

Appendix A. Search strategies used for this review

1. PUBMED

Pulmonary Fibrosis, QOL, and QOL Tests and Questionnaires.

1. pulmonary fibrosis OR “idiopathic pulmonary fibrosis” OR “cryptogenic fibrosing alveolitis” OR “usual interstitial pneumonia” OR “fibrosing alveolitis” OR “usual interstitial pneumonitis” OR “idiopathic interstitial pneumonia” OR (idiopath* [ti] AND pulmon* [ti] AND (fibros* [ti] OR fibrot* [ti])) OR iip [ti] OR “uip” [ti]
lung fibrosis/de
2. lung transplant* OR lung transplantation [mesh]
lung transplantation!
3. sf36 [ti] OR eq 5d [ti] OR euroqol [ti] OR hrql [ti] OR hrqol [ti] OR “health related quality of life” [ti] OR rosser [ti] “standard gamble” [ti] OR ((utility [ti] OR utilities [ti]) AND qaly* [tiab]) OR qwb* [ti] OR (quality [ti] AND wellbeing [ti]) OR “quality of well being” [ti]
4. (quality AND life) OR qol OR hrql OR hrqol OR (quality AND adjusted AND life AND year*) OR health state [tw] OR health status [tw] OR (willingness AND pay) OR wtp OR (george* [tw] AND respiratory [tw] AND questionnaire [tw]) OR sgrq OR (wellbeing OR well being) OR (crq OR (“chronic respiratory disease” AND questionnaire)) OR (whoqol OR (world health organization AND quality of life))
5. quality of life [mesh] OR questionnaires [mesh] OR psychology [sh] OR health status [mesh] OR health status indicators [mesh] OR activities of daily living [mesh] OR health surveys [mesh]
6. quality adjusted life years [mesh] OR treatment outcome [mesh] OR psychometrics [mesh]

- 1 AND (3 OR 4 OR 5 OR 6) = 413 citations
- 2 AND (3 OR 4 OR 5 OR 6) = 815 citations

2. EMBASE

Pulmonary Fibrosis, QOL, and QOL Tests and Questionnaires.

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S pulmonary fibrosis/de OR pulmonary(w)fibrosis OR
 idiopathic(w)pulmonary(w)fibrosis OR cryptogenic(w)fibrosing(w)alveolitis OR
 usual(w)interstitial(w)pneumonia
 S fibrosing(w)alveolitis OR usual(w)interstitial(w)pneumonitis OR
 idiopathic(w)interstitial(w)pneumonia OR (idiopath?/ti AND pulmon?/ti AND (fibros?/ti
 OR fibrot?/ti)) OR iip/ti OR uip/ti OR *lung fibrosis/de*
 s lung(w)transplant? OR *lung transplantation!*

S sf36/ti OR eq(w)5d/ti OR euroqol/ti OR hrql/ti OR hrqol/ti OR
 health(w)related(w)quality(1w)life/ti,ab OR rosseter/ti OR standard(w)gamble/ti
 S (utility/ti OR utilities/ti) AND qaly?/ti,ab OR qwb?/ti OR (quality/ti AND wellbeing/ti)
 s qol OR hrql OR hrqol OR (quality AND adjusted AND life AND year?) OR
 health(w)state/ti,ab OR health(w)status/ti,ab
 s (george?/ti,ab AND respiratory/ti,ab AND questionnaire/ti,ab) OR sgrq
 s wellbeing OR well(w)being OR crq OR (chronic(w)respiratory(w)disease AND
 questionnaire)
 S whoqol OR (world(w)health(w)organization AND quality(1w)life)

S quality of life! OR questionnaire OR px OR health status! OR activities of daily living!

OR health surveys!

S quality-adjusted life years! OR treatment outcome! OR psychometrics!

S health survey/de OR outcomes research/de OR scoring system/de OR rating scale/de

OR functional assessment/de OR self report/de OR questionnaire/de OR quality adjusted

life year/de

- 1 AND (3 OR 4 OR 5 OR 6) = 475 citations
- 2 AND (3 OR 4 OR 5 OR 6) = 739 citations

3. HAPI

(quality of life.de. or qol.mp. or hrqol.mp. or whoqol.mp. or hrql.mp.) and (lung\$ or pulmon\$ or respir\$).mp. [mp=title, acronym, descriptors, abstract] = 25 citations: added to the 77 citations from PubMed (keyword in EndNote: validqollung)

4. Cochrane

(quality of life or qol or hqol or hrqol).ti. and REPLACE WITH IPF/PF/LT hedge...(lung or pulmonary or respiratory).mp

Appendix B. Quality criteria used to assess articles included in the review. Quality domain titles preceded by letters.

A. IPF Case Definition and HRQL Study Subject Assembly

1. Did all IPF subjects undergo VATS or open lung biopsy?
2. Did the authors state that the pathologic specimens of all the IPF patients who underwent VATS or open lung biopsy have patterns consistent with UIP?
3. Was the pathologic pattern confirmed by at least two pathologists?
4. If clinical criteria were used to make the diagnosis of IPF in some patients, did the criteria include HRCT?
5. Was the HRCT pattern of IPF confirmed by at least two radiologists?
6. For the IPF subjects in this study, were known causes of lung fibrosis (e.g., asbestos or bird exposure, medications) excluded before arriving at the diagnosis of IPF?
7. Were the inclusion and exclusion criteria reported?
8. Did the authors state which subjects would complete the HRQL instrument?

B. Clinical Characteristics of the IPF Subjects

9. For the subjects with IPF, is the age distribution given?
10. For the subjects with IPF, is the gender distribution given?
11. For the subjects with IPF, is the race/ethnicity distribution given?
12. For the subjects with IPF, can you discern the # or % of patients who underwent diagnostic lung biopsy?
13. For the subjects with IPF, are there data for at least one of the following: FVC or TLC?
14. For the subjects with IPF, are there data for DLCO?

15. For the subjects with IPF, are there data for at least one of the following: SpO2 or PaO2?

16. For the subjects with IPF, is there an objective measure (e.g., a score a HRCT scoring scale) of the degree of abnormality on HRCT?

17. Were potentially relevant comorbidities discussed?

C. HRQL Instrument Selection

18. IF THIS IS NOT A STUDY DESIGNED TO “VALIDATE” AN INSTRUMENT, did the authors provide a rationale for choosing the particular HRQL instrument(s) for this study?

19. Was the instrument(s) chosen for this study specifically designed to assess HRQL in IPF patients?

20. IF THIS IS NOT A STUDY DESIGNED TO “VALIDATE” AN INSTRUMENT, did the authors discuss (or reference) previously published data that supports the validity of the chosen instrument(s) in IPF patients?

21. IF THIS IS NOT A STUDY DESIGNED TO “VALIDATE” AN INSTRUMENT, did the authors discuss (or reference) previously published data that supports the reliability (e.g., test- retest and internal consistency) of the chosen instrument(s) in IPF patients?

22. IF THIS IS NOT A STUDY DESIGNED TO “VALIDATE” AN INSTRUMENT, did the authors discuss (or reference) previously published data regarding the floor and ceiling effects of the chosen instrument(s) in IPF patients?

23. If a translated instrument was used, did the authors discuss (or reference) data that verifies the cultural validity of the translated instrument?

D. HRQL Endpoints and Instrument Administration

24. Was the hypothesis regarding HRQL stated?
25. Did the authors state which instrument scores (e.g., the total instrument score or specific domain scores) were selected as endpoints?
26. Was the instrument(s) administered in the format (e.g., self- or interviewer-administered) that the instrument developers intended?
27. Did the authors adequately describe the timing of instrument(s) administration (as applicable) in the context of a single administration, an individual study visit, and throughout the course of the study?
28. Did the authors provide details of the scoring methods used?
29. Did the authors provide information on how to interpret scores (e.g., do higher scores indicate better or worse HRQL)?

E. Methods of Statistical Analysis

30. **FOR DRUG TRIALS ONLY**, was the study adequately powered to detect the hypothesized difference in HRQL between groups?
31. **FOR ALL STUDIES**, did the authors describe how missing data (e.g., items missing responses and data from drop-outs) would be accounted for (e.g., by using imputation methods)?
32. **FOR ALL STUDIES**, did the authors define what would deem a subject's HRQL data inadequate (or did they define what constitutes adequate data) for analysis?
33. **FOR ALL STUDIES**, were the statistical methods used to assess (and if applicable, to compare) HRQL described in enough detail that other researchers could repeat the analysis if the full data were made available?
34. **FOR DRUG TRIALS ONLY**, did the authors define what would constitute a clinically important difference in HRQL scores between the treatment groups?

F. Reporting Results

35. Was compliance (% of patients who were asked to complete the instrument and actually completed it) data for each administration given?
36. Did the investigators calculate Internal Consistency Reliability (i.e., Cronbach's alpha) for the instrument (and/or its subscales) in this study's population?
37. Are the floor and ceiling effect levels reported?
38. Were the results of the primary and secondary HRQL analyses presented adequately (e.g., mean or median scores—and where applicable—tests of statistical significance between the placebo and treatment groups) to support the conclusions drawn?
39. Were confidence intervals or p-values reported for the results of the hypothesized HRQL endpoints?
40. Did the authors adequately report missing data (e.g., due to item non-response, due to non-completion of the instrument because of death of the patient, due to non-completion of the instrument for reasons other than death)?
- 41. FOR EACH ARM OF A DRUG TRIAL AND FOR LONGITUDINAL STUDIES**, did the investigators account for all subjects at the end of the study?
42. Were subjects excluded from the HRQL analysis?
 - a. If "Yes" did the investigators describe the circumstances surrounding subjects excluded from the analysis?
43. Was the clinical significance of the HRQL results addressed?

Appendix C. Summaries for the excluded abstract.

In this study, investigators examined HRQL in 34 prevalent and 30 incident cases of IPF.[18] There was no difference between the two groups' scores from the generic HRQL Quality of Well-Being Scale. According to the SF-36, incident cases of IPF had more impaired mental health than prevalent cases. According to the Chronic Respiratory Disease Questionnaire—an obstructive lung disease-specific instrument that has four domains: Dyspnea, Fatigue, Emotional Function, and Mastery—incident cases were more impaired by dyspnea than prevalent cases. Demographic, physiologic, and other important data were not provided.

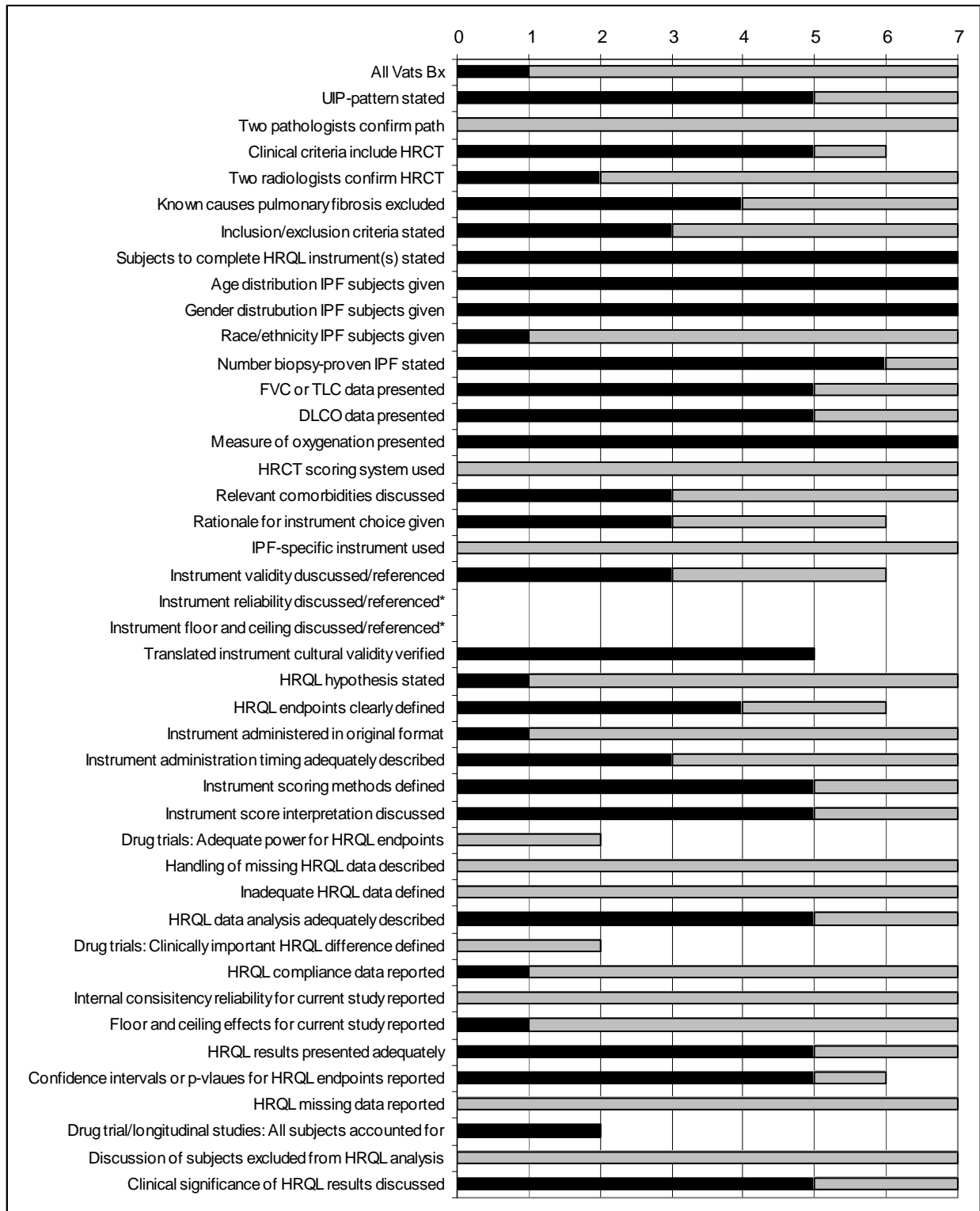
Appendix D Summary of the measurement instruments used in the included studies

	Type of Instrument	Domains Included	Topics Assessed by Specific Items in Each Domain
SGRQ	Obstructive Lung disease-Specific HRQL	Symptoms Activity Impacts	Frequency of cough, sputum production, dyspnea, wheezing/frequency and severity of attacks of chest trouble Activities causing or limited by breathlessness, Impact of chest condition overall and on employment/on inducing feelings of embarrassment, fear or panic, being in control of health/on need for medication/on expectations for health
SF-36	Generic HRQL	Physical Functioning (PF) Role-Physical (RP) Bodily Pain (BP) General Health (GH) Vitality (VT) Social Functioning (SF)	Limitations in walking/climbing stairs/bending or kneeling/ADLs/carrying Decreased time spent/accomplished less/limited kind/had difficulty with usual physical activities Magnitude of pain, degree to which pain interferes with normal activity Sick easier/as healthy as other people, expectations in terms of health, health rating Energy level, feeling worn out/tired/pep/full of life Time and extent to which physical or

Instrument	Type of Instrument	Domains Included	Topics Assessed by Specific Items in Each Domain
WHOQOL-100	Generic QOL	Role-emotional (RE)	emotional health interferes with social activities Extent to which emotional problems have decreased the amount of time spent on work or activities/decreased amount accomplished/impaired care with which work or activities are performed
		Mental Health (MH)	Frequency of feelings—nervous, down in the dumps, blue/sad, peaceful, happy
		Physical health	Pain and discomfort/Energy and fatigue/Sleep and rest
		Psychological	Body image/appearance, positive and negative feelings, self-esteem, thinking/learning/memory/concentration
		Level of Independence	Mobility, ADLs, dependence on medicinal substances/medical aids, work capacity
		Social Relations	Personal relationships, social support, sexual activity
Environment	Financial resources, freedom, physical safety and security, health and social care—accessibility and quality, home environment, opportunities for acquiring new information and skills, participation in and opportunities for recreation/leisure, physical environment (pollution, noise, traffic, climate), transport		

Instrument	Type of Instrument	Domains Included	Topics Assessed by Specific Items in Each Domain
		Spirituality/Religion/Beliefs	Beliefs, meaningfulness of life, understanding and confronting difficulties in life

Appendix E. The number of studies meeting each individual quality criterion.



Black bars represent the number of studies meeting each quality criterion. Hatched bars depict the number of studies for which the given criterion is applicable. *These criteria were not applicable to any study because such data do not exist for patients with IPF.

Appendix F. Correlation coefficients for the relationships between measurement instrument scores and various clinical parameters

Instrument Score	FVC%	FEV1%	DLCO%	SpO2	Dyspnea Scales and Indexes				Arterial Blood Gas at Rest		
	Predicted	Predicted	Predicted	With Exertion	Baseline Dyspnea Index	Medical Research Council Scale	Oxygen Cost Diagram	Bath Breathlessness Scale Total	pH	paO2	paCO2
SF-36											
Physical Functioning	0.43*	0.39*			0.78*,0.81*	-0.75*	-0.71*		-0.54*	0.12	0.15
Role-physical	-0.04	-0.11			0.17	x	x		-0.23	0.002	0.17
Bodily Pain	0.12	0.29			-0.08	x	x		0.13	-0.41*	0.15
General Health	0.4*	0.45*			0.5*,0.47*	x	-0.37*		-0.15	0.05	0.21

Vitality	0.27	0.23			0.65*,0.74*	-0.44*	-0.65*		-0.38*	0.22	0.21
Social Functioning	0.14	0.13			0.49*,0.52*	-0.46*	-0.42*		-0.42*	0.19	0.22
Role- emotional	0.07	0.09			0.08,0.48*	X	-0.41*		-0.36*	0.13	0.25
Mental Health	0.21	0.31			0.39*	X	x		-0.20	0.2	0.34
SGRQ											
Symptoms	-0.35*		-0.32*	-0.38*	-0.55*					-0.21	
Activity	-0.36*		-0.45*	-0.48*	-0.77*					-0.48*	
Impact	-0.15		-0.27	-0.22	-0.53*					-0.29	
Total	-0.30		-0.39*	-0.37*	-0.69*					-0.37*	
WHOQOL-100											
General		0.36*	x	x				-0.56*		0.41*	

Health										
Physical Health		x	x	x				-0.48*		x
Psychological Health		0.39*	x	x				-0.63*		x
Independence		x	x	0.55*				x		x
Social Relationships		0.38*	x	x				x		x
Environment		0.33*	x	x				-0.72*		x
Spirituality		x	x	x				x		x

* = Statistically significant correlation coefficient; † = lowest SpO2 with exertion; x = Correlation that was assessed by study

investigators but not reported in their manuscripts due to lack of statistical significance; When more than one study assessed the same correlation between HRQL and a clinical parameter, all reported coefficients are presented.