Imperial College London

Development & Testing of the Idiopathic Pulmonary Fibrosis Patient Reported Outcome Measure UK & Ireland Multi-Centre IPF-PRoM Study

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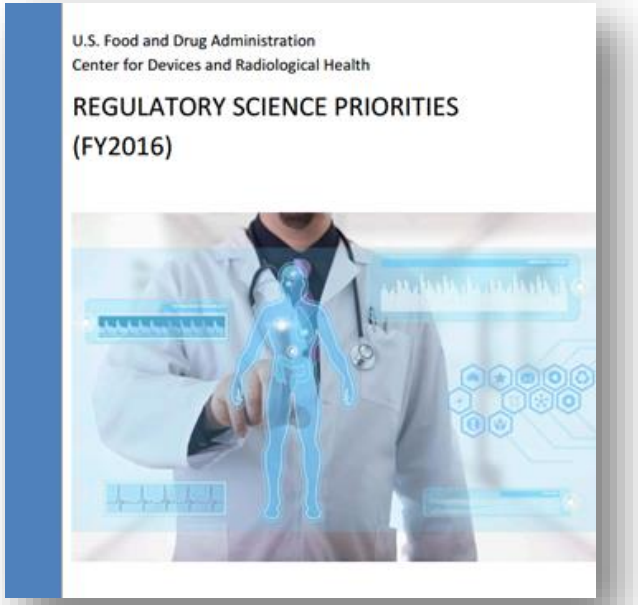
Trainees Coordinating Centre

International Drivers for PROM's

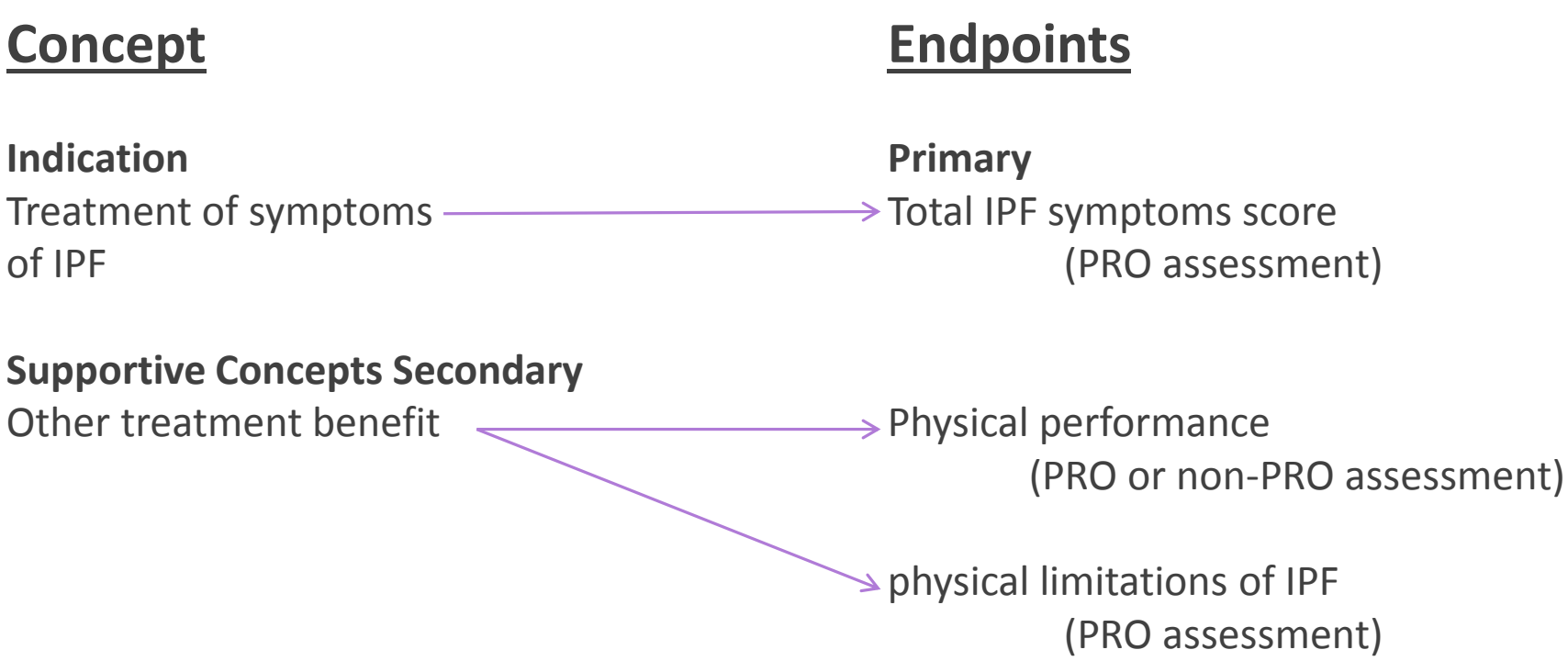
- PROM's needed
  - regulatory decision making
  - medical product development
- The quality and validity of PROMs is highly variable
- There is a need to **develop and validate** PROM's to generate
  - high quality
  - relevant data

on **outcomes of importance to patients**



https://www.fda.gov/downloads/medicaldevices/scienceandresearch/ucm467552.pdf

Endpoint Model:
Treatment of Symptoms Associated with IPF



UK Drivers for PROM's

1820-1910

Early PROM:

- Relieved
- Unrelieved
- Dead

2009 English NHS began collecting PROMs
(four elective procedures)

⇩ Change of government in 2010 ⇩
Outcomes Framework.

PROMs programme stalled

Restructuring of the NHS

PROMs programme shifted DH to NHS England

⇩ PROMs programme rumbled along ⇩

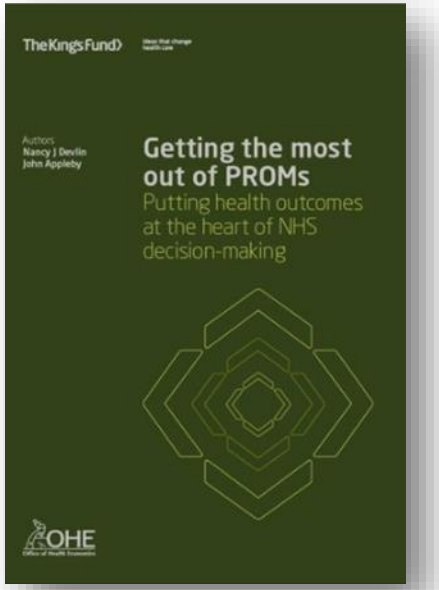
Millions of data points collected

Powerful insights into how surgery improves health

Regaining Momentum

⇩ ?Rolling out to Chronic Conditions? ⇩

https://www.engage.england.nhs.uk/consultation/proms-programme/



Getting the most out of PROMs
Nancy Devlin & John Appleby
Kings Fund March 2010
https://www.kingsfund.org.uk/

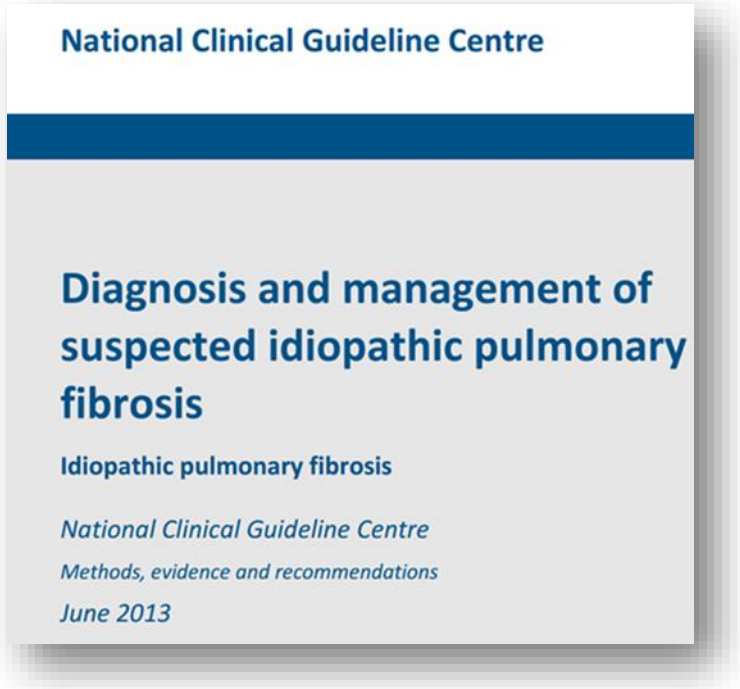
UK Drivers for a PROM for IPF?

- NICE clinical guideline 2013:

  'significant variations in clinical care'
- NICE Quality Standards for IPF 2015: benchmark
- NICE technology appraisal guidance [TA282] 2013

  Pirfenidone for treating idiopathic pulmonary fibrosis
- NICE technology appraisal guidance [TA379] 2016

  Nintedanib for treating idiopathic pulmonary fibrosis



https://www.nice.org.uk/guidance/cg163

U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

Guidance for Industry

Patient-Reported Outcome Measures:
Use in Medical Product Development to Support
Labeling Claims
March, 2009

Technically a template for an evidence dossier

https://www.fda.gov/downloads/drugs/guidances/ucm193282.pdf

The Voice of the Patient

Patient-Focused Drug Development Initiative
Idiopathic Pulmonary Fibrosis
Public Meeting: September 26, 2014
Report Date: March, 2015

https://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM440829.pdf

pcori

The PCORI Methodology Report

PCORI Methodology Committee

November 2013 *(in revision)*

http://www.pcori.org/sites/default/files/PCORI-Methodology-Report.pdf

Patient Centred Research: IPF-PRoM Study

……informed by patients' views & experiences as both **participants** & **partners** in research

- The study protocol reviewed by patients
- A Research support Group was established:
  - Lead researcher
  - Senior Research Nurse
  - Clinical psychologist
  - Patient representatives
  - Care-giver representative
  - Patient & Public Involvement officers

- Quarterly meetings
- Formal Terms of Reference
- Role descriptions agreed at outset
- The remit of the RSG to review study progress
- Have an instrumental role in analysis
- Participate in consensus rounds in phase one
- Contribute to Outputs:
  - Joint publications
  - International conference Presentations

IPF PROM Methodology

- Study Configuration: Multi-centre study
- Patient Centeredness
- Literature Review
  - Qualitative: Focus groups
  - Consensus: Nominal Group of ILD experts
  - Modified NG - Expert Interdisciplinary, Patient & Carer Group
  - Survey: Delphi Method
  - Quantitative: Item reduction
    Psychometrics – Classical Test theory

TRIANGULATION

COnsensus-based Standards for the selection of health Measurement INstruments

- Literature review:
  26 outcome measures in IPF studies
- 14 met the inclusion criteria
- Deconstructed
- 1212 items underwent duplicity screening
- 410 items submitted to consensus rounds

www.cosmin.nl | www.emgo.nl

COSMIN

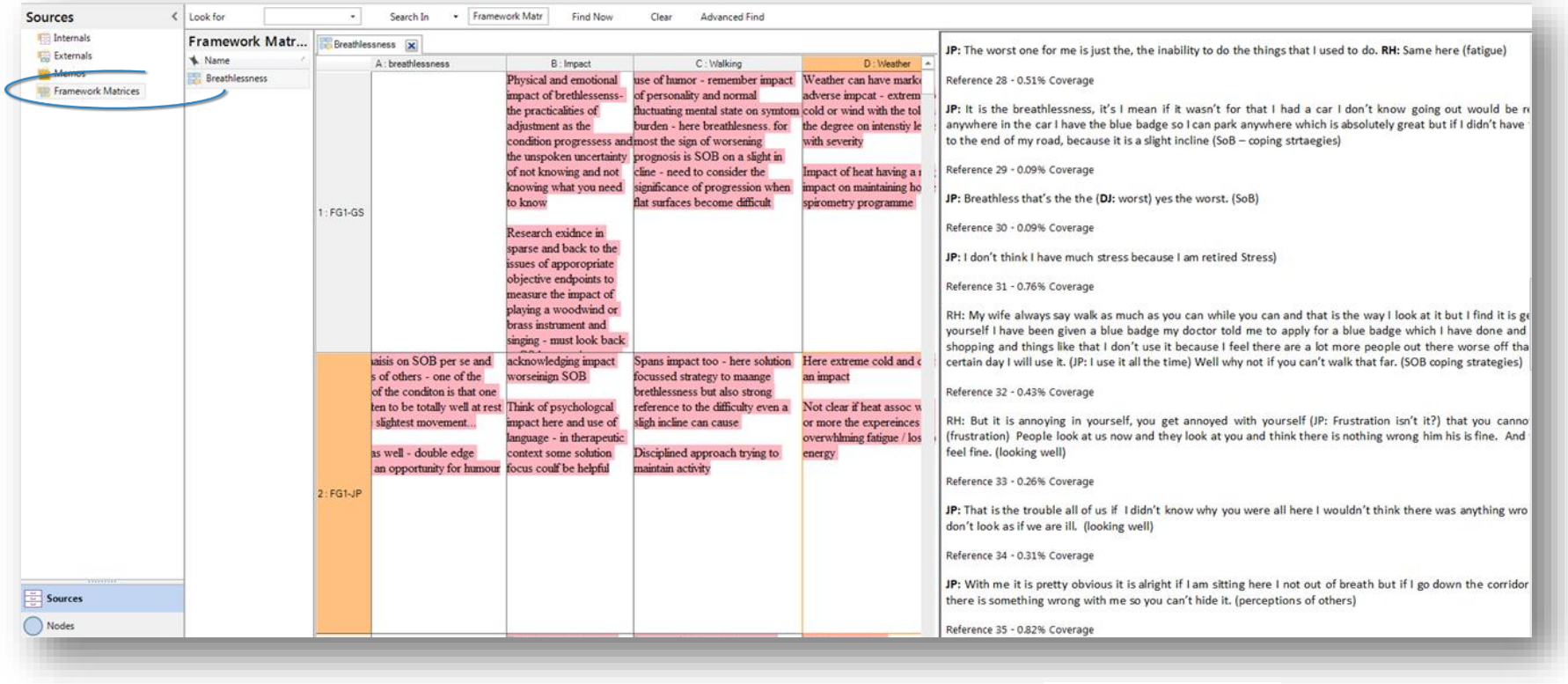
Focus Group: Framework

FG 1
- Brompton Hospital - London
- n= 7 (3f) CPI > 45 No O_2

FG 2
- Brompton Hospital - London
- n= 5 (2f) CPI > 45 On O_2

FG 3
- Pennine Acute Hospitals
- n= 6 (2f) CPI < 45 No O_2

FG 4 / 5
- North Bristol Hospitals
- n= 10 (2f) CPI < 45 No O_2



NatCen
Social Research that works for society

http://www.natcen.ac.uk/our-expertise/methods-expertise/qualitative/framework/

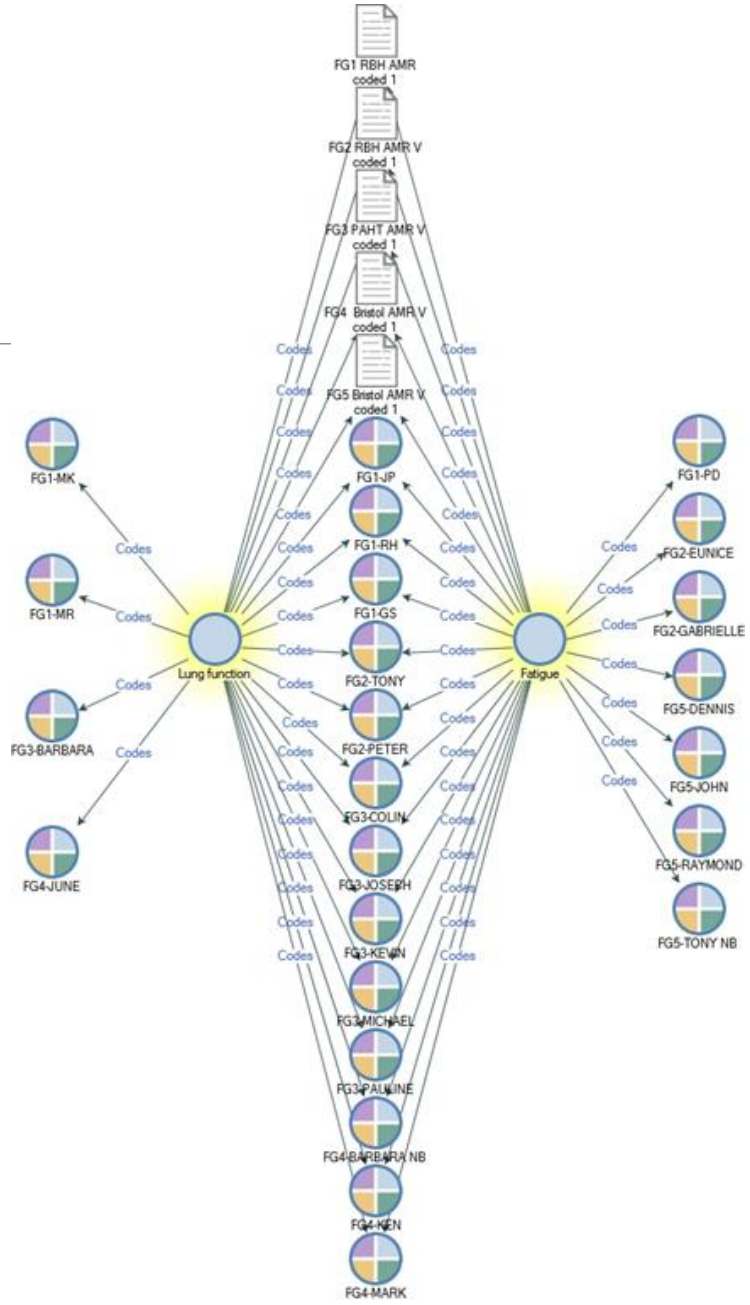
NVIVO

FDA Claim

https://www.fda.gov/downloads/drugs/guidances/ucm193282.pdf

- Content Validity:

- Items cover all aspects of the concept important to patients
- Variations in severity of condition represented
- Population characteristics represented
- Saturation reached
- Source of items traceable
- An item tracking matrix



Ritchie J and Lewis J 2003 Qualitative Research Practice

Delphi*Rounds One and Two

- **305** items included in R1
- **236** items originated from focus group discussions
- Domains ranked by nominal group~
- Importance of statements rated on Likert scale 1-7
- Comments & nominations of other dimensions invited

- Participants:
  - Patients diagnosed with IPF =77
  - Relatives =18
  - Specialist ILD physicians | nurses =29
- Response rates **≥ 93%** in all categories
- **112** items were included in **R2**

(16 new items identified in qualitative analysis)

*Culhs K. http://www.unido.org/fileadmin/import/16959_DelphiMethod.pdf

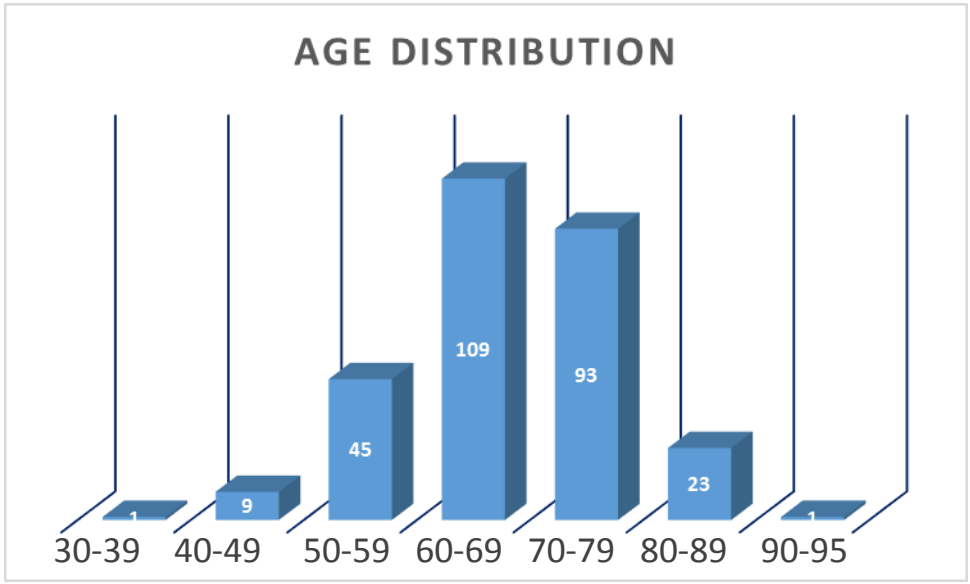
~ Van de Ven AH, Delbecq AL. The nominal group as a research instrument for exploratory health studies. Am J Public Health 1972 Mar;62(3):337-42.

Standardised Inclusion

Statement	Threshold to apply
Definitely include	>=70% of participants rate statement as >=6 OR median rating of >=5
Maybe include	>=70% of participants rate statement as >=5 OR median rating of >=5
Definitely exclude	<70% of participants rate statement as <=4 AND 100% participants understand statement OR median <=4 AND 100% panel understand statement
Review	<70% of panel rate statement as >=6 AND <100% panel understand statement

Delphi Results R3: 105 items

- Accessing survey:510
- Completing survey:281
- Completing hard copy:20
- Partially completing survey:72
- Not permitted to complete survey: 41
- Accessing survey preamble only: 116
- Response categories:
  - Never
  - Occasionally
  - Very often
  - Always

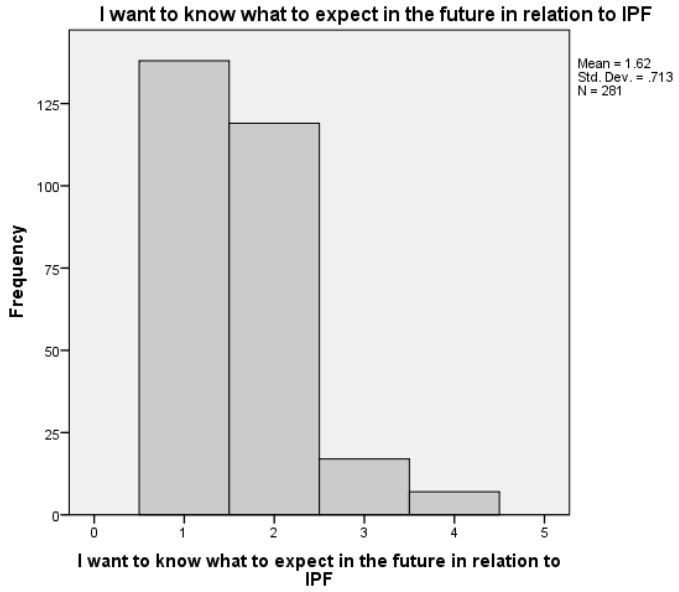


Geographical Distribution Respondents & Centres

Region	N	%
UK: south East	78	27.8
UK: midlands	61	21.7
UK: south West	32	11.4
UK: north West	24	8.5
UK: north East	20	7.1
Ireland	14	5.0
UK: Scotland	14	5.0
UK: Yorkshire & Humber	13	4.6
UK: NI; Wales & other	26	9

- Complete responders male n=181 (65%)
- IP addresses were checked to detect duplication

Descriptive Stats & Item Reduction



I want to know what to expect in the future in relation to IPF

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Strongly Agree	138	49.1	49.1	49.1
	Agree	119	42.3	42.3	91.5
	Disagree	17	6.0	6.0	97.5
	Strongly Disagree	7	2.5	2.5	100.0
	Total	281	100.0	100.0	

- 281 complete responses
- 72 partial responses *(test data set)*
- Questions with a 'non relevant' category removed (30)
  - 57 % (n=161) no experience of oxygen
  - 35% (n=98) do not have a partner
- Ambiguous items were removed (2)

Factor Analysis (FA)

- FA identified 14 factors accounting for 70% of the variance
- Factors with an eigen value ≥1 were retained
- Questions with a factor loading ≥ 0.5 were retained
- Cronbach's alpha assessed internal reliability & consistency of the scale
  - Values ≤ 0.7 were considered too low
  - Values ≥ 0.92 redundant
- Items with a communality ≤ 0.5 were removed
- Face validity was continually assessed by the research team
- Cough items: correlation co-efficient > 0.9 suggested cough was a problematic domain

Fayers P Machin D Quality of Life: The Assessment, Analysis and Interpretation of Patient-reported Outcomes, 2013 2nd Edition Wiley ISBN: 978-1-118-69945-4
Streiner DL Norman GR Health Measurement Scales: A practical guide to their development & use. 2003 3rd Ed Oxford University Press
Kline, P (2000) A psychometrics Primer Free Association Books London ISBN 1853434892

ELSEVIER

CrossMark

Journal of Clinical Epidemiology 68 (2015) 1019–1027

Journal of Clinical Epidemiology

Rasch analysis and impact factor methods both yield valid and comparable measures of health status in interstitial lung disease

Amit S. Patel[a], Richard J. Siegert[b], Sabrina Bajwah[c], Kate Brignall[a], Harry R. Gosker[d], John Moxham[a], Toby M. Maher[e], Elisabetta A. Renzoni[e], Athol U. Wells[e], Irene J. Higginson[c], Surinder S. Birring[a,*]

- KBILD-I KBILD-R - 15 items each – sharing 7 common items
- KBILD-I in contrast to KBILD-R contained a cough item
- The presence of a cough item did not improve the overall clinical performance of the KBILD-I
- Both questionnaires equally able to detect significantly worse health status in patients with ILD and cough compared to those without cough
- It is likely that cough affects a wide range of health status items that capture its impact.
- The absence of a cough item did not significantly reduce the performance of the KBILD-R

The Idiopathic Pulmonary Fibrosis Patient Reported Outcome Measure

12 item questionnaire

Four domains:

Each with 3 items | 4 response options

- Physical experience of breathlessness
- Psychological experience of breathlessness
- Emotional well-being
- Energy

Simple Scoring System

Domain	Alpha Value
1	0.874
2	0.870
3	0.900
4	0.849
Total	0.920

Communalities ≥ 0.5
KMO & Bartletts 0.922

Test Re test Reliability

- 66 patients recruited
- 61 completed TP1 and TP2
- 14 female
- 35 electronically

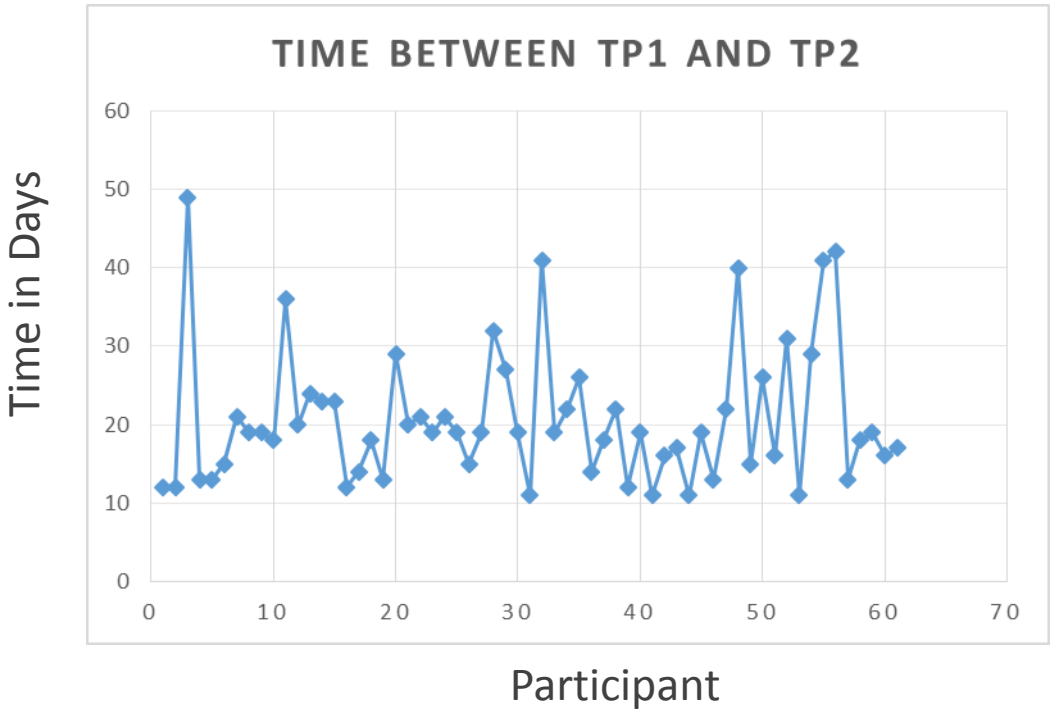
Mean Score	Total	Domain 1	Domain 2	Domain 3	Domain 4
TP1	28.63	7.18	7.73	6.33	7.38
TP2	28.52	7.38	7.52	6.28	7.33
Mean change	0.11	-0.20	0.23	0.05	0.05
Mean absolute difference	2.38	0.87	0.78	0.95	0.88

Test Re test Reliability

Domain	t-statistic	p-value	ICC
1	-1.272	0.209	0.835
2	1.458	0.150	0.895
3	0.273	0.786	0.813
4	0.305	0.761	0.863
Total	0.275	0.784	9.24

No significant difference TP1 – TP2

Mean timeframe 20.69 days



Validation: 12m

Swigris et al. Health and Quality of Life Outcomes 2014, 12:124
http://www.hqlo.com/content/12/1/124

HEALTH AND QUALITY OF LIFE OUTCOMES

REVIEW Open Access

The psychometric properties of the St George's Respiratory Questionnaire (SGRQ) in patients with idiopathic pulmonary fibrosis: a literature review

Jeffrey J Swigris[1*], Dirk Esser[2], Craig S Conoscenti[3] and Kevin K Brown[1]

Abstract

Assessment of health-related quality of life (HRQL) is particularly important in patients with progressive and incurable diseases such as idiopathic pulmonary fibrosis (IPF). The St George's Respiratory Questionnaire (SGRQ) has frequently been used to measure HRQL in patients with IPF, but it was developed for patients with obstructive lung diseases. The aim of this review was to examine published data on the psychometric performance of the SGRQ in patients with IPF. A comprehensive search was conducted to identify studies reporting data on the internal consistency, construct validity, test-retest reliability, and interpretability of the SGRQ in patients with IPF, published up to August 2013. In total, data from 30 papers were reviewed. Internal consistency was moderate for the SGRQ symptoms score and excellent for the SGRQ activity, impact and total scores. Validity of the SGRQ symptoms, activity, impact and total scores was supported by moderate to strong correlations with other patient-reported outcome measures and with a measure of exercise capacity. Most correlations were moderately strong between SGRQ activity or total scores and forced or static vital capacity, the most commonly used marker of IPF severity. There was evidence that changes in SGRQ domain and total scores could detect within-subject improvement in health status, and differentiate groups of patients whose health status had improved, declined or remained unchanged. Although the SGRQ was not developed specifically for use with patients with IPF, on balance, its psychometric properties are adequate and suggest that it may be a useful measure of HRQL in this patient population. However, several questions remain unaddressed, and further research is needed to confirm the SGRQ's utility in IPF.

Keywords: Idiopathic pulmonary fibrosis, Patient-reported outcomes, PROs, St George's Respiratory Questionnaire, SGRQ, Health-related quality of life, HRQL, Psychometrics, Validity, Reliability

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ORIGINAL ARTICLE
INTERSTITIAL LUNG DISEASES

Psychometric properties of the St George's Respiratory Questionnaire in patients with idiopathic pulmonary fibrosis

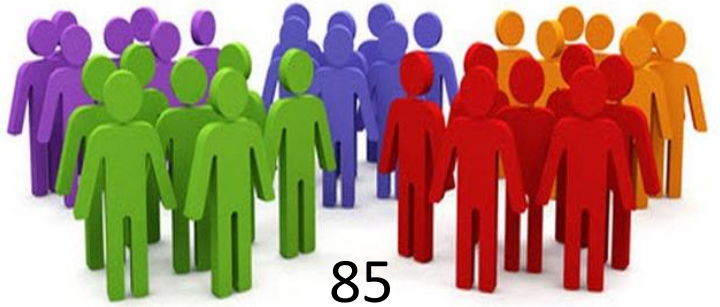
Jeffrey J. Swigris[1], Dirk Esser[2], Hilary Wilson[3], Craig S. Conoscenti[4], Hendrik Schmidt[5], Wibke Stansen[5], Nancy Kline Leidy[3] and Kevin K. Brown[1]

Affiliations: [1]National Jewish Health, Denver, CO, USA. [2]Boehringer Ingelheim GmbH, Ingelheim am Rhein, Germany. [3]Evidera, Bethesda, MD, USA. [4]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA. [5]Boehringer Ingelheim GmbH & Co. KG, Ingelheim am Rhein, Germany.

Correspondence: Jeffrey J. Swigris, Autoimmune Lung Center and Interstitial Lung Disease Program, National Jewish Health, 1400 Jackson Street, Denver, CO 80206, USA. E-mail: swigrisj@njc.org

@ERSpublications
The SGRQ is an acceptable measure of aspects of health-related quality of life in patients with IPF
http://ow.ly/jMjf305bjZ5

Cite this article as: Swigris JJ, Esser D, Wilson H, *et al.* Psychometric properties of the St George's Respiratory Questionnaire in patients with idiopathic pulmonary fibrosis. *Eur Respir J* 2017; 49: 1601788 [https://doi.org/10.1183/13993003.01788-2016].



Furukawa et al. Respiratory Research (2017) 18:18
DOI 10.1186/s12931-017-0503-3

Respiratory Research

RESEARCH Open Access

The St. George's Respiratory Questionnaire as a prognostic factor in IPF

Taiki Furukawa[1], Hiroyuki Taniguchi[1*], Masahiko Ando[2], Yasuhiro Kondoh[1], Kensuke Kataoka[1], Osamu Nishiyama[3], Takeshi Johkoh[4], Junya Fukuoka[5], Koji Sakamoto[6] and Yoshinori Hasegawa[6]

Abstract

Background: It is unclear whether health related quality of life (HRQL) may have a predictive value for mortality in idiopathic pulmonary fibrosis (IPF).
We investigated the relationship between HRQL assessed using the St. George's Respiratory Questionnaire (SGRQ) and survival time in patients with IPF, and tried to determine a clinical meaningful cut off value to predict poorer survival rates.

Methods: We retrospectively analyzed consecutive patients with IPF who underwent an initial evaluation from May 2007 to December 2012. The diagnosis of IPF was made according to the 2011 international consensus guidelines. We used Cox proportional hazard models to identify independent predictors for mortality rate in patients with IPF.

Results: We examined 182 eligible cases, average age was 66 years old, and 86% were male. Mean levels of percent predicted FVC, DLco, six-minute-walk test distance, and the SGRQ total score were around 80%, 58%, 580 m, and 34 points. On multivariate analysis, the SGRQ total score (hazard ratio [HR], 1.012; 95% confidence interval [CI] 1.001–1.023; $P = .029$) and percent predicted FVC (HR, 0.957; 95% CI 0.944–0.971, $P < .001$) were independent predictors for mortality rate. Moreover, a score higher than 30 points in the SGRQ total score showed higher mortality rate (HR, 2.047; 95% CI, 1.329–3.153; $P = .001$).

Conclusions: The SGRQ total score was one of independent prognostic factors in patients with IPF. Total scores higher than 30 points were associated with higher mortality rates.

Trial registration: This study was retrospective, observational study, so it is not applicable.

Keywords: Health related QoL, Idiopathic pulmonary fibrosis, Prognostic factors, The St. George's Respiratory Questionnaire

……SGRQ | EQ-5D | MRC

85

FVC…….

Validation: 3m FVC + interim

ORIGINAL ARTICLE

Daily Home Spirometry: An Effective Tool for Detecting Progression in Idiopathic Pulmonary Fibrosis

Anne-Marie Russell[1,2], Huzaifa Adamali[3], Philip L. Molyneaux[1,2], Pauline T. Lukey[4], Richard P. Marshall[4], Elisabetta A. Renzoni[1,2], Athol U. Wells[1,2], and Toby M. Maher[1,2]

[1]National Institute for Health Research Biomedical Research Unit, Royal Brompton Hospital, London, United Kingdom; [2]Fibrosis Research Group, National Heart and Lung Institute, Imperial College London, London, United Kingdom; [3]Bristol Interstitial Lung Disease Service, North Bristol Lung Centre, Southmead Hospital, Westbury-on-Trym, United Kingdom; and [4]Fibrosis and Lung Injury DPU, GlaxoSmithKline R&D, Stevenage, Herts, United Kingdom

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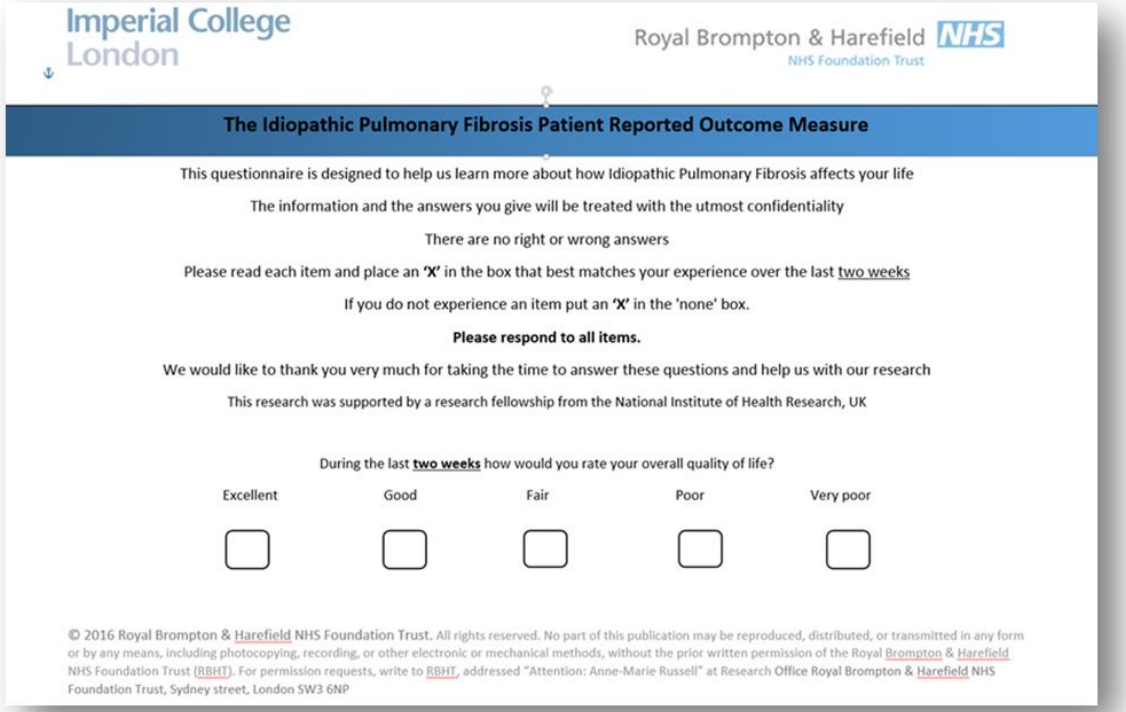
https://youtu.be/IqlkO1KGq90

Validation



Imperial College London

Royal Brompton & Harefield NHS
NHS Foundation Trust

The Idiopathic Pulmonary Fibrosis Patient Reported Outcome Measure

This questionnaire is designed to help us learn more about how Idiopathic Pulmonary Fibrosis affects your life

The information and the answers you give will be treated with the utmost confidentiality

There are no right or wrong answers

Please read each item and place an **'X'** in the box that best matches your experience over the last two weeks

If you do not experience an item put an **'X'** in the 'none' box.

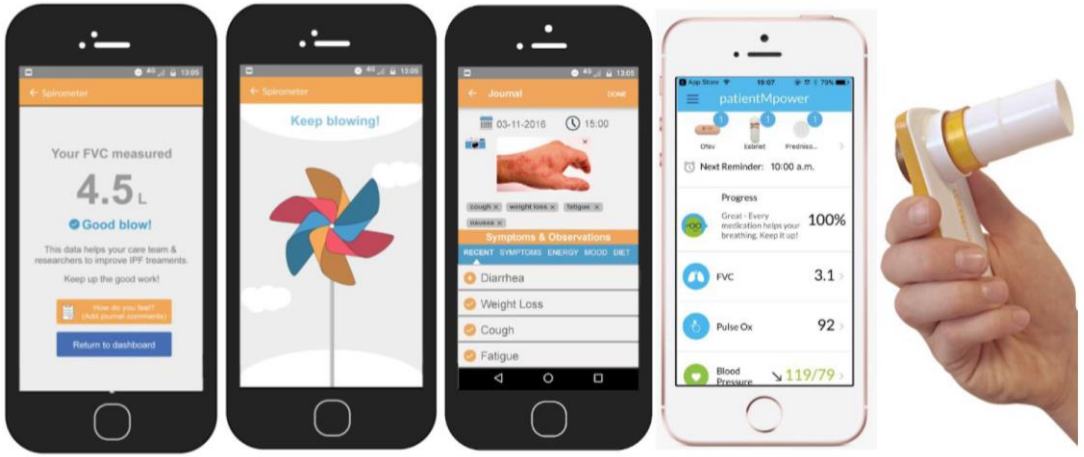
Please respond to all items.

We would like to thank you very much for taking the time to answer these questions and help us with our research

This research was supported by a research fellowship from the National Institute of Health Research, UK

During the last **two weeks** how would you rate your overall quality of life?

Excellent	Good	Fair	Poor	Very poor
☐	☐	☐	☐	☐



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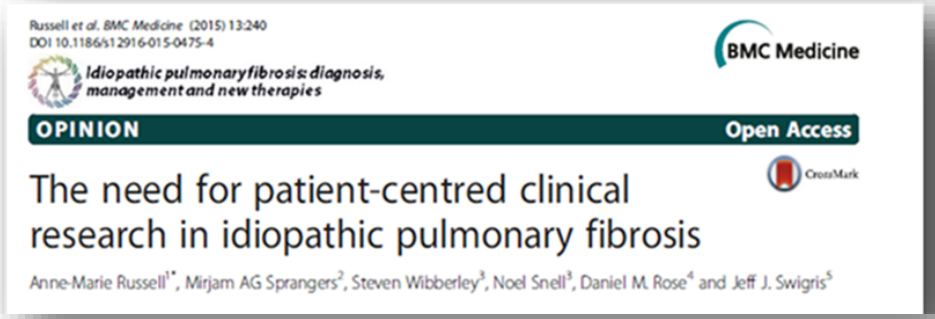
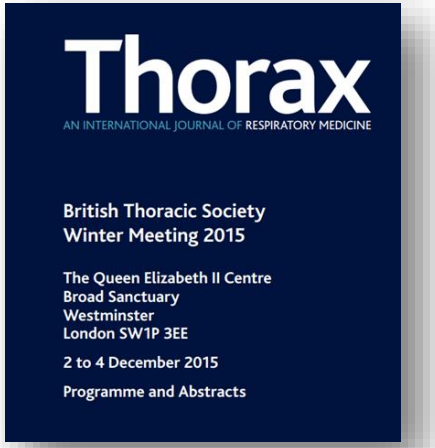
Irish Lung Fibrosis Association
www.ilfa.ie



Research Support Group

Psychological distress in UK patients with IPF; Use of Emotion Thermometers interpreted within a bio-psychosocial constructionist framework

A.-M. Doyle, C.Burdett*, J.Gane*, Z. Aden, A-M. Russell



Patient & carer co-investigators: shared experiences of a research steering group from the IPF-PRoM study

AM Russell, AM Doyle, D Ross*, C Burdett*, J Gane*, S Fleming, Z Aden, P Cullinan

Thank you

2017 ATS Abstract Scholarship