Patient Reported Outcomes (PROs) Tools for Measurement of Health Related Quality of Life

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Overview

- What are PROs?
- Why PROs are Important?
- Some Challenges to PROs
- Best Practices for Creating PROs
- PRO Conceptual Models and Frameworks
Patient Outcomes Assessment

Sources and Examples

- Investigator-Reported
  - For example:
    - Global impression
    - Observation (e.g., physical exam findings)
    - Tests of function

- Physiological
  - For example:
    - Tests (FEV1)
    - Labs (HbA1c)
    - Vital Signs (BP)
    - Tumor size

- Caregiver-Reported
  - For example:
    - HRQL
    - Burden
    - Functional status

- Patient-Reported
  - For example:
    - HRQL
    - Symptoms
    - Global impression
    - Satisfaction with treatment
    - Treatment adherence
What are Patient-Reported Outcomes (PROs)?

- A patient-reported outcome (PRO) is the measurement of any aspect of a patient’s health status that comes directly from the patient (i.e., without the interpretation of the patient’s responses by a physician or anyone else).
What are Patient-Reported Outcomes (PROs)?

• Administration of PROs may be via paper and pencil forms, digital capture (internet, handheld device), or interviewer-administered questionnaires.

• The most commonly used PRO questionnaires assess one of the following:
  • Symptoms (impairments)
  • Functioning (disability)
  • Wellness (health)
  • Health-related quality of life (HRQL)

• **Generic** questionnaires are designed to be used in any population and are meant to cover a broad aspect of the concept being measured (e.g. SF-36, PROMIS Global Health).

• **Targeted**, or disease-specific questionnaires are designed to assess those concerns of most importance for a given population.
Why PROs are Important?

- Unique perspective on treatment effectiveness.
  - Physiological assessments often do not reflect how a patient functions or feels (e.g., FEV1)

- May be more reliable than informal interview

- Some treatment effects are known only to the patient
  - patient’s symptoms (e.g., fatigue, depression)
  - how well the patient feels
  - how well the patient functions
  - how the patient perceives care/treatment
PROs are Important Endpoints

• PROs are used in clinical trials to
  – Describe patients & disease severity
  – Trial eligibility
  – Treatment effects
  – Converge with other outcomes
  – Risk/Benefit Evaluation
Some Challenges for PROs

• Development Limitations
• Unreliable/Unresponsive
• Poor validity
• Sensitivity/Specificity
• Meaningfulness of Scores
• Single vs. Multiple Item?
• Best recall period?
• Response options?
• Mode of administration?
Best Practices for Creating PROs
Consulting the Literature

• Before you set out to develop a new tool, first check what’s available

• If nothing exists or what’s available could be improved upon,

  – Conduct a thorough review of the literature to identify signs, symptoms issues related to your area of interest, including available PRO measures
Consulting Experts

• Open-ended survey or interview to known experts in a particular area to inquire about:
  
  – PROs typically used and why
  – Most important and frequent symptoms, impact on HRQL due to the condition
  – Issues that are most challenging for patients based on experts’ clinical experience

• Rate/rank existing PRO items for relevance, clarity, ease of understanding, etc.
Consulting Target Audience (e.g., Patients)

• Focus Groups

  – Well-established exploratory qualitative research approach to elicit and direct discussion on topics related to one’s experience with a given phenomenon.

  – Draw upon the collective experience, wisdom and group dynamics of individual members coming together around a common goal.

  – Efficient and economical approach that can yield rich data and serve as a starting point for more in-depth follow up work.
Consulting Target Audience (e.g., Patients)

• **Individual Interviews**
  
  – Allow for greater and more in depth exploration of concepts and issues.
  
  – Afford an opportunity to probe and explore sensitive topics that may have been moderated or withheld in focus groups because of the social influences or stigma.
  
  – Corroborate previous exploratory findings from other sources.
Identifying Core Concepts

Triangulation of
Data Sources

Literature, Experts, Focus Groups, Interviews, Surveys

Meaningful, Measurable Concepts
Identification of Core Concepts

• Examine data sources systematically
  – Theoretically-based qualitative analysis approach
  – Constantly comparing with one another
  – Multi-level Coding & Theme creation

• Inter-rater agreement

• Data saturation

• Begin to organize concepts & identify which ones are of interest to be measured
Conceptual Model

- Theoretical representation, which defines the concepts of interest, their interfaces and possible determinants.

- Visual representation of the complex interrelationships among variables and can assist in the selection of target endpoints.

- Generally the basis for a new patient reported outcome measure.
Modified Wilson & Cleary HRQL Model for Dyspnea and Functional Limitations


3 Elements of an Item

1. **Context**
   
2. **Stem**
   
3. **Response**

Please indicate how true each statement has been for you during the past 7 days.

I have nausea.

0  Not at all
1  A little bit
2  Somewhat
3  Quite a bit
4  Very much
Item Writing Guidelines:
Context is Relevant to Concept

• Choose an item context that is relevant to the concept being measured (e.g., past 24 hours, past 7 days, past 2 weeks, past month)

• This can be identified from the literature and/or explored during focus groups or individual interviews
Item Writing Guidelines:

**Use Simple, Universal Language**

- Write clear, unambiguous items
- Use language that is simple and appropriate for the target population
- Avoid colloquialisms and activities that might not be familiar across different age groups, ethnicities, cultures etc.
Item Writing Guidelines:

Make Items Specific

• Ask about specific versus general
  – I enjoy sports.
  – I enjoy watching college football.

• Avoid double-barreled questions
  – Do you approve or disapprove of abortion in cases of incest or threats to the mother’s health?
Item Writing Guidelines:

Pay Attention to Phrasing

• Avoid negatively phrased items
• Write items that require little cognitive processing.
• Try to keep grammar to simple past or present tense

– I don’t have symptoms of nausea (Strongly Disagree, Slightly Disagree, Disagree, etc.)

– I have symptoms of nausea
Item Writing Guidelines:

Key Response Options to Type of Item

- **Opinions**
  - Very important → Not at all important
  - Strongly agree → Strongly disagree

- **Knowledge**
  - True/false
  - Very familiar → Not at all familiar

- **Frequency of Events or Behaviors**
  - Times per day, per week, per month etc.
  - Always/sometimes/never

- **Ratings**
  - Excellent → poor
  - Better/worse/about the same
Expert Item Review I

• Expert Review
  – Review items and rate each candidate item according to relevance and prevalence.
  – Items deemed as irrelevant or low-relevant set aside for further review.
  – Document all decisions on item exclusion, inclusion, or revision to provide an historical account of all items.
Patient Item Review I

– Purpose of Cognitive Interviews
  • To ensure that item content, response scales and instructions are understood as intended
    – Comprehension of the question
    – Processes used to retrieve relevant information from memory
    – Decision processes, such as motivation and social desirability
    – Response processes

– Conduct of Cognitive Interviews
  • Paraphrase the item in their own words
  • Define terminology used in the items
  • Describe any lack of clarity or confusion about the appropriateness of their answer
  • Describe how confident they are about their ability to provide an accurate answer to the item
  • Describe how they arrived at their answer to items that request a numerical or rating response.
Item Changes & Modifications

• Team members review items and modify as needed
Expert & Patient Item Review II

- Second review by experts and patients of modified items
Conceptual Framework

– Illustrates the anticipated associations between the items within a PRO tool and their respective domains.

– Clearly identifies the concepts important to patients and how they should be measured and represents the goals of treatment as “concepts” important in a specific disease and treatment context with a clear description of treatment benefit.
PRO Conceptual Framework Example

Hormone Refractory Prostate Cancer

- Symptoms of Disease
  - U1: Specific symptoms of disease
  - U2
  - U3
  - U4

- Side Effects of Primary Treatment
  - U5
  - U6
  - U7
  - U8

- Quality of Life
  - U9
  - U10
  - U11
  - U12

- U13: Symptoms of disease & side effects of treatment
- U14: Side effects of treatment (e.g., toxicities)
- U15: General aspects of quality of life & well-being

In Sum

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Thank you