Patient-Reported Outcomes Validated in Phase 3 Clinical Trials: A Targeted Literature Review

Antonia Morga, DPhil, MSc, Silvia Dibenedetto, PhD, Rocco Addiutori, PhD, Jun Su, MD

Objective:
- Exploration of how patient reported outcome (PRO) instruments may have been validated during phase 3 studies will help inform the design of future clinical trials
- The objectives of this study were to:
  - Identify PRO instruments that were quantitatively validated (content validity and psychometric assessment) in a phase 3 trial setting
  - Provide information on the methodology and outcomes of the validation
  - Review which validated PROs have been accepted in labeling claims using the same phase 3 study and/or based on subsequent trials or evidence

Methods:
- A targeted literature search of the Medline database (via OVID platform, 3 June 2021)
- Quantitative validation of PROs occurring within the context of phase 3 trials can support label claims
- The targeted literature review identified multiple novel PROs validated in phase 3 clinical trials, in addition to pre-existing PRO instruments validated within phase 3 clinical trials, composed of:
  - 20 novel instruments
  - 58 pre-existing instruments

Results:
- 355 references identified overall
- 68 studies selected for in-depth review

CONCLUSIONS
- The targeted literature review identified multiple novel PROs validated in phase 3 clinical trials, in addition to pre-existing PRO instruments validated for new indications and/or populations in phase 3 trial settings
- Quantitative validation of PROs occurring within the context of phase 3 trials can support label claims

DISCUSSION
- The most frequently validated psychometric properties were internal consistency reliability and known-group validity (Figure 2)
- The targeted literature review identified multiple novel PROs validated in phase 3 clinical trials, in addition to pre-existing PRO instruments validated within phase 3 clinical trials, composed of:
  - 20 novel instruments
  - 58 pre-existing instruments

Table 1. Overall frequency of novel PROs

<table>
<thead>
<tr>
<th>New PROs identified</th>
<th>Number of references</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient-reported Clinical Global Impression of Change (PGIC)</td>
<td>2</td>
</tr>
<tr>
<td>Revised Patient Perception of Migraine Questionnaire (PPMQ-R)</td>
<td>1</td>
</tr>
<tr>
<td>Patient Neurotoxicity Questionnaire (PNQ)</td>
<td>1</td>
</tr>
<tr>
<td>Patient-reported Quality of Life (QoL)</td>
<td>1</td>
</tr>
<tr>
<td>Symptom index for advanced renal cell carcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Nighttime Symptoms of COPD Instrument (NiSCI)</td>
<td>1</td>
</tr>
<tr>
<td>Preference and Satisfaction Questionnaire</td>
<td>1</td>
</tr>
<tr>
<td>Living with Pulmonary Hypertension questionnaire (LPH)</td>
<td>1</td>
</tr>
<tr>
<td>Injection Pen Assessment Questionnaire (IPAQ)</td>
<td>1</td>
</tr>
<tr>
<td>Rheumatoid arthritis-specific Work Productivity Survey (WPS-RA)</td>
<td>1</td>
</tr>
<tr>
<td>Hand Disability in Systemic Sclerosis-Digital Ulcers (HDISS-DU R)</td>
<td>1</td>
</tr>
<tr>
<td>Peyronie’s Disease Questionnaire (PDQ)</td>
<td>2</td>
</tr>
</tbody>
</table>

Figure 1. PRISMA flow chart, Medline search

Figure 2. Frequency of psychometric properties assessed

Poster presented at ISPOR 2022 Conference, 15-18 May 2022; Washington DC, USA Area and Virtual

References
1. PRO-LABELS: Database on Clinical Outcome Assessment (COA) endpoint strategies used to demonstrate efficacy and safety of drugs or devices in the clinical development process. Available at http://www.pro-labels.org (accessed 31 Aug 2022).
2. Data on study design, therapeutic indication and psychometric assessment results extracted from 21 studies for all the 58 pre-existing PROs validated within phase 3 clinical trials, composed of:
   - 20 novel instruments
   - 58 pre-existing instruments

**Abstract number:** 114877

**No information on the validation (n=1):**
- PEP
- PDQ
- OMDQ
- WPS-PS
- WPS-RA

**No information on the validation (n=2):**
- PEPLA
- PRO with a labeling claim (n=5)
- PRO with a labeling claim (n=15)
- No information on the validation (n=2)