |
| Vainshelboim et al, 2013   | Conference abstract                      |
| Vainshelboim et al, 2014   | Conference abstract                      |
| Vainshelboim et al, 2015   | Conference abstract                      |
| Parisien-La Salle et al, 2019 | Non data available for meta-analysis |
| Cockcroft et al, 1981      | Population                               |
| Greening et al, 2014       | Population                               |
| Vainshelboim et al, 2014   | Same data as other included study        |
| Vainshelboim et al, 2016   | Same data as other included study        |
| Liu et al, 2017            | Other language                           |
| Wapenaar et al, 2020       | Non data available for meta-analysis     |
Figure S1  Risk of bias for included studies.

Table S2  Meta-regressions analyses based on age.

| Outcome                  | n  | β       | p     |
|--------------------------|----|---------|-------|
| Lung function (FVC)      | 3  | 0.3499  | 0.489 |
| Exercise capacity (6MWD) | 10 | -0.4345 | 0.499 |
| Health related quality of life | 7 | 0.0913  | 0.413 |
| Dyspnoea                 | 6  | 0.4196  | 0.117 |

Figure S2  Funnel plot showing publication bias results for exercise capacity outcome (measured by 6-MWD).
Figure S3  Funnel plot showing publication bias results for quality of life outcome (measured by St. George Respiratory Questionnaire (SGRQ) or SGRQ-1 (SGRQ specific for idiopathic pulmonary fibrosis)).

Figure S4  Funnel plot showing publication bias results for dyspnoea outcome.