TITLE: Outcome Measures Used in Pulmonary Rehabilitation in Patients With Acute Exacerbation of Chronic Obstructive Pulmonary Disease: A Systematic Review

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Background. Conflicting results about the effects of community-based pulmonary rehabilitation in acute exacerbations of chronic obstructive pulmonary disease (AECOPD) exist, possibly because the variety of outcome measures used and the lack of appropriate measurement properties hinder the development of pulmonary rehabilitation guidelines.

Purpose. The purpose of this study was to identify and review the measurement properties of patient-reported outcome measures (PROMs) and clinical outcome measures of AECOPD that are used in pulmonary rehabilitation and that can be easily applied in a community setting.

Data Sources. PubMed, Web of Science, Scopus, and CINAHL were searched up to July 1, 2016.

Study Selection. Phase 1 identified outcome measures used in pulmonary rehabilitation for AECOPD. Phase 2 reviewed the measurement properties of the identified outcome measures.

Data Extraction. One reviewer extracted the data and 2 reviewers independently assessed the methodological quality of the studies and the measurement properties of the outcome measures by using the Consensus-Based Standards for the Selection of Health Status Measurement Instruments (COSMIN) recommendations.

Data Synthesis. Twenty-three PROMs and 18 clinical outcome measures were found. The outcome measures most used were the St George Respiratory Questionnaire (n = 15/37 studies) and the 6-minute walk test (n = 21/37 studies). Thirty-two studies described the measurement properties of 22 PROMs and 7 clinical outcome measures. The methodological quality of the studies was mostly poor, and the measurement properties were mostly indeterminate. The outcome measure exhibiting more robust properties was the COPD Assessment Test.

Limitations. A number of studies were published without the validated search strategy used and were included *a posteriori*; the fact that 3 studies presented combined results for patients who were stable and patients with exacerbation, affected the conclusions that can be drawn.

Conclusions. A large variety of outcome measures have been used; however, studies on their measurement properties are needed to enhance the understanding of community pulmonary rehabilitation for AECOPD.

Chronic obstructive pulmonary disease (COPD) is frequently punctuated by acute exacerbations (AECOPD).[1] Currently, more than 80% of these events are recommended to be managed within the community since it can shorten the length of hospital stays and/or avoid hospital admittance.[2]

Pulmonary rehabilitation is a well-established, evidenced-based intervention, possible to be applied within the community (ie, in nonspecialized community health services, in community centers, or at the patient's home)[3–6] and with potential to prevent and decrease the harmful effects of acute exacerbations.[7] Costs associated with AECOPD in the United States are estimated in $7100 per patient/per exacerbation[8] and recent economic studies have shown that, compared with usual care, community-based pulmonary rehabilitation provides cost savings of $1098 per patient.[9]

Nevertheless, conflicting results regarding the clinical effects of pulmonary rehabilitation in AECOPD have been reported[10,11] and less than 10% of patients discharged from AECOPD are being referred for pulmonary rehabilitation[12] thus, its implementation is not a common practice. This inconsistency among studies may occur due to the wide variety of outcomes and outcome measures used and/or due to the lack of appropriate measurement properties (ie, reliability, validity and responsiveness) of the outcome measures used in exacerbation periods. It is known that the measurement properties of any outcome measure are population specific[13] and that patients at distinct phases of their chronic disease (stable/exacerbation) differ in the physiologic and ventilatory mechanisms of their lungs.[14] Therefore, it can be hypothesized that instrument measurement properties will also vary in stable and exacerbation periods.

Nevertheless, studies involving pulmonary rehabilitation in patients with AECOPD have been choosing their outcome measures based on the measurement properties established for stable patients with COPD,[15,16] which may hinder the development of pulmonary rehabilitation guidelines and lead instead to publication of recommendations which lack rigorous underpinning evidence in exacerbation periods.

Additionally, attending to patient's level of fragility during exacerbations, the specificities of implementing a pulmonary rehabilitation program in a nonspecialized center and some practical issues, such as the need for specific equipment and sufficient space and time required to complete testing, especially when more than 1 test at baseline is required, may also influence the selection of the outcome measure.[17]

Thus, the 2 aims of this systematic review were to identify patient-reported outcome measures (PROMs) and clinical (non–patient-reported) outcome measures that are used to assess the effects of pulmonary rehabilitation interventions in patients with AECOPD and that can be easily applied in the community (ie, not expensive, not invasive, and quickly implemented) and to synthesize/evaluate their measurement properties.

Methods

This systematic review (PROSPERO registration no. CRD42015023736) was conducted in 2 phases. Phase 1 identified outcome measures used to assess outcomes of pulmonary rehabilitation interventions in patients with AECOPD and that can be easily applied in community-based practice. Phase 2 aimed to assess the measurement properties of the identified outcome measures.

Phase 1: Measures Used in Pulmonary Rehabilitation

Data sources and searches. The effects of pulmonary rehabilitation interventions in patients with AECOPD have been largely reviewed,[10,11,18–21] thus a first search limited to literature reviews was conducted from May to June 2016 in PubMed, Web of Knowledge, Scopus, and CINAHL. The original papers included in these reviews were extracted and searched for the outcome measures.

The latest available literature review on this theme was dated from 2012 and thus, a second search using the same keywords and databases but limited to original studies published from 2010 to June 2016 was also performed to identify all outcome measures most recently used by physiotherapists. An interval of 2 years until the most recent review in the theme seemed appropriate, as studies indicate that time from submission to publication can go up to 2 years.[22] In both searches, the reference lists of the identified studies were scanned for other potential eligible studies. Additionally, a weekly update was conducted until July 2016. The full search strategy can be found in eAppendix 1 (available at: https://academic.oup.com/ptj).

Study selection. Selection of studies was performed by 1 reviewer (A.L.O.) and checked by a second reviewer (A.S.M.). After removing duplicates, 1 reviewer (A.L.O.) performed the initial screening of articles based on type of publication and relevance for the scope of the review. Selection of studies checked by a second reviewer (A.S.M.).

First, title and abstract were screened, and if the articles were considered relevant, full text was analyzed. Studies were included if they met the following 3 criteria: aimed to assess pulmonary rehabilitation or one of its components; assessed patients with an AECOPD within 3 weeks of the onset as this is the mean time needed for recovery[2,23,24]; and were written in English, Spanish, French, or Portuguese. Studies were excluded if they were conducted in

animals; patients requiring emergency intubation, intensive care unit management, and/or mechanical ventilation; patients with compromised neurological status or hemodynamic instability; patients performing self-management programs only; and patients assessed only after discharge for AECOPD. Book chapters, abstracts of communications or meetings, letters to the editor, commentaries to studies, unpublished work and study protocols were excluded.

Data extraction. Data extraction focused on PROMs and clinical outcome measures used to assess pulmonary rehabilitation interventions and that can be easily applied in community-based practice. Thus, data regarding measures not suitable for this setting (eg, arterial blood gases, cardiopulmonary exercise testing, body plethysmography studies, sputum weight and analysis; penetration index of inhaled radioparticles and hospital length of stay) were not extracted. Data extracted were: outcomes, outcome measures, patient characteristics (ie, age and percentage of predicted forced expiratory volume in 1 second (FEV_1) at stability or in acute exacerbation), treatment setting, time from AECOPD to intervention and duration of intervention.

Phase 2: Properties of Measures

Data sources and searches. A systematic electronic literature search was conducted from June to July 2016 on PubMed, Web of Science, Scopus, and CINAHL. A validated sensitive search filter (sensitivity = 97.4%; precision = 4.4%) for finding studies on measurement properties of outcome measures was used.[25] Only outcome measures included in phase 1 were searched in phase 2, however, if new outcome measures feasible to be used in community practice emerged from the search, they were also included. Reference lists of the identified

studies were scanned for other potential eligible studies and a weekly update was conducted until September 2016. The full search strategy can be found in eAppendix 2 (available at: https://academic.oup.com/ptj).

Study selection. Selection of studies was performed by 1 reviewer (A.L.O.) and checked by a second reviewer (A.S.M.). Inclusion and exclusion criteria were as in phase 1. Additionally, studies were included if information was reported regarding 1 or more measurement properties (ie, reliability – internal consistency, reliability, measurement error; validity – content validity, construct validity and criterion validity, responsiveness and interpretability). Studies were excluded if reported on measurement properties of outcome measures not feasible to use in community-based pulmonary rehabilitation programs, separated items of an outcome measure and did not included the full measure.

Data extraction and quality assessment. Data was extracted by 1 reviewer (A.L.O.) using 2 standardized tables, one for PROMs and another for clinical outcome measures. Data extracted were: outcome, outcome measure, author and year of publication, measurement property assessed, quality of the study, quality of the measurement property and costs.

Two independent reviewers (A.L.O. and A.S.M.) evaluated the quality of the included studies using the Consensus-Based Standards for the Selection of Health Status Measurement Instruments (COSMIN) checklist (ie, poor, fair, good, excellent).[26] A consensus method was used to solve disagreements between reviewers.

The quality of the outcome measures reported was determined using the rating system for measurement properties proposed by Terwee et al.[27] For each measurement property a criterion is defined for positive, negative and indeterminate rating.

Data synthesis and analysis. Data on PROMs and clinical outcome measures were separately analyzed. For each measurement property (ie, reliability, validity, responsiveness and interpretability), a synthesis of the quality of the study, using the COSMIN criteria,[26] and of the quality outcome measure, using the system of Terwee et al,[27] was performed.

The consistency of the quality assessment performed by the 2 reviewers was explored with an interrater agreement analysis using the Cohen kappa for each box of the COSMIN criteria. The Cohen kappa value ranges from 0 to 1 and can be categorized as slight (< 0.2), fair (0.21–0.4), moderate (0.41–0.6), substantial (0.61–0.8), or almost perfect (> 0.81) agreement.[28]

Results

Phase 1: Measures Used in Pulmonary Rehabilitation

Study selection. A total of 220 literature reviews were found. After duplicates were removed (n = 66) and exclusions were made on the basis of abstract and title screenings (n = 22), 132 full texts were screened and 15 literature reviews that reported on pulmonary rehabilitation interventions in patients with AECOPD were included. Additionally, 24 original studies included in the 15 reviews were extracted and searched for outcome measures not reported in the reviews.

The search conducted for original studies published after 2010 retrieved 257 original studies. After duplicates were removed (n = 134) and exclusions were made on the basis of abstract and title screenings (n = 23), 100 full texts were screened and 13 original studies were included. Thus, a total of 37 original studies were searched for outcome measures. A flow diagram concerning the literature reviews and original studies search and reasons for studies exclusions can be found in the Figure.

Study characteristics. The 37 studies included were conducted in 19 different countries. A steady increase in the number of studies investigating pulmonary rehabilitation in patients with AECOPD was observed, with only 7 papers published from 1964 to 2000 and 37 by 2016. Most studies were randomized control trials (n = 31)[15,16,29–57] conducted with inpatients (n = 27),[15,16,29,30,33,35,37–41,43,45–48,51–61] followed by hospital outpatient departments (n = 6),[15,37,38,42,44,49] inpatients plus patients' homes (n = 3),[31,32,50] community settings (n = 3),[34,62,63] and patients' homes (n = 1)[36] (Tabs. 1 and 2).

Outcomes and outcome measures. Twenty-three PROMs and 18 clinical outcome measures were identified. The most common patient-reported outcomes assessed were dyspnea (n = 24), using the modified Borg Scale (mBorg)[30,32,38,39,42,44,46,52–55,58,62,63] (n = 14), and health-related quality of life (n = 23), using the St George Respiratory Questionnaire (SGRQ)[16,34-37,39,42,44,49–51,54,56,58,59] (n = 15). The most common clinical outcomes assessed were functional exercise capacity (n = 24), using the 6-minute walk test[16,30-32,37,38,41,43,44,48,49,51–53,56,58,63] (n = 21), and lung function (n = 13), using the FEV_1[16,30,31,36,39,44,55,57,60,61] (n = 10). Other outcomes assessed were anxiety and depression, fatigue, cough, physical activity, strength, activities of daily

living, lung function, peripheral blood gases, subjective airway clearance, and body composition.

Tables 1 and 2 show the patient-reported and clinical outcomes and outcome measures reported.

Phase 2: Properties of Measures

Study selection. The search for measurement properties identified 82 studies. After the removal of duplicates, 41 studies were screened. During the title and abstract screening, 18 studies were excluded. The full text of 23 studies was assessed and another 15 studies were excluded. Therefore, 8 original studies were selected. The search for relevant studies within the reference lists retrieved 24 additional studies. Therefore, a total of 32 studies were included in this review (Figure).

Measurement properties. The measurement properties of 22 PROMs used to assess 5 outcomes (ie, dyspnea [6 outcome measures], health-related quality of life [11 outcome measures], health status [2 outcome measures], activities of daily living [2 outcome measures], and general symptoms [1 outcome measure]) were reported by 26 of 32 studies. The measurement properties of 7 clinical outcome measures used to assess 4 outcomes (ie, oxygen saturation [1 outcome measure], lung function [4 outcome measures], body composition [1 outcome measure], and physical activity [1 outcome measure]) were reported in 8 of 32 studies.

The methodological quality of each study and the quality of the measurement properties of each measure can be found in Tables 3 and 4. The agreement between the 2 independent reviewers using the COSMIN quality assessment was substantial ($\kappa = 0.688$).

The characteristics of the included studies and synthesis of the results per outcome and outcome measure can be found in eAppendix 3 (available at: https://academic.oup.com/ptj; eTab. 1a and eTab. 1b).

Quality and properties of PROMs. Reliability was studied for 5 PROMs in 5 studies of fair to excellent methodological quality (ie, SGRQ, Chronic Respiratory Diseases Questionnaire [CRQ], Clinical COPD Questionnaire [CCQ], and COPD Assessment Test [CAT])[64–68] and in 2 studies of poor methodological quality (ie, CCQ and Exacerbations of Chronic Pulmonary Disease Tool–Patient-Reported Outcome [EXACT-PRO]).[67,69] Studies were rated as poor mainly because an analysis of the unidimensionality of the scale was not preformed.

Measurement properties presented positive results in all reliability categories assessed (ie, internal consistency and test-retest; measurement error has not been assessed) and for all outcome measures (Tab. 3).

Validity was studied for most PROMs, except for the mBorg, visual analog scale, Short-Form 6D, and Nottingham Health Profile, in 21 studies.[64–84] Overall, the methodological quality of the studies was rated from poor to fair, except for structural validity studied in the CRQ and the CAT, which were rated excellent.[64,65] For criterion validity, reasons for rating "poor" were

related with the inadequacy of the gold standard used as comparator. Regarding to construct validity, weaknesses included lack of formulation of hypotheses and lack of description of the comparator instrument.

Criterion validity was indeterminate in 5 studies (ie, modified Medical Research Council [MRC], MRC, extended MRC, CCQ, COPD severity score, EuroQol 5D [EQ-5D], Breathing Problems Questionnaire, London Chest Activities of Daily Living Scale [LCADL], and Manchester Respiratory Activities of Daily Living Questionnaire)[70,71,77,79,81] and positive in 1 study (ie, Global Initiative for Chronic Obstructive Lung Disease plus Symptom Severity Index [GOLD + SSI]).[83] Structural validity presented positive results in 2 studies (ie, CRQ and CAT).[64,65] Construct validity, was indeterminate in 11 studies (ie, Baseline Dyspnea Index and Transition Dyspnea Index [BDI/TDI], SGRQ, CRQ, CCQ, COPD severity score, EQ-5D, Short-Form 6D, Measure Your Medical Outcome Profile, and Medical Outcomes Study 6-Item General Health Survey, modified MRC, SGRQ, EXACT-PRO, and LCADL)[66,68-70,72,75,76,79,80,82], negative in 2 studies (ie, SGRQ and CRQ)[64,73], and positive in 7 studies (ie, SGRQ, CRQ, CCQ, CAT, and Cough and Sputum Assessment Questionnaire)[65,67,74-76,78,84] (Tab. 3).

Responsiveness was studied for most PROMs, except for the modified MRC, MRC, extended MRC, Breathing Problems Questionnaire, GOLD + SSI, Manchester Respiratory Activities of Daily Living Questionnaire, and LCADL, in 19 studies of poor to fair methodological quality.[64,66–69,72–77,79,80,84–89] Common weaknesses of studies included lack of description of the comparator instrument and inadequacy of design and statistical methods used.

Responsiveness was indeterminate in 14 studies (ie, SGRQ, CCQ, COPD severity score, EQ-5D, Short-Form 6D, Nottingham Health Profile, Measure Your Medical Outcome Profile, Medical Outcomes Study 6-Item General Health Survey, EXACT-PRO, Cough and Sputum Assessment Questionnaire, mBorg, visual analog scale, and CCQ),[66–69,73,75,77,79,80,84–87,89] negative in 5 studies (ie, SGRQ, CRQ, CAT, and EQ-5D),[64,72,74,75,79] and positive in 3 studies (ie, BDI/TDI and CAT)[72,76,88] (Tab. 3).

Interpretability was found in 2 studies which presented values of the minimal clinically important difference (MCID) for the CRQ (MCID = 1.01)[64] and the CCQ (MCID = 0.44).[68]

Quality and properties of clinical measures. Reliability was not studied for any of the clinical outcome measures found (Tab. 4).

Validity was studied for all clinical outcome measures in 8 studies of fair to poor methodological quality.[70,72,90–95] For criterion validity, reasons for rating "poor" were related with the inadequacy of the gold standard used as comparator, whereas for construct validity reasons were related to the lack of formulation of hypotheses and the lack of description of the comparator instrument.

Overall, measurement properties presented positive results for criterion validity assessed in 4 studies (ie, peripheral oxygen saturation [SpO_2], forced vital capacity, and computerized respiratory sounds)[70,90,93,94]; however, in 1 study assessing the FEV_1, criterion validity was indeterminate.[70] Regarding to construct validity, indeterminate results were found in 2 studies

(ie, SpO_2, peak expiratory flow [PEF], FEV_1, and forced vital capacity)[70,92] and positive results in 3 studies (ie, SpO_2, PEF, and time spent in weight-bearing activities assessed with an accelerometer)[90,91,95] (Tab. 4).

Responsiveness was studied for the PEF and FEV_1 in 2 studies[72,91] of fair and poor methodological quality, respectively. The study was rated as poor because it did not describe the measurement properties of the comparator instrument.

Responsiveness was rated positive for the PEF[91] and indeterminate for the FEV_1[72] (Tab. 4).

Interpretability was not studied for any of the clinical outcome measures found (Tab. 4).

Discussion

To our knowledge, this is the first systematic review to provide a comprehensive overview of the measurement properties of the outcome measures most used in pulmonary rehabilitation programs during AECOPD and that can be easily applied in a community setting. Twenty-three PROMs and 18 clinical outcome measures were identified in intervention studies. The most used measures were the St George Respiratory Questionnaire (n = 15/37) and the 6-minute walk test (n = 21/37). Several measures have been used only in isolated studies (ie, New York Heart Association Functional Classification, Activities of Daily Living Dyspnea Scale, diaries, Functional Assessment of Chronic Illness Therapy, feeling thermometer, mBorg fatigue, LCADL, 3-minute step test, 3-minute walk test, 2-minute step-in-place test, FEV_1/forced vital capacity, computerized respiratory sounds, fat-free mass index, body mass

index, accelerometer, quadriceps twitch responses, and maximum inspiratory pressure). Measurement properties were only synthesized for 22 PROMs and 7 clinical outcome measures. The methodological quality of most studies was poor, and the results obtained for the measurement properties were indeterminate. The PROMs and clinical outcome measures exhibiting the most appropriate measurement properties were the CAT and SpO_2, respectively.

The most used PROMs were the mBorg and the SGRQ. Dyspnea and health-related quality of life have been reported as the outcomes that better reflect the overall impact of the disease[96] and, therefore their monitoring during AECOPD, with appropriate outcome measures, is essential to guide health professionals on the most effective interventions. Nevertheless, the measurement properties of the mBorg have been little reported and, when reported, in studies of poor methodological quality. The BDI/TDI, although not commonly used, was the only outcome measure which rated fair and positive for responsiveness on dyspnea. The SGRQ has shown appropriate test retest reliability but inconclusive validity and responsiveness. Although, the SGRQ has strong measurement properties in stable patients with COPD,[24,97] it reports to the past month, 3 months and 1 year. These inappropriate timeframes to assess improvements from an AECOPD, which usually takes 1 to 3 weeks to be meaningful to patients,[23,98] might explain some of the divergent results found. Measurement properties of CAT have been assessed in a reasonable number of studies of fair methodological quality[65,75,76,78,88] and positive results have been found. Therefore, the BDI/TDI and CAT may be promising PROMs to assess the effectiveness of community-based pulmonary rehabilitation in patients with AECOPD.

The most used clinical outcome measures were the FEV_1 and the 6-minute walk test. However, the measurement properties of the FEV_1 were found in studies of poor methodological quality and no studies were found reporting on the measurement properties of the 6-minute walk test in patients with AECOPD which impaired conclusions regarding its use. Similarly to exercise tolerance, no studies were found reporting on measurement properties of muscle strength. Currently, it is known that the inflammatory effects of AECOPD are not confined to the lungs but also impair peripheral muscle strength and exercise tolerance.[1] Declines in these outcomes are independent predictors of hospitalizations and mortality.[99,100] Early rehabilitation may play a crucial role in preventing and reducing losses in exercise capacity, muscle strength and musculoskeletal dysfunction,[16,43] thus possibly reverting this cascade of events. Nevertheless, there is the urgent need to establish the measurement properties of clinical outcome measures for AECOPD to assess patients' dysfunctions, plan interventions, and verify their effectiveness.

This systematic review evidenced that the conflicting results of pulmonary rehabilitation programs in patients with AECOPD[10,15,16,50] may not be related to the quality of treatment but with the lack of appropriateness of measurement proprieties of the outcome measures used. Additionally, whilst the methodology of this review target only measures that could be implemented in community settings (ie, simple and accessible measures), our results can also be applicable to other clinical settings where these measures are available. Nevertheless, since most AECOPD are recommended to be managed in the community and community-based pulmonary rehabilitation might be a promising intervention for minimizing a patient's decline and prevent recurrence, robust studies on the validity, reliability and responsiveness, as well as on availability, cost and interpretability (ie, by establishing the MCID), of outcome

measures are urgently needed. These studies will contribute to clarify the role of community-based pulmonary rehabilitation in patients with AECOPD.

Study Limitations

This study has some limitations that need to be acknowledged. Several relevant studies for this systematic review[67–69,71–73,75,77–79,81–83,85,86,88–95] were not found with the validated search strategy used and were only included after searching through the reference lists of the reviewed studies. Relevant studies may have fallen out of the search due the absence of keywords related to measurement properties in their title, abstract or keywords, which impaired the filter used to identify them. Adequate use of the Medical Subject Headings (MESH) terms is warranted to identify the purpose of the studies and improve the quality of the results found in future systematic reviews.

This systematic review has followed the COSMIN recommendations to assess the quality of the included studies. The COSMIN was originally developed for health-related PROMs, such as questionnaires,[26] and thus its validity, reliability and adequacy for assessing the methodological quality of clinical studies and outcome measures, may be questioned. Nonetheless, in the absence of a measure specifically designed to evaluate such studies and outcome measures, the COSMIN is indicated as an adequate alternative tool.[101,102]

The selection of studies was performed by 1 reviewer which could have caused bias in the studies selection. This limitation has been mitigated by consulting a second reviewer when uncertainties were found and by defining strict inclusion and exclusion criteria prior to studies selection.

Finally, 3 of the studies included presented combined results of stable and exacerbated patients with COPD[69,73,74] which could have affected some of the conclusions established. Nevertheless, the results of these studies have been considered within the universe of all studies included, and thus we believe that any potential bias that could have been introduced was diluted. Future studies should focus on patients with AECOPD only, so that recommendations regarding its measurement properties can be established with confidence.

Conclusions

Although a large number of outcome measures easy to implement in a community-based setting have been used to assess pulmonary rehabilitation in patients with AECOPD, their measurement properties have been poorly studied. Given the wide availability of measures it does not seem necessary to develop new outcome measures to be used in community-based pulmonary rehabilitation of patients with AECOPD. Instead, studies following the COSMIN standards to evaluate the measurement properties (ie, reliability, validity and responsiveness) of the existing outcome measures are recommended. Such studies would contribute to clarify the role of community-based pulmonary rehabilitation in patients with AECOPD and guide the development of core outcome sets.

Author Contributions

Concept/idea/research design: A.L. Oliveira, A.S. Marques
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Disclosures

The authors completed the ICJME Form for Disclosure of Potential Conflicts of Interest. No disclosures were reported.

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Table 1.

Patient-Reported Outcomes Used in Pulmonary Rehabilitation of Patients With Acute Exacerbation (AE) of Chronic Obstructive Pulmonary Disease (COPD)[a]

Outcome	Outcome Measure	Patient Characteristics					Intervention Setting	Intervention Timing	Intervention Duration
		No. of Patients	Age (y)	FEV_1pp (%)	FEV_1ppAE (%)	FEV_1ppST (%)			
Dyspnea	BDI/TDI[30–32]	26–30	62.3–69		34.1–60		Inpatient and home	4–8 d after hospital presentation	11 d–18 mo
	VAS[35,60]	1–27	68.4–74	NS			Inpatient	At hospital presentation to 2 d after hospital presentation	45 min–2 mo
	Borg Scale[33,36,41]	26–110	61–75			35–42	Inpatient and home	At hospital presentation to hospital discharge	Until hospital discharge to 6 wk
	mBorg[30,32,38,39,42,44,46,52–55,58,62,63]	19–1,826	45–78.8		34.1–69.4	50.5–56	Inpatient, hospital outpatient department, and	At hospital presentation to 3 wk after discharge	60 min–19 mo

							community		
	MRC[36,39,49,52,59]	19–94	58.4–73.9		38–53.3	29–56	Inpatient, hospital outpatient department, and home	At hospital presentation to 2 wk after discharge	Until hospital discharge to 12 wk
	mMRC[15,38,44,48,51,63]	19–97	56.8–73.8 (mean)		35–69.4	37.3–44.4	Inpatient, hospital outpatient department, and community	At hospital presentation to 3 wk after discharge	Until hospital discharge to 12 wk
	NYHA[41]	38	61	NS			Inpatient	As soon as stable	Until hospital discharge
	ADLDS[52]	94	69.2–73.9		38–39		Inpatient	2 d after hospital presentation	Until hospital discharge
HRQL	Diary[32]	26	64–69		34.9–37.5		Inpatient and home	4–7 d after admission	19 mo
	CRQ[15,31,32,34,37,38,42,52]	19–97	64–73.9		34.1–52	36.7–42.7	Inpatient, hospital outpatient department, community, and home	As soon as stable to 3.7 wk after hospital presentation	Until hospital discharge to 18 mo

	SGRQ[16,34–37,39,42,44,49–51,54,56,58,59]	19–1,826	58.4–78.8		35.6–56.1	29–56	Inpatient, hospital outpatient department, community, and home	As soon as stable to 2 wk after hospital presentation	Until hospital discharge to 12 wk
	SF-36[34,38,44]	24–97	69.6–73.8		35–56.1	36.7–41.7	Inpatient, hospital outpatient department, and community	After discharge to 3 wk after hospital presentation	8 wk
	EQ-5D[36,42,55,56]	16–526	65–73.7		52	38–42	Inpatient, hospital outpatient department, and home	As soon as stable to 1 wk after hospital discharge	Until hospital discharge to 8 wk
	CAT[52,61]	11–94	69.2–78		34–39		Inpatient	1–2 days after hospital presentation	2 d to until hospital discharge
	FACIT fatigue[59]	19	71			29	Inpatient	Immediately at hospital presentation	6 wk
	Feeling thermometer[15]	19	67.5			42.7	Inpatient or hospital outpatient department	2 wk after hospital presentation	12 wk

Anxiety and depression	HADS[38,55]	49–97	69.7–73.7	35–41			Inpatient and hospital outpatient department	As soon as stable to immediately after discharge	Until hospital discharge to 8 wk
Fatigue	mBorg[42]	60	65–67	52			Hospital outpatient department	1 wk after discharge	8 wk
Sputum	VAS sputum[53,61]	11–61	68–78		34–39		Inpatient	As soon as stable	2–4 d
General symptoms	BCSS[51,56,61,62]	11–90	56.8–78		34–69.4	37.3–44.4	Inpatient and community	At hospital presentation to 72 h after hospital presentation	60 min to until hospital discharge
ADL	Barthel Index[33,57]	21–110	68–75		45.1–46.1	35–38	Inpatient	At hospital presentation to 72 h after hospital presentation	Until hospital discharge
	LCADL[54]	44	77.4–78.8		41.8–41.4		Inpatient	As soon as stable	8–9 d
Composite measure	BODE Index[38,48,51,52]	50–97	65.1–73.9		35–39	37.3–44.4	Inpatient and hospital outpatient department	At hospital presentation to 2 d after hospital presentation	Until hospital discharge to 8 wk

[a]ADL = activities of daily living; ADLDS = Activity of Daily Living Dyspnea Scale; AE = acute exacerbation; BCSS = Breathlessness, Cough, and Sputum Scale; BDI/TDI = Baseline Dyspnea Index and Transition Dyspnea Index; BODE = body mass index, airflow obstruction, dyspnea, and exercise capacity; CAT = COPD Assessment Test; CRQ = Chronic Respiratory Disease Questionnaire; EQ-5D = EuroQol 5D; FACIT = Functional Assessment of Chronic Illness Therapy; FEV_1pp = percentage predicted forced expiratory volume in 1 s; HADS = Hospital Anxiety and Depression Scale; HRQL = Health-Related Quality of Life; LCADL = London Chest Activities of Daily Living Scale; mBorg = modified Borg Scale; MRC = Medical Research Council; mMRC = modified MRC; NS = not stated; NYHA = New York Heart Association Functional Classification; SF-36 = Short Form (36-Item) Health Survey; SGRQ = St George Respiratory Questionnaire; ST = stable; VAS = visual analog scale.

Table 2.

Clinical Outcomes Used in Pulmonary Rehabilitation of Patients With Acute Exacerbation (AE) of Chronic Obstructive Pulmonary Disease (COPD)[a]

Outcome	Outcome Measure	Patient Characteristics					Intervention Setting	Intervention Timing	Intervention Duration
		No. of Patients	Age (y)	FEV_1pp	FEV_1ppAE	FEV_1ppST			
Functional exercise capacity	6MWT[16,30–32,37,38,41,43,44,48,49,51–53,56,58,63]	28–1,826	61–73.9		34.1–69.4	50.5	Inpatient, hospital outpatient department, community, and home	At hospital presentation to 3 wk after discharge	4 d–18 mo
	ISWT[34,36,42,50]	26–196	65–71.1		52	36.7–51.9	Inpatient, hospital outpatient department, community, and home	Immediately to 10 d after discharge	6–8 wk
	ESWT[42,47,50]	20–196	65–70.1		52	39.8–51.9	Inpatient, hospital outpatient department, and home	At hospital presentation to 1 wk after discharge	Until hospital discharge to 8 wk

	3-min step test[36]	26	65–67			38–42	Home	Immediately after discharge	6 wk
	3-min walk test[57]	21	68–73.6		45.1–46.1		Inpatient	48 h after hospital presentation	Until hospital discharge
	2-minute step-in-place test[55]	49	72.4–73.7		39–41		Inpatient	As soon as stable	Until hospital discharge
Oxygen saturation	SpO_2[30,38–40,52,55,56,60,62]	1–526	56.8–73.9		35–69.4	52–56	Inpatient, hospital outpatient department, and community	At hospital presentation to 8 d after hospital presentation	45 min–8 wk
Lung function	FEV_1[16,30,31,36,39,44,55,57,60,61]	1–60	62.3–78		34–56.1	38–56	Inpatient, hospital outpatient department, and home	At hospital presentation to 3 wk after hospital discharge	45 min–18 mo
	FVC[30,31,36,39,61]	11–59	62.3–78		34–39	38–56	Inpatient and home	At hospital presentation to immediately after hospital discharge	2 d–18 mo

	FEV_1/FVC[39]	59	70.2			57.9–64.4	Inpatient	At hospital presentation	7 d
	PEF[40,41]	38–45	61	NS			Inpatient	At hospital presentation	Until hospital discharge
	CRS[62]	19	56.8		69.4		Community	Within 48 to 72 h after hospital presentation	3 wk
Body composition	Fat-free mass index[42]	60	65–67		52		Hospital outpatient department	1 wk after hospital discharge	8 wk
	BMI[51]	90	67.8–69.5		35.9–35.6	37.3–44.4	Inpatient	2 d after hospital presentation	Until hospital discharge
Physical activity	Accelerometer[16]	29	67.8–64.1		39.1–41.7		Inpatient	3 d after hospital presentation	At least 3 sessions
Strength	MVIC[16,36,42,43,45,47,50,54,55,57]	11–196	65–78.8		39.1–52	38–51.9	Inpatient, hospital outpatient department, and home	At hospital presentation to 1 wk after hospital discharge	7 d–8 wk
	TwQ[42]	60	65–67		52		Hospital outpatient	1 wk after hospital	8 wk

							department	discharge	
	MIP[30]	28	62.3 – 65.6		38		Inpatient	6–8 d after hospital presentation	11 d

[a]6MWT = 6-min walk test; AE = acute exacerbation; BMI = body mass index; CRS = computerized respiratory sounds; ESWT = endurance shuttle walk test; FEV_1 = forced expiratory volume in 1 s; FEV_1pp = percentage predicted FEV_1; FVC = forced vital capacity; ISWT = incremental shuttle walk test; MIP = maximum inspiratory pressure; MVIC = maximal voluntary isometric contraction; NS = not stated; PEF = peak expiratory flow; SpO_2 = peripheral oxygen saturation; ST = stable; TwQ = quadriceps twitch responses.

760 **Table 3.**

761 Consensus-Based Standards for the Selection of Health Status Measurement Instruments (COSMIN) Evaluation, Quality of the Measurement

762 Property, and Cost of Patient-Reported Outcomes[a]

Outcome	Outcome Measure	Study	Reliability		Validity			Responsiveness	Cost
			Internal Consistency	Test-Retest	Criterion Validity	Structural Validity	Construct Validity (Hypothesis Testing)		
Dyspnea	mBorg	Kendrick et al, 2000[85]						Poor/?	Free
	VAS	Lemasson et al, 2007[86]						Poor/?	Free
	mMRC	Güryay et al, 2007[70]			Poor/ ?		Poor/?		Free
	MRC	Steer et al, 2012[71]			Poor/ ?				Free
	eMRC	Steer et al, 2012[71]			Poor/ ?				No information
	BDI/TDI	Aaron et al, 2002[72]					Poor/?	Fair/+	Not free for commercial use
HRQL	SGRQ	Doll et al, 2003[73]					Fair/−	Poor/?	Free
		Bourbeau et al, 2004[74]					Fair/+	Fair/−	
		Menn et al, 2010[87]						Poor/?	
		Katsoulas et al, 2010[66]		Fair/+			Good/?	Poor/?	
		Jones et al, 2012[75]					Poor/?	Poor/?	
		Tu et al, 2014[76]					Poor/?		
	CRQ	Bourbeau et al, 2004[74]					Fair/+	Fair/−	Not free
		Tsai et al,	Excellent/+			Excellent/	Poor/−	Fair/−	

		2008[64]				+			
		Aaron et al, 2002[72]					Poor/?	Fair/−	
	CCQ	Trappenburg et al,2010[77]			Fair/?			Poor/?	Not free
		Antoniu et al, 2014[67]	Poor/+	Fair/+			Fair/+	Poor/?	
		Kocks et al, 2006[68]					Poor/?	Poor/?	
	CAT	Jones et al, 2009[65]	Excellent/+			Excellent/+	Fair/+		Not free for commercial use
		Jones et al, 2011[78]					Fair/+		
		Jones et al 2012[75]					Fair/+	Poor/−	
		Mackay et al, 2012[88]						Fair/+	
		Tu et al, 2014[76]					Poor/+	Fair/+	
	COPDSS	Miravitlles et al, 2011[79]			Fair/?		Poor/?	Poor/?	Free
	EQ-5D	Menn et al, 2010[87]						Poor/?	Not free for clinical and commercial use
		Goossens et al, 2011[89]						Poor/?	
		Miravitlles et al, 2011[79]			Fair/?		Poor/?	Fair/−	
		Paterson et al, 2000[80]					Poor/?	Poor/?	
	SF-6D	Menn et al, 2010[87]						Poor/?	Not free for commercial use
	BPQ	Yohannes et al, 2005[81]			Poor/?				Not free for commercial use
	NHP	Doll et al, 2003[73]						Poor/?	Not free; copyright held by Galen Research
	MYMOP	Paterson et al, 2000[80]					Poor/?	Poor/?	Free

	MOS-6A	Paterson et al, 2000[80]					Poor/?	Poor/?	Free
Health status	EXACT-PRO	Leidy et al, 2014[82]					Poor/?		Not free for commercial use
		Leidy et al, 2011[69]	Poor/+				Poor/?	Poor/?	
	GOLD + SSI	Hutchinson et al, 2010[83]			Poor/+				Free
ADL	MRADL	Yohannes et al, 2005[81]			Poor/?				Not free for commercial use
	LCADL	Miravitlles et al, 2011[79]			Fair/?		Poor/?		Free
General symptoms	CASA-Q	Monz et al, 2010[84]					Poor/+	Poor/?	No information

[a]ADL = activities of daily living; BDI/TDI = Baseline Dyspnea Index and Transition Dyspnea Index; BPQ = Breathing Problems Questionnaire; CASA-Q = Cough and Sputum Assessment Questionnaire; CAT = COPD [Chronic Obstructive Pulmonary Disease] Assessment Test; CCQ = Clinical COPD Questionnaire; COPDSS = COPD severity score; CRQ = Chronic Respiratory Disease Questionnaire; eMRC = extended Medical Research Council (MRC); EQ-5D = EuroQol 5D; EXACT-PRO = Exacerbations of Chronic Pulmonary Disease Tool–Patient-Reported Outcome; GOLD = Global Initiative for Chronic Obstructive Lung Disease; HRQL = Health-Related Quality of Life; LCADL = London Chest Activities of Daily Living Scale; mBorg = modified Borg Scale; mMRC = modified MRC; MOS-6A = Medical Outcomes Study 6-Item General Health Survey; MRADL = Manchester Respiratory Activities of Daily Living Questionnaire; MYMOP = Measure Your Medical Outcome Profile; NHP = Nottingham Health Profile; SF-6D = Short-Form 6D; SGRQ = St George Respiratory Questionnaire; SSI = Symptom Severity Index; VAS = visual analog scale; + = positive; − = negative; ? = indeterminate.

Table 4.

Consensus-Based Standards for the Selection of Health Status Measurement Instruments (COSMIN) Evaluation, Quality of the Measurement Property, and Cost of Clinical Outcomes[a]

Outcome	Outcome Measure	Study	Reliability		Validity		Responsiveness	Cost
			Internal Consistency	Test-Retest	Criterion Validity	Construct Validity (Hypothesis Testing)		
Oxygen saturation	SpO_2 (%)	Güryay et al, 2007[70]			Fair/+	Poor/?		Not free
		Kelly et al, 2001[90]			Fair/+	Poor/+		
Lung function	PEF (pp)	Emerman et al, 1996[91]				Poor/+	Fair/+	Not free
		Güryay et al, 2007[70]				Poor/?		
	FEV_1 (pp or L)	Güryay et al, 2007[70]			Poor/?	Poor/?		Not free
		Aaron et al, 2002[72]					Poor/?	
		White et al, 2005[92]				Poor/?		
	FVC (pp)	Güryay et al, 2007[70]				Poor/?		Not free
	CRS	Morillo et al, 2013[93]			Fair/+			Not free
Body composition	BMI (kg/m^2)	Tsimogianni et al, 2009[94]			Poor/+			Free
Physical activity	Time spent in weight-bearing activities (min)	Pitta et al, 2006[95]				Poor/+		Not free

[a]BMI = body mass index; CRS = computerized respiratory sounds; FEV_1 = forced expiratory volume in 1 s; FVC = forced vital capacity; PEF = peak expiratory flow; pp = percentage of predicted normal value; SpO_2 = peripheral oxygen saturation; + = positive; − = negative; ? = indeterminate.

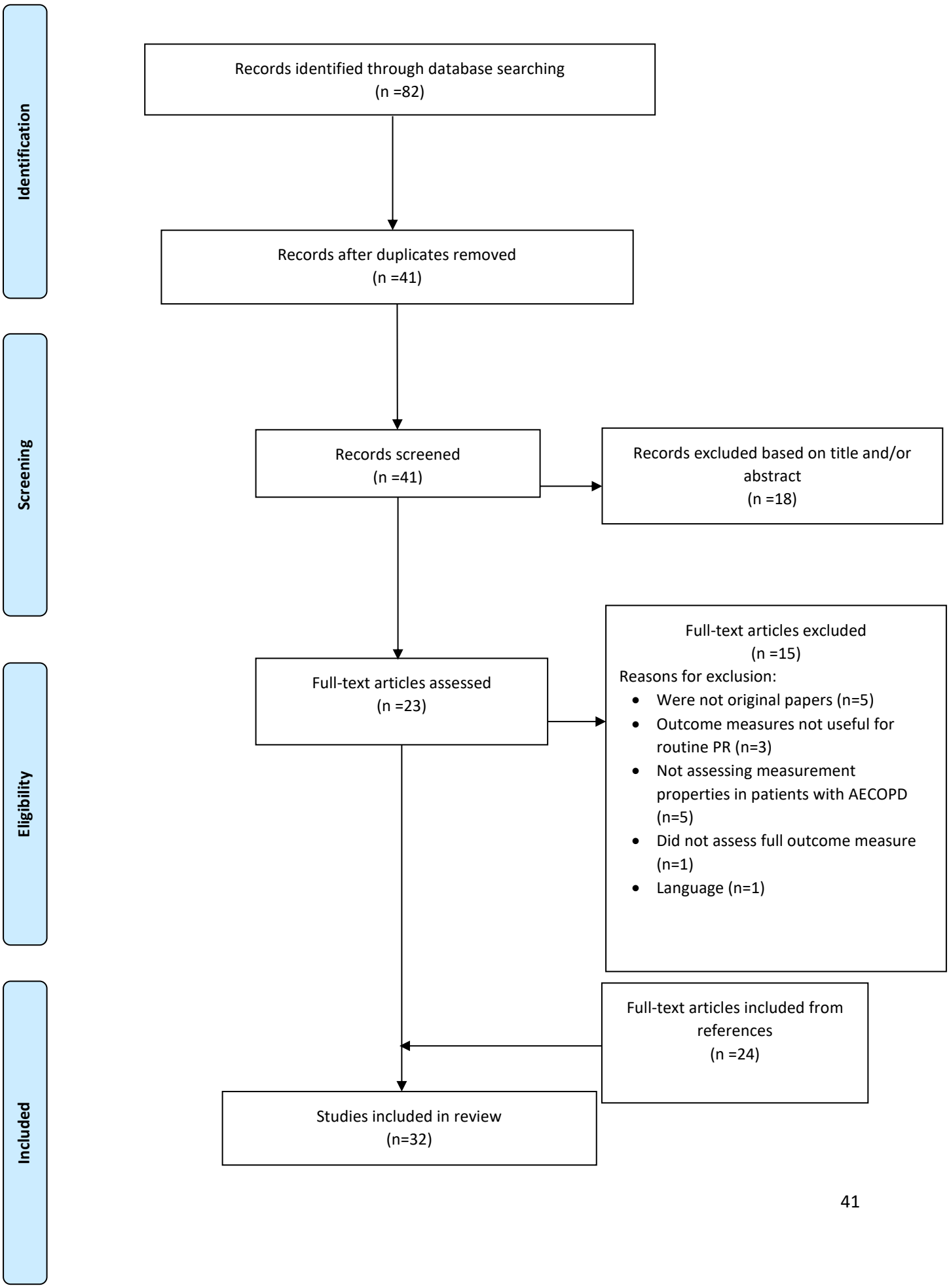
Identification
Screening
Eligibility
Included
Records identified through database searching
(n =82)
Records after duplicates removed
(n =41)
Records screened
(n =41)
Records excluded based on title and/or abstract
(n =18)
Full-text articles assessed
(n =23)
Full-text articles excluded
(n =15)
Reasons for exclusion:
Were not original papers (n=5)
Outcome measures not useful for routine PR (n=3)
Not assessing measurement properties in patients with AECOPD (n=5)
Did not assess full outcome measure (n=1)
Language (n=1)
Full-text articles included from references
(n =24)
Studies included in review
(n=32)

Figure.

Flow diagram of the studies assessing the measurement proprieties of the outcome measures used in the pulmonary rehabilitation (PR) of patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) (phase 2).