Supplementary file: Full detailed description of the methodology of the systematic review

Search strategy

PubMed, EMBASE and the Cochrane Library were searched to identify relevant literature. The search strategy included various terms for the MCID determination of HRQoL questionnaires and/or health status measurement tools and/or PROs in adults with COPD (Supplementary Table 1). The search was conducted on the 9th of June 2015 and updated regularly with the final update on the 16th of June 2017. It included all studies and research designs prior to this.

Study criteria

Studies were considered eligible if they included approaches and original measurement data for the MCID of a generic or disease-specific HRQoL questionnaire and/or health status instrument and/or PRO used in a COPD population. HRQoL and health status instruments were considered eligible when they captured more than one domain of the concepts physical, psychological and social functioning [1-2]. In COPD patients, this would include concepts such as breathlessness, fatigue, cough, sputum production, physical functioning, social functioning, mental well-being and exacerbations [16]. The term health status will be used for future reference in this review. Only full-text studies containing original data were included. Conference abstracts, editorials and opinion articles were excluded. Reviews were initially included to explore the references. Non-English publications were translated if considered eligible.

Study selection

Titles and abstracts of the identified articles were screened by two authors (HA and CdJ) independently. The screening process included: (1) the study design and type was identified; (2) the measurement tool was identified; (3) a judgement was made whether the tool was a questionnaire or PRO, which measured health status according to the predefined inclusion definition; (4) the population was identified and screened for adults with COPD; (5) the aim of the study was identified, which needed to determine the instrument's MCID; (6) a description of the MCID methodology and final quantitative estimates should be available; (7) final judgement for eligibility was made. Independent results from both authors were compared. Where disagreement occurred, this was discussed and consensus was reached, or a third author (IT, TvdM or RS) was consulted. Full-text articles were retrieved for the selected studies and again checked according to the above stated seven steps. The

reference lists of the selected articles were screened for additional titles. The abstracts of the additional titles were screened accordingly for meeting the pre-defined inclusion criteria.

Quality assessment and risk of bias

Eligible full text articles were assessed for their quality and risk of bias by two authors (HA and CdJ) independently. Disagreement was discussed and consensus was reached. The authors composed a quality assessment and risk of bias tool by selecting 31 relevant items from various sources, because there was no specific evaluation tool available for evaluating studies that measure an instrument's MCID (Supplementary Table 2). Furthermore, various research designs were included, which made it difficult to use one checklist.

Items on study methodology and questionnaire design were selected from the Cochrane Risk of Bias tool [67] and the COSMIN checklist [68]. These items concerned the attrition and missing data procedures; selective outcome reporting; risk of funding and ownership bias; availability of at least two health status measurements; time interval of measurement stated; similar test conditions for both measurements; follow-up completed; validation and properties of the health status tool described; floor- and ceiling effects described; whether the MCID was calculated; and whether criterion/anchors used were considered golden standard. Additional items were retrieved from the systematic reviews by Bohannon et al. [58-59]: clear inclusion/exclusion criteria; systematic enrollment of patients; missing data percentage less than 25%; more than one anchor used; and the use of Receiver Operating Characteristics (ROC) Curves with an Area Under the Curve (AUC) of at least 0.70. The current authors added the following items based upon recommendations in the literature [2, 33, 45, 69]: adequate description of the anchor and its properties; anchor correlations at least 0.50; Global Rating of Change (GRC) used with 11 or more scoring options; type of clinical criterion used; more than one distribution-based method used; MCID for more than one population measured; and whether the MCID was determined for improvement, deterioration or both.

The general scoring of the quality assessment and risk of bias included the answering options "yes", "no", "unclear" and "not applicable", as deducted from the COSMIN checklist [68]. "Not applicable" was selected for MCID related items that were not relevant for the corresponding study. Positive answers / low bias items were scored two points; unclear items were scored one point; and negative answers / high bias / not applicable items were scored zero points. Individual items were scored and presented. An overall total score with a maximum of 62 could be obtained. Five categories were defined for the overall quality stratification, which were required for

triangulation procedures. Summed scores of 0-12 were qualified one star; 13-25 two stars; 26-37 three stars; 38-49 four stars; and 50-62 five stars as overall risk of bias and quality rating.

Data extraction, synthesis and analysis

Data were extracted using a standardized form including the general article properties; study properties; patient characteristics; health status measurements; and MCID properties (methodology, type of change, type of MCID, MCID estimates, and missing data procedures). Results from the full-text analysis were categorized per identified health status tool. Data were presented in tables and figures. A narrative synthesis of the MCID results, its methodology and its quality was prepared per instrument including forest plots. Primary outcome measures were the quality assessment of the MCIDs for health status tools in COPD, an overview of its MCID methods and estimates; as well as triangulation of the MCIDs where multiple studies per instrument existed. Since no standard for triangulation exists, the authors determined the final triangulation as following: Triangulation was executed by first determining an anchor-based and distribution-based MCID per included study. The anchor-based result received a weight of 2/3, while the distribution-based method received a weight of 1/3. The results were multiplied by a weighted factor for its study size (N) and quality rating (1-5 stars). An overall weighted triangulated mean MCID was calculated per health status tool.

Supplementary Table S1: Search strategy (PICO) and search dates for PubMed, EMBASE and the Cochrane Library

Database	Search terms	Search date
PubMed	P - Concept Patients with COPD "Pulmonary Disease, Chronic Obstructive"[Mesh] OR COPD [tw] OR Chronic Obstructive Pulmonary Dis* [tw] OR Obstructive Pulmonary Dis* [tw] OR Pulmonary Dis* [tw] OR Chronic Obstructive Airway Dis* [tw] OR Obstructive Airway Dis* [tw] OR Airflow Limitation* [tw] OR Airflow Obstruction* [tw] OR Chronic Bronchitis [tw] OR Bronchitis [tw] OR Emphysema [tw] OR Chronic Airway Dis* [tw] OR Respiratory Dis* [tw] AND I - Concept Patient reported health status questionnaires Patient-reported outcome*[tw] OR Patient Reported Outcome*[tw] OR PRO [tw] OR "Health Status"[Mesh] OR health status[tw] OR "Health Status Indicators"[Mesh] OR "Quality of Life"[Mesh] OR Quality Of Life [tw] OR QoL [tw] OR "Questionnaires"[Mesh] OR Questionnaire* [tw] AND C – none AND O – Minimal Clinically Important Difference (MCID) MCID [tw] OR MID [tw] OR minimum clinically important difference*[tw] OR minimum clinical important difference*[tw] OR minimum important difference*[tw] OR minimal clinically important difference*[tw] OR minimal clinical important difference*[tw] OR minimal important difference* [tw] OR minimally important difference*[tw] OR minimally clinical important difference*[tw] OR minimally clinically important difference*[tw] OR minimum clinically important change*[tw] OR minimum clinical important change* [tw] OR minimum important change*[tw] OR minimal clinically important change*[tw] OR minimal clinical important change* [tw] OR minimally important change*[tw] OR minimally clinically important change*[tw] OR minimally clinical important change* [tw] OR minimum clinically important improvement*[tw] OR minimum clinical important improvement* [tw] or minimum important improvement* [tw] OR minimal clinically important improvement*[tw] OR minimal clinical important improvement* [tw] or minimal important improvement* [tw] OR minimally clinical important improvement*[tw] OR minimally clinically important improvement*[tw]OR minimally important improvement*[tw] OR clinically meaningful difference*[tw] OR clinically meaningful change*[tw] OR clinically meaningful improvement*[tw] OR clinical meaningful difference*[tw] OR clinical meaningful change* [tw] OR clinical meaningful improvement* [tw]	Initial search on the 9th of June 2015. Updated on the 28th of January 2016 and the 13th of June 2017
EMBASE	P - Concept Patients with COPD 'obstructive airway disease'/exp OR 'chronic obstructive lung disease'/exp OR 'COPD':ab,ti OR 'Chronic Obstructive Pulmonary Disease':ab,ti OR 'Obstructive Pulmonary Disease':ab,ti OR 'Pulmonary Disease':ab,ti OR 'Chronic Obstructive Airway Disease':ab,ti OR 'Obstructive Airway Disease':ab,ti OR 'Airflow Limitation':ab,ti OR 'Airflow Obstruction':ab,ti OR 'Chronic Bronchitis':ab,ti OR 'Bronchitis':ab,ti OR 'Emphysema':ab,ti OR 'Chronic Airway Disease':ab,ti OR 'Respiratory Disease':ab,ti OR 'Chronic Obstructive Pulmonary Diseases':ab,ti OR 'Obstructive Pulmonary Diseases':ab,ti OR 'Pulmonary Diseases':ab,ti OR 'Chronic Obstructive Airway Diseases':ab,ti OR 'Obstructive Airway Diseases':ab,ti OR 'Airflow Limitations':ab,ti OR 'Airflow Obstructions':ab,ti OR 'Chronic Airway Diseases':ab,ti OR 'Respiratory Diseases':ab,ti OR 'Chronic Obstructive Pulmonary Disorder':ab,ti OR 'Obstructive Pulmonary Disorder':ab,ti OR 'Pulmonary Disorder':ab,ti OR 'Chronic Obstructive Airway Disorder':ab,ti OR 'Obstructive Airway Disorder':ab,ti OR 'Chronic Airway Disorder':ab,ti OR 'Respiratory Disorder':ab,ti OR 'Chronic Obstructive Pulmonary Disorders':ab,ti OR 'Obstructive Pulmonary Disorders':ab,ti OR 'Pulmonary Disorders':ab,ti OR 'Chronic Obstructive Airway Disorders':ab,ti OR 'Obstructive Airway Disorders':ab,ti OR 'Chronic Airway Disorders':ab,ti OR 'Respiratory Disorders':ab,ti AND I - Concept Patient reported health status questionnaires 'general health status assessment'/exp OR 'health status'/exp OR 'health status indicator'/exp OR 'quality of life'/exp OR 'quality of life assessment'/exp OR 'Patient Health Questionnaire'/exp OR 'questionnaire'/exp OR 'Patient-reported outcome':ab,ti OR 'Patient Reported Outcome':ab,ti OR 'PRO':ab,ti OR 'Health Status':ab,ti OR 'Quality Of Life':ab,ti or 'QoL':ab,ti OR 'Questionnaire':ab,ti OR 'Patient-reported outcomes':ab,ti OR 'Patient Reported Outcomes':ab,ti OR 'Questionnaires':ab,ti AND C - none	Initial search on the 15th of June 2015. Updated on the 28th of January 2016 and the 13th of June 2017

	AND O – Minimal Clinically Important Difference (MCID) 'MCID':ab,ti OR 'MID':ab,ti OR 'minimum clinically important difference':ab,ti OR 'minimum clinical important difference':ab,ti OR 'minimum important difference':ab,ti OR 'minimal clinically important difference':ab,ti OR 'minimal clinical important difference':ab,ti OR 'minimal important difference':ab,ti OR 'minimally important difference':ab,ti OR 'minimally clinical important difference':ab,ti OR 'minimally clinically important difference':ab,ti OR 'minimum clinically important change':ab,ti OR 'minimum clinical important change':ab,ti OR 'minimum important change':ab,ti OR 'minimal clinically important change':ab,ti OR 'minimal clinical important change':ab,ti OR 'minimally important change':ab,ti OR 'minimally clinically important change':ab,ti OR 'minimally clinical important change':ab,ti OR 'minimum clinically important improvement':ab,ti OR 'minimum clinical important improvement':ab,ti OR 'minimum important improvement':ab,ti OR 'minimal clinically important improvement':ab,ti OR 'minimal clinical important improvement':ab,ti OR 'minimal important improvement':ab,ti OR 'minimally clinical important improvement':ab,ti OR 'minimally clinically important improvement':ab,ti OR 'minimally important improvement':ab,ti OR 'clinically meaningful difference':ab,ti OR 'clinically meaningful change':ab,ti OR 'clinically meaningful improvement':ab,ti OR 'clinical meaningful difference':ab,ti OR 'clinical meaningful change':ab,ti OR 'clinical meaningful improvement':ab,ti OR 'minimum clinically important differences':ab,ti OR 'minimum clinical important differences':ab,ti OR 'minimum important differences':ab,ti OR 'minimal clinically important differences':ab,ti OR 'minimal clinical important differences':ab,ti OR 'minimal important differences':ab,ti OR 'minimally important differences':ab,ti OR 'minimally clinical important differences':ab,ti OR 'minimally clinically important differences':ab,ti OR 'minimum clinically important changes':ab,ti OR 'minimum clinical important changes':ab,ti OR 'minimum important changes':ab,ti OR 'minimal clinically important changes':ab,ti OR 'minimal clinical important changes':ab,ti OR 'minimally important changes':ab,ti OR 'minimally clinically important changes':ab,ti OR 'minimally clinical important changes':ab,ti OR 'minimum clinically important improvements':ab,ti OR 'minimum clinical important improvements':ab,ti OR 'minimum important improvements':ab,ti OR 'minimal clinically important improvements':ab,ti OR 'minimal clinical important improvements':ab,ti OR 'minimal important improvements':ab,ti OR 'minimally clinical important improvements':ab,ti OR 'minimally clinically important improvements':ab,ti OR 'minimally important improvements':ab,ti OR 'clinically meaningful differences':ab,ti OR 'clinically meaningful changes':ab,ti OR 'clinically meaningful improvements':ab,ti OR 'clinical meaningful differences':ab,ti OR 'clinical meaningful changes':ab,ti OR 'clinical meaningful improvements':ab,ti AND [embase]/lim Conference abstracts were excluded using the filter option	
COCHRANE LIBRARY	#1 MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees #2 COPD or "Chronic Obstructive Pulmonary Dis*" or "Obstructive Pulmonary Dis*" or "Pulmonary Dis*" or "Chronic Obstructive Airway Dis*" or "Obstructive Airway Dis*" or "Airflow Limitation*" or "Airflow Obstruction*" or "Chronic Bronchitis" or Bronchitis or Emphysema or "Chronic Airway Dis*" or "Respiratory Dis*":ti,ab,kw (Word variations have been searched) #3 MeSH descriptor: [Health Status] explode all trees #4 MeSH descriptor: [Health Status Indicators] explode all trees #5 MeSH descriptor: [Quality of Life] explode all trees #6 MeSH descriptor: [Questionnaires] explode all trees #7 "Patient-reported outcome*" or "Patient Reported Outcome*" or PRO or "health status" or "Quality of Life" or QoL or Questionnaire*:ti,ab,kw (Word variations have been searched) #8 MCID or MID or "minimum clinically important difference*" or "minimum clinical important difference*" or "minimum important difference*" or "minimal clinically important difference*" or "minimal clinical important difference*" or "minimal important difference*" or "minimally important difference*" or "minimally clinical important difference*" or "minimally clinically important difference*" or "minimum clinically important change*" or "minimum clinical important change*" or "minimum important change*" or "minimal clinically important change*" or "minimal clinical important change*" or "minimally important change*" or "minimally clinically important change*" or "minimally clinical important change*" or "minimum clinically important improvement*" or "minimum clinical important improvement*" or "minimum important improvement*" or "minimal clinically important improvement*" or "minimal clinical important improvement*" or "minimal important improvement*" or "minimally clinical important improvement*" or "minimally clinically important improvement*" or "minimally important improvement*" or "clinically meaningful difference*" or "clinically meaningful change*" or "clinically meaningful improvement*" or "clinical meaningful difference*" or "clinical meaningful change*" or "clinical meaningful improvement*":ti,ab,kw (Word variations have been searched) #9 (#1 OR #2) AND (#3 OR #4 OR #5 OR #6 OR #7) AND #8 Option trials was selected	Initial search on the 9th of July 2015. Updated on the 28th of January 2016 and the 16th of June 2017

Supplementary Table S2: Risk of bias and quality assessment form

Selected item	**Scoring method (points)**
1. Were participant inclusion criteria clearly defined?	Yes (2) No (0) Unclear (1)
2. Were participant exclusion criteria clearly defined?	Yes (2) No (0) Unclear (1)
3. Were patients systematically enrolled?	Yes (2) No (0) Unclear (1)
4. Was follow-up completed?	Yes (2) No (0) Unclear (1)
5. Were missing data procedures reported?	Yes (2) No (0) Unclear (1)
6. Which % lost in follow up?	<25% (2) ≥25% (0) Unclear (1)
7. Were at least two health status measurements (pre and post) available?	Yes (2) No (0) Unclear (1)
8. Was the time interval for follow-up stated?	Yes (2) No (0) Unclear (1)
9. Were test conditions similar for both measurements?	Yes (2) No (0) Unclear (1)
10. Was there an adequate description given of measurement instrument?	Yes (2) No (0) Unclear (1)
11. Was the instrument validated in the current study, or is made reference to other study?	Yes (2) No (0) Unclear (1)
12. Were floor effects described	Yes (2) No (0) Unclear (1)
13. Were ceiling effects described	Yes (2) No (0) Unclear (1)
14. Was the M(C)ID or MIC calculated?	Yes (2) No (0) Unclear (1)
15. Was an adequate description given of the anchor(s)?	Yes (2) No (0) Unclear (1) Not Applicable = N/A (0)
16. Were measurement properties of the anchor(s) described?	Yes (2) No (0) Unclear (1) Not Applicable = N/A (0)
17. Can the anchor(s) be considered a gold standard?	Yes (2) No (0) Unclear (1) Not Applicable = N/A (0)
18. Were >1 anchor used to determine M(C)ID?	Yes (2) No (0) Unclear (1) Not Applicable = N/A (0)
19. Were anchor correlations calculated?	Yes (2) No (0) Unclear (1) Not Applicable = N/A (0)
20. Were anchor correlations ≥0.50?	Yes (2) No (0) Unclear (1) Not Applicable = N/A (0)
21. Were ROC curves produced?	Yes (2) No (0) Unclear (1) Not Applicable = N/A (0)
22. Was the Area Under the Curve (AUC) ≥0.70?	Yes (2) No (0) Unclear (1) Not Applicable = N/A (0)
23. Was a Global Rating of Change used?	Yes (2) No (0) Unclear (1) Not Applicable = N/A (0)
24. Number of GRC anchor questions?	<11 (0) ≥11 (2) Unclear (1) Not Applicable = N/A (0)

25. What criterion was used?	Exacerbation (2) Hospital admission (1) Death (0) Other (1) Not Applicable = N/A (0)
26. Was more than one distribution-based method used?	Yes (2) No (0) Unclear (1) Not Applicable = N/A (0)
27. Was more than one population used in MCID?	Yes (2) No (0) Unclear (1)
28. MCID calculated for:	Improvement (1) Deterioration (1) Both (2)
29. Was there selective outcome reporting?	Yes (0) No (2) Unclear (1)
30. Was there funding bias?	Yes (0) No (2) Unclear (1)
31. Was there ownership bias?	Yes (0) No (2) Unclear (1)

Supplementary file: Full description of the included HRQoL and health status instruments

CAT

The CAT contains eight questions with item scores ranging zero (no limitations) up to five (maximum limitations) [90]. The total score derives from summing all items (min:0, max:40).

CCQ

The CCQ contains ten questions with item scores ranging zero (no limitations) to six (maximum limitations) [91]. Total and domain scores (symptoms, functional and mental status) result from summing relevant scores and dividing this by the number of items (min: 0, max: 6).

(SF-)CRQ

The CRQ consists of 20 items scored on a seven-point scale ranging one (most troubles) to seven (no troubles) on the domains dyspnea (five items), fatigue (four items), emotional function (seven items), and mastery (four items) [92]. Domain scores are determined by summing the scores or determining the mean of the summed items. [7, 80, 88]. The SF-CRQ includes two selected items per domain [71].

The eDiary

The eDiary contains five symptom items and two impact items, resulting in scores ranging from zero (best possible state/no problems) to 10 (worst possible state) [77].

EQ-5D Utilities Index and VAS

The EQ-5D contains the five dimensions mobility, self-care, usual activities, pain/discomfort, and anxiety/depression with each three (EQ-5D-3L) or five levels (EQ-5D-5L) in scoring severity [93-94]. A scoring algorithm results in an Utility Index (UI) between -0.590 (worst health) and +1.000 (best health) for the 3L version; and -0.208 to +1.000 for the 5L version. In addition, a Visual Analogue Scale (VAS) score must be marked from zero (worst health) to 100 (best health).

Feeling Thermometer (FT)

The FT is a VAS ranging from zero (worst state) to 100 (best score) [81].

Quality of Life for Respiratory Illness Questionnaire (QOLRIQ)

The QOLRIQ contains 55 items regarding breathing problems, physical problems, emotions, situations triggering or enhancing breathing problems, general activities, daily and domestic activities, and social activities, relationships and sexuality [84]. Scores range on a seven-point scale with higher scores representing more impairment.

SF-6D and SF-36

The SF-36 contains 36 items divided over eight domains each scoring between zero (worst health) and 100 (best health) [95]. The SF-6D includes six dimensions resulting in a health state ranging 0.29 (worst health) to 1.00 (full health) [85].

St. George's Respiratory Questionnaire (SGRQ)

The SGRQ is a 50-item questionnaire containing the domains symptoms, activities and impact with total and domain scores ranging zero (best health status) to 100 (worst health status) [96].

Visual Simplified Respiratory Questionnaire (VSRQ)

The VSRQ contains eight items covering dyspnea, anxiety, depression, sleep, energy, daily activities, social activities, and sexual life [79]. Scores range from zero to ten with lower scores indicating higher impact on patients' HRQoL.

Supplementary Table S3: Overview of excluded studies during the full-text analysis stage in alphabetical order

Title:	**Author(s):**	**Journal and year:**	**Reason for exclusion:**
A comparison between the EQ-5D and the SF-6D in patients with Chronic Obstructive Pulmonary Disease (COPD)	J. Chen; C.K.H. Wong; S.M. McGhee; P.K.P. Pang; Wai-Cho Yu	PLOS one 2014; 9: 11	No MCID calculations.
A comparison of clinically important differences in health-related quality of life for patients with chronic lung disease, asthma, or heart disease.	K.W. Wyrwich; W.M. Tierney; A.N. Babu; K. Kroenke; F.D. Wolinsky	Health Services Research 2005; 40: 2	No clinical data.
A measure of quality of life for clinical trials in chronic lung disease	G.H. Guyatt; L.B. Berman; M. Townsend; S.O. Pugsley; L.W. Chambers	Thorax 1987; 42: 773-778	No MCID calculations.
Analysis of the factors related to mortality in chronic obstructive pulmonary disease	T. Oga, K. Nishimura, M. Tsukino, S. Sato, T. Hajiro	American Journal of Respiratory and Critical Care Medicine 2002; 167: 544-549	No MCID calculations.
A systematic overview of the measurement properties of the chronic respiratory questionnaire	Y. Lacasse; E Wong; G. Guyatt	Canadian Respiratory Journal 1997; 4: 3	No original data.
Bridging the gap: Using triangulation methodology to estimate Minimal Clinically Important Differences (MCIDs)	N. Kline Leidy; K.W. Wyrwich	COPD: Journal of Chronic Obstructive Pulmonary Disease 2005; 2: 157-165	No original data. No health status tool.
Clinically important changes in health-related quality of life for patients with chronic obstructive pulmonary disease: an expert consensus panel report.	K.W. Wyrwich; S.D. Fihn; W.M. Tierney; K. Kroenke; A.N. Babu; F.D. Wollinsky	Journal of General Internal Medicine Volume 2003; 18	No clinical data.
Creating scenarios of the impact of COPD and their relationship to COPD assessment test (CAT) scores	P.W. Jones; M. Tabberer; W-H Chen	BMC Pulmonary Medicine 2011; 11: 42	No MCID calculations.
Development and first validation of the COPD Assessment Test	P.W. Jones, G. Harding, P. Berry, et al.	European Respiratory Journal 2009; 34: 648-654	No MCID calculations.
EQ-5D-derived health utilities and minimally important differences for chronic health conditions: 2011 Commonwealth Fund Survey of Sicker Adults in Canada.	K. Tsiplova, E. Pullenayegum, T. Cooke, F. Xie	Quality of Life Research 2016; 25: 3009-3016	COPD combined with asthma.
Estimation and application of the minimum clinically important difference in COPD	P.W. Jones	The Lancet Respiratory Medicine 2014; 2	No original data.
Evaluating the Clinical COPD Questionnaire: A systematic review.	Z. Zhou, A. Zhou, Y. Zhao, P. Chen	Respirology 2017; 22: 251-262	No original data.
Examining the Minimal Clinically Important Difference in the St. George's Respiratory Questionnaire	M. Decramer; B. Celli; D.P. Tashkin; D. Liu; S. Kesten	American Journal of Respiratory and Critical Care Medicine 2011; 183: A1514	No full text available.

Factors associated with the minimal clinically important difference for health-related quality of life after physical conditioning in patients with COPD	V.Z. Dourado; C. de Oliveira Antunes; S.E. Tanni; I. Godoy	Journal of Brasilian Pneumology 2009; 35(9): 846-853	No MCID calculations.
Further evidence supporting an SEM-based criterion for identifying meaningful intra-individual changes in health-related quality of life	K.W. Wyrwich; W.M. Tierney; F.D. Wolinsky	Journal of Clinical Epidemiology 1999; 52 (9): 861-873	No MCID calculations.
Half standard deviation estimate of the minimally important difference in HRQOL scores?	S.S. Farivar; H. Liu; R.D. Hays	Expert Review Pharmacoeconomics Outcomes Research 2004; 4(5)	No original data.
Health-related quality of life and mortality in male patients with chronic obstructive pulmonary disease.	A. Domingo-Salvany, R. Lamarca, M. Ferrer, J. Garcia-Aymerich, J. Alonso, M. Felez, A. Khalaf Marrades	American Journal of Respiratory and Critical Care Medicine 2002; 166: 680-685	No MCID calculations.
How can we assess outcomes of clinical trials: The MCID approach	B. Make	COPD: Journal of Chronic Obstructive Pulmonary Disease 2007; 4: 191-194	No original data.
Improving the interpretation of quality of life evidence in meta-analyses: the application of minimal important difference units	B.C. Johnston; K. Thorlund; H.J. Schünemann; F. Xie; M. Hassan Murad; V.M. Monton; G.H. Guyatt	Health and Quality of Life Outcomes 2010; 8: 116	No original data. No MCID calculations.
Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation	G.R. Norman; J.A. Sloan; K. Wyrwich	Medical Care 2003; 41 (5): 585-592	No original data.
Interpretation of changes in HRQL outcomes: The relationship between distribution- and anchor-based approaches	G.R. Norman; C.R. Dennison	European Respiratory Review 2002	No full text available.
Interpreting results from clinical trials: Understanding Minimal Clinically Important Differences in COPD outcomes	B. Make; R. Casaburi; N. Kline Leidy	COPD: Journal of Chronic Obstructive Pulmonary Disease 2005; 2: 1-5	No original data.
Interpreting score differences in the SF-36 Vitality scale: using clinical conditions and functional outcomes to define the minimally important difference	J.B. Bjorner; G.V. Wallenstein; M.C. Martin; P. Lin; B. Blaisdell-Gross; C. Tak Piech; S.H. Mody	Current Medical Research and Opinions 2007; 23(4): 731-739	No MCID calculations.
Interpreting thresholds for a clinically significant change in health status in asthma and COPD	P.W. Jones	European Respiratory Journal 2002; 19: 398-404	No original data.
Limitations of calculating “true” regression slope: impact on estimates of minimal important difference	J.W. Dodd, P.W. Jones	European Respiratory Journal 2011; 37: 1296-1301	No original data.
Linking clinical relevance and statistical significance in evaluating intra-individual changes in health-related quality of life	K.W. Wyrwich; N.A. Nienaber; W.M. Tierney; F.D. Wolinsky	Medical Care 1999; 37 (5): 469-478	No original data. No COPD.

Meaningful effect size and patterns of response of the transition dyspnea index	T.J. Witek Jr.; D.A. Mahler	Journal of Clinical Epidemiology 2003; 56(3): 248-55	No health status tool.
Measurement properties and interpretability of the Chronic Respiratory Disease Questionnaire (CRQ)	H.J. Schünemann; M. Puhan; R. Goldstein; R. Jaeschke; G.H. Guyatt	COPD: Journal of Chronic Obstructive Pulmonary Disease 2005; 2: 81-89	No original data.
Measures of dyspnea in pulmonary rehabilitation	E. Crisafulli; E.M. Clini	Multidisciplinary Respiratory Medicine 2010; 5(3): 202-210	No original data.
Minimally Clinically Important Difference for the UCSD Shortness of Breath Questionnaire, Borg Scale, and Visual Analog Scale	A.L. Ries	COPD: Journal of Chronic Obstructive Pulmonary Disease 2005; 2: 105-110	No original data. No health status tool.
Minimal Clinically Important Differences in Pharmacological Trials	P.W. Jones; K.M. Beeh; K.R. Chapman; M. Decramer; D.A. Mahler; J.A. Wedzicha	American Journal of Respiratory and Critical Care Medicine 2014; 189 (3)	No original data.
Minimal Clinically Important Differences (MCIDs) of the Thai Version of the Leicester Cough Questionnaire for Subacute and Chronic Cough	P. Pornsuriyasak, P. Thungtitigul, T. Kawamatawong, S.S. Birring, T. Pongmesa	Value in Health Regional Issues 2017; 12C: 57-62	No COPD
Minimal important difference of the transition dyspnea index in a multinational clinical trial	T.J. Witek Jr.; D.A. Mahler	European Respiratory Journal 2003; 21: 267-272	No health status tool.
Minimal Important Difference thresholds and the Standard Error of Measurement: Is there a connection?	K.W. Wyrwich	Journal of Biopharmaceutical Statistics 2004; 14(1): 97-110	No original data.
New methods can extend the use of minimal important difference units in meta-analyses of continuous outcome measures	B.C. Johnston; K. Thorlund; B.R. da Costa; T.A. Furukawa; G.H. Guyatt	Journal of Clinical Epidemiology 2012; 65: 817-826	No original data.
Power of outcome measurements to detect clinically significant changes in pulmonary rehabilitation of patients with COPD.	J.P. de Torres; V. Pinto-Plata; E. Ingenito; P. Bagley; A. Gray; R. Berger; B. Celli	Chest 2002; 121: 4	No MCID calculations.
Properties of the COPD assessment test in a cross-sectional European Study	P.W. Jones; G. Bruselle; R.W. Dal Negro; M. Ferrer; P. Kardos; M.L. Levy; T. Perez; J.J. Soler Cataluna; T. van der Molen; L. Adamek; N. Banik	European Respiratory Journal 2001; 38: 29-35	No MCID calculations.
Quality of life and hospital readmission in patients with chronic obstructive pulmonary disease	L.M. Osman; D.J. Godden; J.A.R. Friend; J.S. Legge; J.G. Douglas	Thorax 1997; 52: 67-71	No MCID calculations.
Quality of life changes in COPD patients treated with Salmeterol	P.W. Jones; T.K. Bosh	American Journal of Respiratory and Critical Care Medicine 1997; 155: 1283-1289	No MCID calculations.

Quality of life in patients with chronic respiratory disease: the Spanish version of the chronic respiratory questionnaire	R. Guell; P. Casan; M. Sangenis; F. Morante; J. Belda; G.H. Guyatt	European Respiratory Journal 1998; 11: 55-60	No MCID calculations.
Quality of life, symptoms and pulmonary function in asthma: long-term treatment with nedocromil sodium examined in a controlled multicentre trial. Nedocromil Sodium Quality of Life Study Group	P.W. Jones and the Nedocromil Sodium Quality of Life Study Group	European Respiratory Journal 1994; 7: 55-62	No MCID calculations. No COPD
Relation of distribution- and anchor-based approaches in interpretation of changes in Health Related Quality of Life	G.R. Norman; F. G. Sridhar; G.H. Guyatt; S.D. Walter	Medical Care 2001; 39(10): 1039-47	No original data.
Responsiveness of the COPD Assessment Test: The Minimal Clinically Important Difference does matter	J.W.H. Kocks; I.G. Tsiligianni; T. van der Molen	Chest 2012; 142: 1	No original data.
Self-complete measure of health status for chronic airflow limitation. The St. George's Respiratory Questionnaire	P.W. Jones; F.H. Quirk; C.M. Baveystock; P.A. Littlejohns	American Journal of Respiratory and Critical Care Medicine 1992; 145(6): 1321-7	No MCID calculations.
Statistical interpretations of health-related quality of life outcomes in COPD: Alternatives to the MCID	G.R. Norman	European Respiratory Review 2002	No full text available.
Statistical interpretation of HRQL changes in COPD: Development of the MCID standards and related	K.W. Wyrwich	European Respiratory Review 2002	No full text available.
St. George's Respiratory Questionnaire: MCID	P.W. Jones	COPD: Journal of Chronic Obstructive Pulmonary Disease 2005; 2: 75-79	No original data.
Small, moderate, and large changes, and the Minimum Clinically Important Difference in the University of California, San Diego Shortness of Breath Questionnaire	N. Horita; N. Miyazawa; S. Morita; R. Kojima; N. Kimura; T. Kaneko; Y. Ishigatsubo	COPD: Journal of Chronic Obstructive Pulmonary Disease 2014; 11: 26-32	No health status tool.
The COPD assessment test: a systematic review	N. Gupta; L.M. Pino; A. Morogan; J. Bourbeau	European Respiratory Journal 2014; 44: 873-884	No original data.
The Minimal Clinically Important Difference in Generic Utility-Based Measures	R.M. Kaplan	COPD: Journal of Chronic Obstructive Pulmonary Disease 2005; 2: 91-97	No health status tool. No original data.
The minimal detectable change cannot reliably replace the minimal important difference.	D. Turner; H.J. Schünemann; L.E. Griffith; D.E. Beaton; A.M. Griffiths	Journal of Clinical Epidemiology 2010; 63: 28-36	No original data.
The minimal important difference of the hospital anxiety and depression scale in patients with chronic obstructive pulmonary disease	M.A. Puhan; M. Frey; S. Büchi; H.J. Schünemann	Health and Quality of Life Outcomes 2008, 6: 46	No health status tool.
The minimal important difference of the pulmonary functional status and dyspnea questionnaire in patients with severe chronic obstructive pulmonary disease	E.M.G. Regueiro; C. Burtin; P. Baten; D. Langer; H. Van Remoortel; V.A. Pires Di Lorenzo; D. Costa; W. Janssens; M. Decramer;	Respiratory Research 2013; 4: 58	No health status tool.

	R. Gosselink; T. Troosters		
The precision of health state valuation by members of the general public using the standard gamble	K. Stein; M. Dyer; R. Milne; A. Round; K. Ratcliffe; J. Brazier	Quality of Life Research 2009; 18: 509-518	No health status tool.
The responsiveness of the Anxiety Inventory for Respiratory Disease Scale following Pulmonary Rehabilitation.	A.M. Yohannes, S. Dryden, N.A. Hanania	Chest 2016; 150(1): 188-195	No health status tool.
The St George's Respiratory Questionnaire	P.W. Jones; F.H. Quirk; C.M. Baveystock	Respiratory Medicine 1991, 85 (Supplement B): 25-31	No MCID calculations.
Trial end-point in Chronic Obstructive Pulmonary Disease (COPD): Minimal Clinically Important Difference	A. Gillissen; R. Buhl; P. Kardos; M. Puhan; K.F. Rabe; T. Rothe; R. Sauer; T. Welte; H. Worth; G. Menz	Pneumologie 2008; 62: 149-157	No original data.

Supplementary Table S4: Patient characteristics and health status scores of the included studies

First author(s):	Male (%):	Age:	Spirometry (FEV1%pred):	Baseline health status:	Health status change score:
COPD Assessment Test (CAT)					
Alma [70]	65	57.87±6.56	50.4±15.11	20.23±7.33	-3.11±5.59
Dodd [72]	62.7	69.2±9.3	50.9±18.9	20.5±7.4	-2.9±5.6
Jones study 1 [73]	49	64±9	47±21	21.44±7.7	-1.4±5.3
Jones study 2 [73]	61	67±8	50±17	17.9±6.5	-2.2±5.3
Kon study 1 [75]	58	70±9	47.6 (CI 45.9-49.3)	21.4 (CI 20.8-22.0)	-2.5 (CI -3.0 - to -1.9)
Kon study 2 [75]	60	71±11	42 (CI 39-46)	23.5 (CI 22.3-24.8)	-3.0 (-4.4 to -1.6)
Kon study 3 [75]	NR	70±8	47.6 (CI 44.4-50.8)	20.1 (CI 19.1-21.2)	0.6 (-0.4 to 1.5)
Smid [82]	55.4	64.3±8.8	48.9±20	21.5±6.6	-3.0±6.8
Tsiligianni [83]	90	67 (IQR 58-75)	GOLD I/II/III/IV %: 16.7/46.7/30/0.7	NR	NR
Clinical COPD Questionnaire (CCQ)					
Alma [70]	65	57.87±6.56	50.4±15.11	2.86±1.17 (CCQ total) 2.87±1.24 (CCQ symptoms) 2.86±1.34 (CCQ functional) 2.86±1.74 (CCQ mental)	-0.58±0.92 (CCQ total) -0.59±1.16 (CCQ symptoms) -0.56±1.00 (CCQ functional) -0.62±1.49 (CCQ mental)
Kocks [74]	NR	71 (IQR 43-84)	37.7	NR	NR
Kon [76]	57.9	71 (CI 70-72)	49.8 (CI 47.3-52.3)	2.8 (CI 2.6-2.9)	-0.5 (CI -0.6 to -0.3)
Smid [82]	55.4	64.3±8.8	48.9±20	2.6±1.0	-0.6±0.9
Tsiligianni [83]	90	67 (IQR 58-75)	GOLD I/II/III/IV %: 16.7/46.7/30/0.7	NR	NR
(Short-Form) Chronic Respiratory Questionnaire ((SF-)CRQ)					
Chu-Lin Tsai [71] – SF-CRQ	45	69 (IQR 62-75)	NR	3 (IQR 2-4) dyspnea 2 (IQR 1.5-3.5) fatigue 3.5 (IQR 2.5-5) emotional 3.5 (IQR 2.5-4.5) mastery	2 (IQR 0.5-3.5) dyspnea 1 (IQR 0-2.5) fatigue 1 (IQR 0-2.5) emotional 1.5 (IQR 0-3) mastery
Jaeschke study 1 [7] – CRQ	NR	64.6±4.1	1.10±0.45 liters (FEV1)	NR	NR
Jaeschke study 2 [7] – CRQ	96	66±7.3	0.93±0.34 liters (FEV1)	NR	NR
Redelmeier [80] – CRQ	47	67±10	0.975±0.40 liters (FEV1)	3.5 (R 1.2-7.0) dyspnea 4.4 (R 1.0-7.0) fatigue 5.2 (R 1.7-7.0) emotion 5.0 (R 2.0-7.0) mastery	NR
Wyrwich study 1 [88] – CRQ	NA	NA	NA	NA	NA

Wyrwich study 2 [88] – CRQ	64.4	50-54 yrs: 11,5% 55-64 yrs: 32% 65-74 yrs: 37.4% ≥75 yrs: 19.2%	NR	NR	NR
Wyrwich study 3 [88] – CRQ	NA	NA	NA	NR	NR
EQ-5D Utility Index (UI) and VAS					
Nolan study 1 [78] - EQ-5D-5L UI and VAS	59.7	70.4±9.3	46.1±19.6	0.68±0.24 (UI) 61.0±20.6 (VAS)	Only baseline
Nolan study 2 [78] - EQ-5D-5L-UI and VAS	59.3	70.2 (CI 69.2-71.2)	49.8 (CI 47.5-52.0)	0.697 (CI 0.673-0.720) (UI) 61.1 (CI 58.9-63.3) (VAS)	0.065 (CI 0.047 – 0.083) (UI) 8.6 (CI 6.5-10.7) (VAS)
Walters and Brazier [86] – EQ-5D-3L-UI	48.7	67±10.4 (men) 62±10.3 (women)	47	NR	NR
Zanini [89] – EQ-5D-3L-VAS	82.9	71±9	55±20	58±17 (VAS)	14±12 (VAS)
St. George's Respiratory Questionnaire (SGRQ)					
Alma [70]	65	57.87±6.56	50.4±15.11	50.69±17.33 (SGRQ total) 63.66±21.77 (SGRQ symptoms) 63.58±19.82 (SGRQ activity) 39.21±18.81 (SGRQ impact)	-9.04±12.11(SGRQ total) -14.22±21.69 (SGRQ symptoms) -6.71±13.44 (SGRQ activity) -8.78±13.95 (SGRQ impact)
Schünemann [81]	54.8	65.8±7.6	NR	52.8±12.7	-8.1±20.4
Tsiligianni [82]	90	67 (IQR 58-75)	GOLD I/II/III/IV %: 16.7/46.7/30/0.7	NR	NR
Welling [87]	36.5	60±8.8	26±9	62±10.9	-9.8±13.8 (1 month) -7.5±15.8 (6 months)
SF-6D and SF-36					
Walters [85] –SF-6D	48.7	67±10.4 (men) 62±10.3 (women)	47	NR	NR
Walters [86] – SF-6D	48.7	67±10.4 (men) 62±10.3 (women)	47	NR	NR
Wyrwich study 1 [88] – SF-36	NA	NA	NA	NA	NA
Wyrwich study 2 [88] – SF-36	64.4	50-54 yrs: 11,5% 55-64 yrs: 32% 65-74 yrs: 37.4% ≥75 yrs: 19.2%	NR	NR	NR
Wyrwich study 3 [88] – SF-36	NA	NA	NA	NR	NR
Kulich [77] – the eDiary	67	<65 yrs: 44% ≥65- <75 yrs: 38.3% ≥75 yrs: 17.7%	NR	Mean range 2.12-3.20	Mean range 1.68-2.60 (follow-up score)
Perez [79] – VSRQ	84.9	64.3±10.0	46.81	44.58±15.96	49.72±16.44 (follow-up score)
Schünemann [81] – FT	54.8	65.8±7.6	NR	56.8±20.6	10.9±20.4

Van Stel [84] - QOLRIQ	53.6	60.4±11	36.6±14.1	3.77±0.90	0.82

Data: Age (yrs) reported as mean±SD, mean (95%CI), or median (IQR). Spirometry reported for FEV1% predicted as mean±SD or mean (95%CI); for GOLD category as %; for FEV1 mean±SD in liters. Health status baseline, follow-up and/or change scores reported as mean±SD, mean (95%CI), median (IQR), mean (R) or mean range of scores.

Abbreviations: 95%CI, 95% Confidence Interval; CAT, COPD Assessment Test; CCQ, Clinical COPD Questionnaire; (SF-)CRQ, (Short-Form) Chronic Respiratory Questionnaire; EQ-5D-3L-UI, EuroQol 5 Dimension 3 Levels Utility Index; EQ-5D-3L-VAS, EuroQol 5 Dimension 3 Levels Visual Analogue Scale; EQ-5D-5L-UI, EuroQol 5 Dimension 5 Levels Utility Index; EQ-5D-5L-VAS, EuroQol 5 Dimension 5 Levels Visual Analogue Scale; FEV1, Forced Expiratory Volume in 1 second; FEV1%pred, Forced Expiratory Volume in 1 second % predicted; FT, Feeling Thermometer; GOLD, Global Initiative for Obstructive Lung Diseases; IQR, InterQuartile Range; N, Number of Patients; NA, Not Applicable; NR, Not Reported; QOLRIQ, Quality of Life for Respiratory Illness Questionnaire; R, Range; SD, Standard Deviation; SF-6D/SF-36, Short-Form 6D/36; VSRQ, Visual Simplified Respiratory Questionnaire; Yrs, Years.

Supplementary Table S5: Overview of patients' inclusion- and exclusion criteria of the included studies in alphabetical order

First author(s):	Inclusion- and exclusion criteria:
Alma [70]	Patients ≥18 years diagnosis COPD GOLD II-IV with informed consent and ability to understand questionnaires. No hypercapnic failure; no contra-indications for IMT; no co-morbidities greater than COPD; no other respiratory co-morbidities; no α1-antitrypsin deficiency.
Chu-Lin Tsai [71]	Patients ≥55 years, physician-based COPD diagnosis, presenting at ED with COPD exacerbation (increasing shortness of breath, worsening cough, or change in sputum production), ability to give informed consent.
Dodd [72]	Patients with clinical diagnosis of COPD, referred for PR.
Jaeschke [7]	Study 1) Eligible for PR; shortness of breath during ≥3 daily activities; FEV1 < 70% of predicted; informed consent. No previous admission to PR; no inability to complete questionnaires; no inability to perform 6MWD. Study 2) FEV1 <70% predicted and ratio <0.7 with FVC. No reversibility. Signs of exertional dyspnea with inability to perform ≥3 daily activities. Excluded if in previous clinical trial with oral steroids FEV1 improved 25% or more. No asthma diagnosis. No prior hospitalization or exacerbation in previous two months.
Jones [73]	Study 1) Patients 40-80 years, physician-based COPD diagnosis (GOLD criteria), ability to read English. No asthma; no other active chronic respiratory disease; no other severe uncontrolled co-morbidity. Study 2) Like study 1, except patients had to be stable for 6 weeks. No history of unstable angina or myocardial infarction in past month; no resting heart rate >120 beats/min; no systolic blood pressure >180 mm Hg; no diastolic blood pressure >100mm Hg.
Kocks [74]	Patients ≥40 years, with COPD diagnosis (ATS criteria), admitted with acute exacerbation, smoking history of >10 pack-years, informed/written consent. No asthma; no prednisolone allergy; no chest X-ray not consistent with COPD; no participation other trial; no acidosis; no severe comorbidity; no inability to follow instructions.
Kon [75]	Study 1) Stable patients ≥35 years, diagnosis of COPD, ability to walk 5m, no contra-indications for PR, ability to read and understand English. Study 2) Patients ≥35 years, acute COPD exacerbation as diagnosed by physician, admission >24 hours to acute ward, ability to read and understand English. Study 3) Stable patients ≥35 years, diagnosis of COPD, no exacerbation past 4 weeks, ability to read and understand English.
Kon [76]	COPD diagnosis (GOLD criteria), clinical indication for PR (BTS guidelines), no exacerbation past 6 weeks, no contra-indication for exercise, no neurologic limitations to walking, no PR in previous 12 months.
Kulich [77]	Patients ≥40 years, COPD GOLD II or III, packyears ≥10.
Nolan [78]	Study 1) COPD patients (GOLD criteria) in outpatient clinics Harefield Hospital. Study 2) COPD patients (GOLD) in PR clinics Harefield Hospital. Able to walk 5m without assistance. No contra-indications for aerobics.
Perez [79]	Patients ≥40 years, clinical diagnosis mild/moderate/severe COPD (ATS criteria), smoking history ≥10 years, no asthma; no allergic rhinitis; no atopy; no oxygen usage; no recent respiratory tract infection previous 6 weeks; no history of myocardial infarction or arrhythmias previous 6 months; no hospitalization for pulmonary edema or heart failure previous 3 years.
Redelmeier [80]	COPD patients in PR, came from community, maximal medical therapy, agreed to participate. No other active comorbidities; no poor motivation; no unrealistic expectations; no inadequate comprehension; no acute exacerbation.
Schünemann [81]	All inpatients and outpatients with Chronic Airflow Limitation (CAL) enrolled in PR. No α1-antitrypsin deficiency, silicosis, sarcoidosis, asbestosis, lupus, or cancer, and no inability to complete questionnaires.
Smid [82]	Patients 40-85 years with mild-very severe COPD (GOLD guidelines), enrolled in PR at CIRO institute after assessment in Horn, the Netherlands, providing informed consent.
Tsiligianni [83]	Patients ≥45 years, smoking history ≥10 years, COPD diagnosis by physician and spirometry (FEV1/FVC <0.7), no asthma; no unstable cardio-vascular disease; no other respiratory conditions.
Van Stel [84]	Pulmonologist diagnosis of asthma and/or COPD (ERS), patients enrolled in and completing PR, able to speak and understand Dutch.
Walters [85]	Patients ≥35 years, native English speaking, clinical COPD diagnosis. No asthma; no occupational lung fibrosis; no

	pulmonary malignancy; no spirometry with FEV1>70%FVC or FEV1<70%FVC with reversibility.
Walters [86]	Patients ≥35 years, native English speaking, clinical COPD diagnosis. No asthma; no occupational lung fibrosis; no pulmonary malignancy; no spirometry with FEV1>70%FVC or FEV1<70%FVC with reversibility.
Welling [87]	Different per individual trial: COPD patients included if follow-up at 1 or 6 months was available incl. SGRQ assessment.
Wyrwich [88]	Study 1) Expert Panel, MEDLINE search for CRQ and SF-36, north-American authors, 1995-1999. Study 2) Outpatients ≥50 years, physician confirmed COPD, breathing problems past 4 weeks, telephone, adequate hearing. Study 3) Primary care physicians with a substantial amount of COPD patients in study 2.
Zanini [89]	COPD patients (GOLD criteria), ≥4 sessions PR/week. No exacerbation past 4 weeks; no inability to perform 6MWD; no exacerbation or unstable condition during PR leading to incompletion; no contra-indications for PR (musculo-skeletal disorders, malignant diseases, unstable cardiac condition); no lack of adherence to PR.

Abbreviations: 6MWD, Six Minute Walking Distance; ATS, American Thoracic Society; BTS, British Thoracic Society; CAL, Chronic Airflow Limitations; COPD, Chronic Obstructive Pulmonary Disease; ED, Emergency Department; ERS, European Respiratory Society; FVC, Forced Vital Capacity; FEV1, Forced Expiratory Volume in 1 Second; GOLD, Global Initiative for Obstructive Lung Diseases; IMT, Inspiratory Muscle Training; PR, Pulmonary Rehabilitation; SF-36, Short-Form 36; SGRQ, St. George's Respiratory Questionnaire.

Supplementary Table S6: Overview of all MCID methods and estimates

Study:	Type:	Description Method:	MCID:	Distribution:	N:
CAT					
Alma [70]	Anchor	15-point GRC: mean change patient minimal improvement	-3.12	95%CI -3.86- to -2.37	196
Dodd [72]	Anchor	5-point GRC: mean change patient "feeling little better"	-1.30	SD 4.50	88
Jones study 1 [73]	Anchor	6-point GRC: mean change score for responders	-2.80	SD 4.60	33
Dodd [72]	Anchor	5-point GRC: mean change patient "feeling little worse"	+2.00	SD 0.00	3
Kon study 1 [75]	Anchor	5-point GRC: mean change patient "feeling little better"	-1.60	95%CI -2.60 to -0.80	207
Tsiligianni [83]	Anchor	7-point GRC: mean change patient with minimal change	---	---	9
Jones study 1 [73]	Anchor	6-point GRC by the physician: mean change score for responders	-2.60	SD 4.40	34
Alma [70]	Anchor	Criterion: difference score patients with and without exacerbation during PR	-2.96	95%CI -5.20 to -0.71	449
Alma [70]	Anchor	MCID CCQ total (-0.4): Linear regression analysis	-2.45	95%CI -2.77 to -2.14	449
Alma [70]	Anchor	MCID CCQ total (-0.4): mean difference change score between patients failing and patients achieving the anchor's MCID	-2.74	---	449
Alma [70]	Anchor	MCID CCQ total (-0.4): ROC Curves	-3.00	---	449
Alma [70]	Anchor	MCID CCQ total (-0.5): Linear regression analysis	-2.81	95%CI -3.08 to -2.54	449
Alma [70]	Anchor	MCID CCQ total (-0.5): mean difference change score between patients failing and patients achieving the anchor's MCID	-2.82	---	449
Alma [70]	Anchor	MCID CCQ total (-0.5): ROC Curves	-3.00	---	449
Alma [70]	Anchor	MCID SGRQ total (-4): Linear regression analysis	-1.86	95%CI -2.27 to -1.46	449
Kon study 1 [75]	Anchor	MCID of SGRQ total (-4): Linear regression analysis	-2.30	95% CI -2.70 to -1.80	565
Kon study 2 [75]	Anchor	MCID of SGRQ total (-4): Linear regression analysis	-2.80	95% CI -3.70 to -1.90	147
Kon study 3 [75]	Anchor	MCID of SGRQ (-4): Linear regression analysis	-1.20	95%CI -2.50 - 0.00	164
Smid [82]	Anchor	MCID of SGRQ total (-4): Linear regression analysis	-3.50	---	419
Alma [70]	Anchor	MCID SGRQ total (-4): mean difference change score between patients failing and patients achieving the anchor's MCID	-2.45	---	449
Alma [70]	Anchor	MCID SGRQ total (-4): ROC Curves	-3.00	---	449
Kon study 1 [75]	Anchor	MCID of SGRQ total (-4): ROC Curves	-2.00	---	565
Kon study 2 [75]	Anchor	MCID of SGRQ total (-4): ROC Curves	-2.00	---	147
Kon study 3 [75]	Anchor	MCID of SGRQ (-4): ROC Curves	-1.00	---	164
Kon study 3 [75]	Anchor	MCID of SGRQ (+4): ROC Curves	+1.00	---	164
Smid [82]	Anchor	MCID of SGRQ total (-4): ROC Curves	-1.70	---	419
Alma [70]	Anchor	MCID SGRQ total (-7): Linear regression analysis	-2.61	95%CI -2.91 to -2.32	449
Alma [70]	Anchor	MCID SGRQ total (-7): mean difference change score between patients failing and patients achieving the anchor's MCID	-2.86	---	449
Alma [70]	Anchor	MCID SGRQ total (-7): ROC Curves	-3.00	---	449
Jones study 1 [73]	Anchor	MCID of the SGRQ (4) used in direct mapping: 40/100 x MCID SGRQ	1.60	---	65
Kon study 1 [75]	Anchor	MCID CRQ total (+10): ROC Curves	-2.00	---	565
Kon study 1 [75]	Anchor	MCID CRQ total (+10): Linear regression analysis	-1.80	95%CI -2.60 to -1.00	565
Kon study 1 [75]	Anchor	MCID CRQ dyspnea (+2.5): Linear regression analysis	-1.70	95%CI -2.50 to -1.00	565
Kon study 1 [75]	Anchor	MCID CRQ fatigue (+2.0): Linear regression analysis	-2.00	95%CI -2.70 to -1.20	565
Kon study 1 [75]	Anchor	MCID CRQ emotion (+3.5): Linear regression analysis	-2.30	95%CI -3.20 to -1.50	565
Kon study 1 [75]	Anchor	MCID CRQ mastery (+2.0): Linear regression analysis	-2.20	95%CI -2.90 to -1.50)	565
Alma [70]	Distribution	0.5SD	2.80	---	449
Kon study 1 [75]	Distribution	0.5SD	3.80	---	565
Kon study 2 [75]	Distribution	0.5SD	3.70	---	147
Kon study 3 [75]	Distribution	0.5SD	3.80	---	164
Smid [82]	Distribution	0.5SD	3.40	---	419
Alma [70]	Distribution	SEM	3.28	---	449
Kon study 1 [75]	Distribution	SEM	3.30	---	565
Kon study 2 [75]	Distribution	SEM	3.30	---	147
Kon study 3 [75]	Distribution	SEM	3.40	---	164
Smid [82]	Distribution	SEM	2.90	---	419
Tsiligianni [83]	Distribution	SEM	1.92	---	90
Alma [70]	Distribution	1.96SEM	6.43	---	449
Tsiligianni [83]	Distribution	1.96 SEM	3.76	---	90

CCQ					
Alma [70]	Anchor	15-point GRC: mean change patient minimal improvement	-0.56 (T)	95%CI -0.68 to -0.44	196
Kocks [74]	Anchor	15-point GRC day 2: mean change patient minimal improvement	---	---	15
Kocks [74]	Anchor	15-point GRC day 3: mean change patient minimal improvement	-0.44 (T)	SD 0.66	20
Alma [70]	Anchor	Like CCQ Total	-0.55 (S)	---	196
Kocks [74]	Anchor	Like CCQ Total	-0.70 (S)	SD 1.09	15
Kocks [74]	Anchor	Like CCQ Total	-0.74 (S)	SD 0.93	20
Alma [70]	Anchor	Like CCQ Total	-0.55 (F)	---	196
Kocks [74]	Anchor	Like CCQ Total	---	---	15
Kocks [74]	Anchor	Like CCQ Total	---	---	20
Alma [70]	Anchor	Like CCQ Total	-0.58 (M)	---	196
Kocks [74]	Anchor	Like CCQ Total	-1.00 (M)	---	15
Kocks [74]	Anchor	Like CCQ Total	---	---	20
Tsiligianni [83]	Anchor	7-point GRC: mean change patient with minimal change	---	---	9
Alma [70]	Anchor	Criterion: difference score patients with and without exacerbation during PR	-0.62 (T)	95%CI -0.98 to -0.27	449
Kocks [74]	Anchor	Criterion: difference score patients at day 42 between death/rehospitalization and survival/no rehospitalization during 12 months follow-up	-0.39 (T)	95%CI -0.71 to -0.07	168
Alma [70]	Anchor	Like CCQ Total	-0.47 (S)	---	449
Kocks [74]	Anchor	Like CCQ Total	---	---	168
Alma [70]	Anchor	Like CCQ Total	-0.67 (F)	---	449
Kocks [74]	Anchor	Like CCQ Total	-0.77 (F)	95%CI -1.19 to -0.34	168
Alma [70]	Anchor	Like CCQ Total	-0.86 (M)	---	449
Kocks [74]	Anchor	Like CCQ Total	0 (M)	---	168
Alma [70]	Anchor	MCID CAT (-2): Linear regression analysis	-0.48 (T)	95%CI -0.53 to -0.42	449
Alma [70]	Anchor	MCID CAT (-2): mean difference change score between patients failing and patients achieving anchor's MCID	-0.48 (T)	---	449
Kon [76]	Anchor	MCID CAT (-2): mean difference change score between patients failing and patients achieving anchor's MCID	-0.43 (T)	---	261
Alma [70]	Anchor	MCID CAT (-2): ROC Curves	-0.50 (T)	---	449
Kon [76]	Anchor	MCID CAT (-2): ROC Curves	-0.40 (T)	---	261
Alma [70]	Anchor	MCID CAT (-3): Linear regression analysis	-0.57 (T)	95%CI -0.61 to -0.53	449
Alma [70]	Anchor	MCID CAT (-3): mean difference change score between patients failing and patients achieving anchor's MCID	-0.56 (T)	---	449
Alma [70]	Anchor	MCID CAT (-3): ROC Curves	-0.60 (T)	---	449
Alma [70]	Anchor	MCID SGRQ total (-4): Linear regression analysis	-0.34 (T)	95%CI -0.40 to -0.28	449
Smid [82]	Anchor	MCID SGRQ total (-4): Linear regression analysis	-0.40 (T)	---	419
Alma [70]	Anchor	MCID SGRQ total (-4): mean difference change score between patients failing and achieving anchor's MCID	-0.46 (T)	---	449
Kon [76]	Anchor	MCID SGRQ (-4): mean difference change score between patients failing and achieving anchor's MCID	-0.47 (T)	---	261
Alma [70]	Anchor	MCID SGRQ total (-4): ROC Curves	-0.50 (T)	---	449
Kon [76]	Anchor	MCID SGRQ total (-4): ROC Curves	-0.40 (T)	---	261
Smid [82]	Anchor	MCID SGRQ total (-4): ROC Curves	-0.40 (T)	---	419
Alma [70]	Anchor	MCID SGRQ total (-7): Linear regression analysis	-0.48 (T)	95%CI -0.53 to -0.44	449
Alma [70]	Anchor	MCID SGRQ total (-7): mean difference change score between patients failing and achieving anchor's MCID	-0.53 (T)	---	449
Alma [70]	Anchor	MCID SGRQ total (-7): ROC Curves	-0.60 (T)	---	449
Kon [76]	Anchor	MCID CRQ total (+10): ROC Curves	-0.40 (T)	---	261
Kon [76]	Anchor	MCID CRQ total (+10): mean difference change score between patients failing and achieving anchor's MCID	-0.40 (T)	---	261
Alma [70]	Distribution	0.5SD	0.46 (T)	---	449
Kon [76]	Distribution	0.5SD	0.48 (T)	---	261
Smid [82]	Distribution	0.5SD	0.50 (T)	---	419
Alma [70]	Distribution	SEM	0.29 (T)	---	449
Kocks [74]	Distribution	SEM	0.21 (T)	---	168
Kon [76]	Distribution	SEM	0.29 (T)	---	261
Smid [82]	Distribution	SEM	0.20 (T)	---	419
Tsiligianni [83]	Distribution	SEM	0.21 (T)	---	90
Alma [70]	Distribution	1.96SEM	0.56 (T)	---	449
Tsiligianni [83]	Distribution	1.96 SEM	0.41 (T)	---	90
Kon [76]	Distribution	MDC95	0.80 (T)	---	168

(SF)-CRQ					
Chu-Lin Tsai [71]	Anchor	5-point GRC: mean change patient “feeling little better”	1.01 (T)	95%CI 0.72 to 1.31	---
Chu-Lin Tsai [71]	Anchor	5-point GRC: mean change patient “feeling little better”	1.60 (D)	---	---
Chu-Lin Tsai [71]	Anchor	5-point GRC: mean change patient “feeling little better”	0.80 (F)	---	---
Chu-Lin Tsai [71]	Anchor	5-point GRC: mean change patient “feeling little better”	0.30 (E)	---	---
Chu-Lin Tsai [71]	Anchor	5-point GRC: mean change patient “feeling little better”	1.10 (M)	---	---
Chu-Lin Tsai [71]	Anchor	5-point GRC: mean change patient “feeling little worse”	-0.60 (D)	---	---
Chu-Lin Tsai [71]	Anchor	5-point GRC: mean change patient “feeling little worse”	-0.10 (F)	---	---
Chu-Lin Tsai [71]	Anchor	5-point GRC: mean change patient “feeling little worse”	-0.60 (E)	---	---
Chu-Lin Tsai [71]	Anchor	5-point GRC: mean change patient “feeling little worse”	-0.06 (M)	---	---
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small improvement	2.00 (D)	---	212
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small improvement	1.00 (F)	---	266
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small improvement	1.00 (E)	---	197
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small improvement	1.00 (M)	---	247
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small deterioration	-1.00 (D)	---	313
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small deterioration	-2.00 (F)	---	208
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small deterioration	-1.00 (E)	---	349
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small deterioration	-2.00 (M)	---	158
Jaeschke study 1 [7]	Anchor	15-point GRC: mean change patient minimal change	2.38 (D)	---	16
Jaeschke study 1 [7]	Anchor	15-point GRC: mean change patient minimal change	2.20 (F)	---	15
Jaeschke study 1 [7]	Anchor	15-point GRC: mean change patient minimal change	5.60 (E)	---	5
Jaeschke study 2 [7]	Anchor	15-point GRC: mean change patient minimal change	3.11 (D)	---	9
Jaeschke study 2 [7]	Anchor	15-point GRC: mean change patient minimal change	2.70 (F)	---	10
Jaeschke study 2 [7]	Anchor	15-point GRC: mean change patient minimal change	4.00 (E)	---	8
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small improvement	5.00 (D)	---	15
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small improvement	2.00 (F)	---	15
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small improvement	1.00 (E)	---	15
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small improvement	0 (M)	---	15
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small deterioration	-1.00 (D)	---	30
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small deterioration	-2.00 (F)	---	30
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small deterioration	0 (E)	---	30
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small deterioration	-1.00 (M)	---	30
Redelmeier [80]	Anchor	7-point Subjective Comparison Ratings Scale between patients: mean difference scores for patients feeling “a little better” or “little worse” compared to others	0.09 (D)	---	---
Redelmeier [80]	Anchor	7-point Subjective Comparison Ratings Scale between patients: mean difference scores for patients feeling “a little better” or “little worse” compared to others	0.50 (F)	---	---
Redelmeier [80]	Anchor	7-point Subjective Comparison Ratings Scale between patients: mean difference scores for patients feeling “a little better” or “little worse” compared to others	0.87 (E)	---	---
Redelmeier [80]	Anchor	7-point Subjective Comparison Ratings Scale between patients: mean difference scores for patients feeling “a little better” or “little worse” compared to others	0.23 (M)	---	---
Redelmeier [80]	Anchor	7-point Subjective Comparison Ratings Scale between patients: mean difference scores for patients feeling “a little better” or “little worse” compared to others	0.53 (pooled)	95% CI 0.39-0.67	---
Chu-Lin Tsai [71]	Distribution	SEM	0.55	---	301
Wyrwich study 1 [88]	Opinion	Delphi rounds of consensus by expert panel	3.00 (D)	---	9
Wyrwich study 1 [88]	Opinion	Delphi rounds of consensus by expert panel	2.00 (F)	---	9
Wyrwich study 1 [88]	Opinion	Delphi rounds of consensus by expert panel	5.00 (E)	---	9
Wyrwich study 1 [88]	Opinion	Delphi rounds of consensus by expert panel	3.00 (M)	---	9

EQ-5D-UI and VAS					
Nolan study 2 [78]	Anchor	5-point GRC: mean change patient “feeling little better”	6.99 (VAS)	95% CI 3.78 to 10.20	124
Nolan study 2 [78]	Anchor	5-point GRC: mean change patient “feeling little better”	0.054 (UI)	95%CI 0.028 to 0.08	124
Walters [86]	Anchor	5-point GRC: mean change patient “somewhat better” after 6 months	-0.128 (UI)	SD 0.155	9
Walters [86]	Anchor	5-point GRC: mean change patient “somewhat better” after 12 months	0.013 (UI)	SD 0.185	9
Walters [86]	Anchor	5-point GRC: mean change patient “somewhat worse” after 6 months	0.039 (UI)	SD 0.222	21
Walters [86]	Anchor	5-point GRC: mean change patient “somewhat worse” after 12 months	-0.007 (UI)	SD 0.236	16
Walters [86]	Anchor	5-point GRC: mean change patient “somewhat better” and “somewhat worse” after 6 months	-0.011 (UI)	SD 0.216	30
Walters [86]	Anchor	5-point GRC: mean change patient “somewhat better” and “somewhat worse” after 12 months	0.000 (UI)	SD 0.215	25
Nolan study 2 [78]	Anchor	MCID CRQ dyspnea (+2.5): Linear regression analysis	6.50 (VAS)	---	324
Nolan study 2 [78]	Anchor	MCID CRQ dyspnea (+2.5): ROC Curves	6.50 (VAS)	---	324
Nolan study 2 [78]	Anchor	MCID CRQ fatigue (+2.0): Linear regression analysis	7.20 (VAS)	---	324
Nolan study 2 [78]	Anchor	MCID CRQ fatigue (+2.0): ROC Curves	6.50 (VAS)	---	324
Nolan study 2 [78]	Anchor	MCID CRQ emotion (+3.5): Linear regression analysis	8.00 (VAS)	---	324
Nolan study 2 [78]	Anchor	MCID CRQ emotion (+3.5): ROC Curves	6.50 (VAS)	---	324
Nolan study 2 [78]	Anchor	MCID CRQ mastery (+2.0): Linear regression analysis	7.60 (VAS)	---	324
Nolan study 2 [78]	Anchor	MCID CRQ mastery (+2.0): ROC Curves	6.50 (VAS)	---	324
Nolan study 2 [78]	Anchor	MCID CRQ total (+10): Linear regression analysis	6.70 (VAS)	---	324
Nolan study 2 [78]	Anchor	MCID CRQ total (+10): ROC Curves	6.50 (VAS)	---	324
Zanini [89]	Anchor	MCID of BDI/TDI (+1): ROC Curves	8.00 (VAS)	---	439
Nolan study 2 [78]	Anchor	MCID CRQ emotion (+3.5): Linear regression analysis	0.063 (UI)	---	324
Nolan study 2 [78]	Anchor	MCID CRQ emotion (+3.5): ROC Curves	0.046 (UI)	---	324
Nolan study 2 [78]	Anchor	MCID CRQ mastery (+2.0): Linear regression analysis	0.062 (UI)	---	324
Nolan study 2 [78]	Anchor	MCID CRQ mastery (+2.0): ROC Curves	0.038 (UI)	---	324
Nolan study 2 [78]	Anchor	MCID CRQ total (+10): Linear regression analysis	0.059 (UI)	---	324
Nolan study 2 [78]	Anchor	MCID CRQ total (+10): ROC Curves	0.037 (UI)	---	324
Nolan study 2 [78]	Distribution	0.5SD	10.1 (VAS)	---	324
Nolan study 2 [78]	Distribution	0.5SD	0.109 (UI)	---	324
Walters [86]	Distribution	0.5SD 6 months	0.15 (UI)	---	97
Walters [86]	Distribution	0.5SD 12 months	0.12 (UI)	---	81
Walters [86]	Distribution	ES 6 months	-0.04 (UI)	---	97
Walters [86]	Distribution	ES 12 months	0.00 (UI)	---	81
Walters [86]	Distribution	SRM 6 months	-0.05 (UI)	---	97
Walters [86]	Distribution	SRM 12 months	0.00 (UI)	---	81
SF-6D					
Walters [85]	Anchor	5-point GRC: mean change patient “somewhat better”	0.006	SD 0.074	10
Walters [86]	Anchor	5-point GRC: mean change patient “somewhat better” after 6 months	0.054	SD 0.107	9
Walters [86]	Anchor	5-point GRC: mean change patient “somewhat better” after 12 months	-0.004	SD 0.071	9
Walters [85]	Anchor	5-point GRC: mean change patient “somewhat worse”	0.012	SD 0.095	19
Walters [86]	Anchor	5-point GRC: mean change patient “somewhat worse” after 6 months	0.028	SD 0.083	21
Walters [86]	Anchor	5-point GRC: mean change patient “somewhat worse” after 12 months	0.019	SD 0.100	16
Walters [85]	Anchor	5-point GRC: mean change patient “somewhat better” and “somewhat worse”	0.010	SD 0.087	29
Walters [86]	Anchor	5-point GRC: mean change patient “somewhat better” and “somewhat worse” after 6 months	0.036	SD 0.090	30
Walters [86]	Anchor	5-point GRC: mean change patient “somewhat better” and “somewhat worse” after 12 months	0.011	SD 0.090	25
Walters [85]	Distribution	SRM	0.11	95%CI -0.28 to 0.58	60
Walters [86]	Distribution	SRM 6 months	0.41	---	97
Walters [86]	Distribution	SRM 12 months	0.12	---	81
Walters [86]	Distribution	ES 6 months	0.37	---	97
Walters [86]	Distribution	ES 12 months	0.12	---	81
Walters [85]	Distribution	0.5SD	0.044	---	60
Walters [86]	Distribution	0.5SD 6 months	0.05	---	97
Walters [86]	Distribution	0.5SD 12 months	0.05	---	81

SF-36					
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small improvement	4.00 (Physical F)	---	188
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small improvement	8.00 (R Physical)	---	139
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small improvement	6.00 (Bodily Pain)	---	144
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small improvement	3.00 (Gen Health)	---	218
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small improvement	5.00 (Vitality)	---	199
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small improvement	6.00 (Social)	---	122
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small improvement	7.00 (Emotional)	---	150
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small improvement	4.00 (Mental)	---	181
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small deterioration	-2.00 (Physical F)	---	242
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small deterioration	-3.00 (R Physical)	---	284
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small deterioration	-3.00 (bodily pain)	---	314
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small deterioration	-3.00 (Gen Health)	---	406
Wyrwich study 2 [86]	Anchor	15-point GRC: mean change patient small deterioration	-5.00 (Vitality)	---	368
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small deterioration	-6.00 (Social)	---	200
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small deterioration	-5.00 (Emotional)	---	208
Wyrwich study 2 [88]	Anchor	15-point GRC: mean change patient small deterioration	-6.00 (Mental)	---	195
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small improvement	5.00 (Physical F)	---	15
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small improvement	9.00 (R Physical)	---	15
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small improvement	2.00 (Bodily Pain)	---	15
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small improvement	11.00 (Gen Health)	---	15
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small improvement	2.00 (Vitality)	---	15
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small improvement	6.00 (Social)	---	15
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small improvement	2.00 (Emotional)	---	15
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small improvement	6.00 (Mental)	---	15
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small deterioration	-1.00 (Physical F)	---	30
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small deterioration	3.00 (R Physical)	---	30
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small deterioration	-2.00 (bodily pain)	---	30
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small deterioration	-1.00 (Gen Health)	---	30
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small deterioration	0 (Vitality)	---	30
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small deterioration	-5.00 (Social)	---	30
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small deterioration	1.00 (Emotional)	---	30
Wyrwich study 3 [88]	Anchor	15-point GRC: mean change physician small deterioration	4.00 (Mental)	---	30
Wyrwich study 1 [88]	Opinion	Delphi rounds of consensus by expert panel	10.00 (Physical F)	---	9
Wyrwich study 1 [88]	Opinion	Delphi rounds of consensus by expert panel	12.50 (R Physical)	---	9
Wyrwich study 1 [88]	Opinion	Delphi rounds of consensus by expert panel	10.00 (Bodily Pain)	---	9
Wyrwich study 1 [88]	Opinion	Delphi rounds of consensus by expert panel	10.00 (Gen Health)	---	9
Wyrwich study 1 [88]	Opinion	Delphi rounds of consensus by expert panel	12.50 (Vitality)	---	9
Wyrwich study 1 [88]	Opinion	Delphi rounds of consensus by expert panel	12.50 (Social)	---	9
Wyrwich study 1 [88]	Opinion	Delphi rounds of consensus by expert panel	8.33 (Emotional)	---	9
Wyrwich study 1 [88]	Opinion	Delphi rounds of consensus by expert panel	10 (Mental)	---	9

SGRQ					
Alma [70]	Anchor	15-point GRC: mean change patient minimal improvement	-8.40 (T)	95%CI -10.07 to -6.73	196
Alma [70]	Anchor	Like SGRQ Total	-13.12 (S)	---	196
Alma [70]	Anchor	Like SGRQ Total	-5.90 (A)	---	196
Alma [70]	Anchor	Like SGRQ Total	-8.24 (I)	---	196
Tsiligianni [83]	Anchor	7-point GRC: mean change patient minimal change	---	---	9
Alma [70]	Anchor	Criterion: difference score patients with and without exacerbation during PR	-9.28 (T)	95% CI -14.56 to-3.99	449
Alma [70]	Anchor	Criterion: difference score patients with and without exacerbation during PR	--- (S)	---	449
Alma [70]	Anchor	Criterion: difference score patients with and without exacerbation during PR	-10.61 (A)	---	449
Alma [70]	Anchor	Criterion: difference score patients with and without exacerbation during PR	-9.93 (I)	---	449
Alma [70]	Anchor	MCID CAT (-2): Linear regression analysis	-7.73 (T)	95%CI -8.48 to -6.98	449
Alma [70]	Anchor	MCID CAT (-2): mean difference change score between patients failing and patients achieving the anchor's MCID	-7.78 (T)	---	449
Alma [70]	Anchor	MCID CAT (-2): ROC Curves	-7.50 (T)	---	449
Alma [70]	Anchor	MCID CAT (-3): Linear regression analysis	-8.89 (T)	95%CI -9.47 to -8.31	449
Alma [70]	Anchor	MCID CAT (-3): mean difference change score between patients failing and patients achieving the anchor's MCID	-8.69 (T)	---	449
Alma [70]	Anchor	MCID CAT (-3): ROC Curves	-8.00 (T)	---	449
Alma [70]	Anchor	MCID CCQ total (-0.4): Linear regression analysis	-7.51 (T)	95%CI -8.16 to -6.86	449
Alma [70]	Anchor	MCID CCQ total (-0.4): mean difference change score between patients failing and patients achieving the anchor's MCID	-8.14 (T)	---	449
Alma [70]	Anchor	MCID CCQ total (-0.4): ROC Curves	-8.30 (T)	---	449
Alma [70]	Anchor	MCID CCQ total (-0.5): Linear regression analysis	-8.35 (T)	95% CI -8.90 to -7.79	449
Alma [70]	Anchor	MCID CCQ total (-0.5): mean difference change score between patients failing and patients achieving the anchor's MCID	-8.36 (T)	---	449
Alma [70]	Anchor	MCID CCQ total (-0.5): ROC Curves	-8.63 (T)	---	449
Schünemann [81]	Anchor	MCID CRQ dyspnea (0.5): Linear regression analysis	-3.05 (T)	95% CI -5.71 to -0.39	84
Welling [87]	Anchor	MCID of FEV1 (100ml): Linear regression analysis 1M	-9.20 (T)	---	110
Welling [87]	Anchor	MCID of FEV1 (100ml): Linear regression analysis 6M	-7.80 (T)	---	86
Welling [87]	Anchor	MCID of 6MWD (26m): Linear regression analysis 1M	-8.50 (T)	---	110
Welling [87]	Anchor	MCID of 6MWD (26m): Linear regression analysis 6M	-6.30 (T)	---	86
Welling [87]	Anchor	MCID of RV (400ml): Linear regression analysis 1M	-8.70 (T)	---	110
Welling [87]	Anchor	MCID of RV (400ml): Linear regression analysis 6M	-6.40 (T)	---	86
Schünemann [81]	Distribution	0.2SD	2.40 (T)	---	84
Alma et al. [70]	Distrubution	0.5SD	6.06 (T)	---	449
Schünemann [81]	Distribution	0.5SD	5.90 (T)	---	84
Welling [87]	Distribution	0.5ES (1 month)	6.90 (T)	---	110
Welling [87]	Distribution	0.5ES (6 months)	7.90 (T)	---	86
Schünemann [81]	Distribution	0.8SD	9.40 (T)	---	84
Alma et al. [70]	Distrubution	SEM	5.20 (T)	---	449
Tsiligianni [83]	Distribution	SEM	2.47 (T)	---	90
Alma et al. [70]	Distrubution	1.96SEM	10.19 (T)	---	449
Tsiligianni [83]	Distribution	1.96 SEM	4.84 (T)	---	90

Other tools: The eDiary					
Kulich [77]	Anchor	7-point GRC: mean change score patients scoring "a little better" on the domain "Overall Impact" of the eDiary	-0.61	---	---
Kulich [77]	Anchor	7-point GRC: mean change score patients scoring "a little better" on the domain "COPD Severity" of the eDiary	-0.58	---	---
Kulich [77]	Anchor	TDI rating: mean change score for patient indicating a "minor improvement" for the functional impairment domain	-0.64	---	---
Kulich [77]	Anchor	TDI rating: mean change score for patient indicating a "minor improvement" for the magnitude of task domain as anchor	-0.52	---	---
Kulich [77]	Anchor	TDI rating: mean change score for patient indicating a "minor improvement" for the magnitude of effort domain as anchor	-0.55	---	---
Other tools: VSRQ					
Perez [79]	Anchor	15-point GRC: mean change score patients reporting a minimal improvement	3.40	---	185
Perez [79]	Anchor	Median of the Cumulative Response Curves for the minimally improved group drawn upon the dyspnea Overall Treatment Effect	3.50	---	185
Perez [79]	Anchor	MCID SGRQ (-4): Linear regression analysis	3.20	---	373
Other tools: Feeling Thermometer					
Schünemann [81]	Anchor	MCID CRQ fatigue domain (0.5): Linear regression analysis	6.08	95%CI 1.87 to 10.28	84
Schünemann [81]	Anchor	MCID SGRQ activity domain (4): Linear regression analysis	8.01	95%CI 4.12 to 11.90	84
Schünemann [81]	Anchor	MCID SGRQ impact domain (4): Linear regression analysis	6.47	95%CI 2.55 to 10.38	84
Schünemann [81]	Anchor	MCID SGRQ total (4): Linear regression analysis	6.83	95%CI 3.03 to 10.63	84
Schünemann [81]	Distribution	0.2SD	4.10	---	84
Schünemann [81]	Distribution	0.5SD	10.20	---	84
Schünemann [81]	Distribution	0.8SD	16.30	---	84
Other tools: QOLRIQ					
Van Stel [84]	Anchor	5-point GRC: mean absolute difference between patients unchanged and improved	0.51	95%CI 0.04 to 0.98	55
Van Stel [84]	Anchor	5-point GRC: mean absolute difference between patients unchanged and deteriorated	0.49	95%CI -0.11 to 1.09	28
Van Stel [84]	Anchor	Mean absolute change matching a 1 unit change in improved self-assessed health status	0.64	---	---
Van Stel [84]	Anchor	Mean absolute change matching a 1 unit change in deteriorated self-assessed health status	0.37	---	---
Van Stel [84]	Distribution	0.2ES	0.18	---	108
Van Stel [84]	Distribution	0.5ES	0.45	---	108
Van Stel [84]	Distribution	SEM	0.22	---	108

Abbreviations: 6MWD, Six Minute Walking Distance; A, Activity score; BDI/TDI, Baseline Dyspnea Index / Transition Dyspnea Index; CAT, COPD Assessment Test; CCQ, Clinical COPD Questionnaire; CI, Confidence Interval; (SF-)CRQ, (Short-Form) Chronic Respiratory Questionnaire; D, Dyspnea score; E, Emotion score; EQ-5D-3L-UI, EuroQol 5 Dimension 3 Levels Utility Index; EQ-5D-3L-VAS, EuroQol 5 Dimension 3 Levels Visual Analogue Scale; EQ-5D-5L-UI, EuroQol 5 Dimension 5 Levels Utility Index; EQ-5D-5L-VAS, EuroQol 5 Dimension 5 Levels Visual Analogue Scale; ES, Effect Size; F, Functional Status or Fatigue score; FEV1, Forced Expiratory Volume in 1 Second; GRC, Global Ratings of Change scale; I, Impact score; M, Mental or Mastery score; MCID, Minimal Clinically Important Difference; MDC95, 95% Minimal Detectable Change level; N, Number of Patients; NS, Not Significant; PR, Pulmonary Rehabilitation; QOLRIQ, Quality of Life for Respiratory Illness Questionnaire; ROC, Receiver Operating Characteristics; RV, Residual Volume; S, Symptoms score; SD, Standard Deviation; SEM, Standard Error of Measurement; SF-36, Short-Form 36; SF-6D, Short Form 6 Dimensions; SGRQ, St. George's Respiratory Questionnaire; SRM, Standardized Response Mean, T, Total score; VSRQ, Visual Simplified Respiratory Questionnaire;