Optimising Outcomes: Patient Centred Research

Anne-Marie Russell

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## Disclosures

| Sponsorship or research funding | • National Institute Heath Research  
| • InterMune / Hoffman La Roche  
| • Pulmonary Fibrosis Trust UK  
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| • Boehringer Ingelheim  
| • Novartis |
| Other relationships | • ILD Interdisciplinary Network  
| • Action for Pulmonary Fibrosis  
| • British Lung Foundation |
- All cause Mortality (ACM)
- Clinician-reported outcome (ClinRO)
- Observer-reported outcome (ObsRO)
- Patient-reported outcome (PRO)
- Performance outcome (PerFO)
What is a Patient Reported Outcome Measure (PROM)?

- Acknowledges the patient is the best source of information about how he or she feels - **expert**
- Reveal information patients might not disclose spontaneously
- A report of the status of a patient’s health condition **directly from the patient** without interpretation of the patient’s response by a clinician
- Quantify a person’s **perception** of things such as health status, symptoms, or quality of life (QOL)

## Definitions of Selected Terms Related to Quality-of-Life

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional status</td>
<td>An individual's effective performance of or ability to perform those roles, tasks, or activities that are valued (e.g. going to work, playing sport, or housework)</td>
</tr>
</tbody>
</table>
| HRQoL        | Personal health status  
HRQoL usually refers to aspects of life dominated or significantly influenced by mental or physical well-being |
| QoL          | An evaluation of all aspects of our lives, including where we live, how we live, & how we play. It encompasses life factors such as family circumstances, finances, housing & job satisfaction |
| Well-being  | Subjective bodily and emotional states; how an individual feels; a state of mind distinct from functioning that pertains to behaviours and activities   |
Drivers: Department Health PRoMs Prog 2009

- DH led programme supported by Health and Social Care Information Centre (HSCIC)
- Pre-operative & post-operative PROMs, questionnaire data under the terms of the Standard NHS Contract for Acute Services:
  - unilateral hip & knee replacements, groin hernia & varicose vein surgeries
  - Expanding to a range of chronic conditions, including diabetes, asthma, stroke, (COPD) and others

Devlin N & Appleby J Getting the most out of proms: Putting health outcomes at the heart of NHS decision-making The King’s Fund 2010
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] Pirfenidone for treating idiopathic pulmonary fibrosis 2013
• NICE technology appraisal guidance [TA379] Idiopathic pulmonary fibrosis – Nintedanib

• Patient Centeredness
• Effectiveness of care from the patient’s own perspective

Patient-centred management in idiopathic pulmonary fibrosis: similar themes in three communication models

Wim A. Wuyts¹, Fedro A. Peccatori² and Anne-Marie Russell³

Eur Respir Rev 2014; 23: 231–238
DOI: 10.1183/09059180.00001614
‘We advocate a pragmatic approach in selecting methodologies best suited to the research problem; mixed methods that employ both quantitative & qualitative designs acknowledging the limitations and complementary nature of both, followed by the involvement of patients in the research process as active investigators, and finally, paying closer attention to the choice of patient-centred outcomes to ensure we are measuring what is important to patients.’

The selection of patient-reported outcomes (PROs) based on familiarity is no longer acceptable.
Clinical Trials

Acknowledgement: Prof Luca Richeldi
Ongoing Clinical Trials

- Galapagos: phase (2) study
- Boehringer.227 efficacy & safety of oral nintedanib Systemic Sclerosis
- Boehringer.229 Drug-drug interaction nintedanib & pirfenidone
- TIPAC: phase 3
- RECITAL: CTD-ILD Rituximab or Cyclophosphamide
- Pirfenidone in the Chronic HP Treatment (Picheon)
- Effect of Pirfenidone on Cough in IPF (Cough-IPF)

https://clinicaltrials.gov
Ley B, Collard HR, King TE Jr et al Clinical course and prediction of survival in idiopathic pulmonary fibrosis. 
Am J Respir Crit Care Med 2011; 183:431–440
Guidance for Industry

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

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

December 2009
Clinical/Medical
Study Objectives and Purpose:

- Develop a psychometrically sound instrument that:
  - Captures the patient perspective
  - Measures symptoms experienced by patients with IPF
  - Concordant with the PROM approval criteria of the European Medicines Agency (EMA) & US FDA

- Identify concepts & descriptors of IPF attributes which are important to patients
- Explore the utility of the Delphi survey method with patients with IPF
- Test the reliability and reproducibility of the IPF-PROM
- Validate the IPF-PROM against measures of FVC, questionnaires & clinical status

IPF PROM Methodology

- Patient Centeredness – Research Steering Group
- 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

Study Configuration: Multi-centre study across Four sites
Developing the Delphi - Qualtrics®

- Domains (n=13) and items (n=329: 45 from Lit Rev / 284 from FG’s)
  - Rate the importance on a Likert scale 1-7 (very important - not at all important)
  - Give comments and suggestions in the blank fields available under each question (subjected to qualitative analysis)
  - Nominate other dimensions and related items to be included

- Pilot round – age matched controls
- Pilot with patients diagnosed with IPF
Delphi Round 1 and 2

- Patients; Care-givers and ILD physicians and nurses

- Patients (n=79) – response rate 93.6%
- Healthcare professional (n=32) – response rate 96.5%
- Care-givers (n=19) – response rate 94.7%
## Analytical Approach of Delphi Data

<table>
<thead>
<tr>
<th>Statement result</th>
<th>Threshold to apply</th>
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</thead>
<tbody>
<tr>
<td><strong>Definitely include</strong></td>
<td>&gt;=70% of participants rate statement as &gt;=6&lt;br&gt;OR Median rating of &gt;=5</td>
</tr>
<tr>
<td><strong>Maybe include</strong></td>
<td>&gt;=70% of participants rate statement as &gt;=5&lt;br&gt;OR Median rating of &gt;=5</td>
</tr>
<tr>
<td><strong>Definitely exclude</strong></td>
<td>&lt;70% of participants rate statement as &lt;=4&lt;br&gt;AND 100% participants understand statement&lt;br&gt;OR Median &lt;=4&lt;br&gt;AND 100% panel understand statement</td>
</tr>
<tr>
<td><strong>Review</strong></td>
<td>&lt;70% of panel rate statement as &gt;=6&lt;br&gt;AND&lt;br&gt;&lt;100% panel understand statement</td>
</tr>
</tbody>
</table>
Results:

- R1: 98 items were retained for R2 and 18 additional items added from analysis of comments.
- R2: Repeating the process 12 items were eliminated after R2. Response rate >93%.
- A greater number of items than anticipated remained resulting in a high a ratio of respondents per item.
- Round two confirmatory for round one.
- How many respondents per item required?
Round 3: UK and Ireland national survey

- 304 respondents diagnosed with IPF: 104 item questionnaire.
- Participants were recruited through IPF charities & support groups.
- An electronic link to the questionnaire was hosted on the charity websites / facebook.
- Self-selecting participants, confirming they had a diagnosis of IPF, anonymously recorded their level of agreement / experience with 104 statements about IPF on 4 point Likert scales.
Delphi Results

- Participants accessing survey n=510;
- Completing survey n=281;
- Completing hard copy n= 20;
- Partially completing survey n=70;
- not able to complete survey as diagnosis not IPF n=41
- 108 participants accessed the survey but did not proceed to the questions.
- Complete responses male n=181 (65%)
- IP addresses were checked to detect duplicate responses

<table>
<thead>
<tr>
<th>Years</th>
<th>N (%)</th>
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<tbody>
<tr>
<td>≤59y</td>
<td>55 (19.5%)</td>
</tr>
<tr>
<td>60-69</td>
<td>109 (39%)</td>
</tr>
<tr>
<td>70-79</td>
<td>93 (33%)</td>
</tr>
<tr>
<td>range ≥ 80y</td>
<td>24 (8.5%).</td>
</tr>
</tbody>
</table>
### Geographical distribution of Respondents

<table>
<thead>
<tr>
<th>Region</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK: South East</td>
<td>78</td>
<td>27.8</td>
</tr>
<tr>
<td>UK: Midlands</td>
<td>61</td>
<td>21.7</td>
</tr>
<tr>
<td>UK: South West</td>
<td>32</td>
<td>11.4</td>
</tr>
<tr>
<td>UK: North West</td>
<td>24</td>
<td>8.5</td>
</tr>
<tr>
<td>UK: North East</td>
<td>20</td>
<td>7.1</td>
</tr>
<tr>
<td>Ireland</td>
<td>14</td>
<td>5.0</td>
</tr>
<tr>
<td>UK: Scotland</td>
<td>14</td>
<td>5.0</td>
</tr>
<tr>
<td>UK: Yorkshire &amp; Humber</td>
<td>13</td>
<td>4.6</td>
</tr>
<tr>
<td>UK: NI; Wales &amp; other</td>
<td>26</td>
<td>9</td>
</tr>
</tbody>
</table>
Discussion:

- Taking a rigorous patient centred approach to item generation and reduction is multifaceted.
- Working with IPF charities is feasible, reliable and an efficient way to gather a large volume of responses across the UK and Ireland in a short period of time (4 months) from patients diagnosed with IPF.
- The journey of each item retained in the final questionnaire can be traced to it’s point of origin in the process.
Work in progress

- Classical: Factor Analysis
- 8 item IPF PRoM
- Test the reliability and reproducibility of the IPF-PROM
- Validation of IPF-PROM against measures of 3 monthly FVC
  - EQ-5D
  - MRC scale
  - SGRQ
  - Clinical status
Use of PRoMs in IPF

- SGRQ not developed specifically for use with patients with IPF
- its psychometric properties are adequate
- it is a useful measure of HRQL in this population
User’s Guide to Implementing Patient-Reported Outcomes Assessment in Clinical Practice

Version: November 11, 2011

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