Patient reported outcomes in health care sector: A brief review

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Abstract
Nowadays in the healthcare sector the concept of patient reported outcomes is emerging significantly. The following article covers almost all the relevant areas related to the PROs including PRO instruments, selection criteria of PRO instruments, ideal properties of pro instrument, development of PRO instrument, administration of PRO instrument and data collection, ways to present PRO results and barriers to patient-reported outcomes measurement. This is useful for the healthcare industry including physicians, policy makers, pharmacist, healthcare providers and patients for the improvement, enhancement and assessment of the therapy or the treatment

Keywords: patient reported outcomes, PRO instruments

1. Introduction
The outcomes from any clinical intervention obtained by the patient i.e. patient-reported outcomes (PROs) are seemed to be of more importance in future than any other outcomes like physiological, clinical or caregiver-reported etc [1]. PROs can be used at group level in research and quality improvement and at individual patient level to support clinical decision-making and ensure optimal efficient use of resources [2].

Patient-Reported Outcomes (PRO) is known as the status of individual patient’s health status which is directly obtained from the patients without elucidation of the patient’s response by physicians or any other healthcare professionals [3]. PRO instrument can be used to measure the impact of an intervention on one or more aspects of patients’ health status, hereafter referred to as PRO concepts, which are ranging from the symptomatic (response of a headache) to more complex concepts (e.g., ability to carry out activities of daily living), to extremely complex concepts such as quality of life, which is widely understood to be a multi-domain concept with psychological, social and physical components. Data obtained from a PRO instrument can provide evidence of a treatment benefit from the patient perspective [4, 5].

Patient-reported outcomes (PROs) play important role within the healthcare system to gain information related to patient’s views on the outcome of a treatment. The goal of health services is to increase health gain for patients in terms of both healthcare professional assessments of the presence, and severity, of a disease, and patient self-assessments of health. Therefore, outcomes within health services need to include both these dimensions; that is, clinical observations, laboratory measures and other examinations need to be combined with patients’ own assessments of their perceived physical, mental and social well-being and functional ability [6].

PROs consist two terms (patient-reported and outcome) which mean any report coming directly from patients, without interpretation by physicians or others, about how they feel with respect to a health condition and its therapy. Absolute terms (e.g., severity of a symptom, sign, or state of a disease) or as a change from a previous measure are used to measure the outcomes.

In addition “PRO” usually refer to the things being measured i.e. domains and concepts (discrete concepts within a multi-domain concept), the instrument used to measure the concepts (e.g. diaries, interview, questionnaires etc.) and the actual end points (i.e., the outcomes as analyzed in a particular clinical trial).

Moreover PROs are “a useful terminology as an organizing tool for the many concepts and applications of self-reports in treatment evaluations and population surveys” [7]. The patient-reported outcomes (PROs)—also known as patient-generated health data (PGHD). According
to National Quality Forum (NOF) PROs are “any report of the status of a patient’s health condition that comes directly from the patient, without interpretation of the patient’s response by a clinician or anyone else.” PRO tools are used for the assessment of patient-reported health data for mental, physical, social well-being. PGHD includes, but are not limited to treatment history, biometric data, symptoms, health history and lifestyle choices. Besides it, Patient-reported outcomes (PROs) play an important role in assessing the treatment benefit of new medical products. It is observed that PRO measures must be used when assessing concepts best known by the patient or best measured from the patient’s perspective. As a result, there is growing emphasis on well defined and reliable PRO measures. Moreover advancement of technology have significantly increased electronic PRO (ePRO) data collection capabilities. The flow from paper based towards ePRO data capture has enhanced the accuracy and integrity of clinical trial data [8].

In addition, patient reported outcomes (PROs) are the calculated scores based on validated and standardized survey tools, using data collected through patient questionnaires. The obtained numeric scores are graphed which give care providers a quick overview of a patient’s current condition and comparison with previous results. Data generated from PROs can be compared to normative values to monitor exceptions or alarming deviations from expected results. This data can be used by care providers to monitor and change the patient’s treatment plan or to aggregate the data at population level to research care plan effectiveness and identify new best practices [9].

Functional characteristics of PROs [9]
- Patient responses are collected on the basis of standardized or custom online questionnaires
- Responses obtained from PROs can be associated with metric values
- For standardized scoring calculations, response metrics are used as input
- Scoring is graphed and compared against prior results and/or normative data

Nowadays PROs are gaining the importance in clinical world as survival is not the ultimate goal of the treatment but quality of life also plays an essential role in the treatment. Types of PROs currently used in medical research
- QoL (Quality Of Life)
- HRQL (Health Related Quality Of Life)
- Symptoms (Impairment)
- Utility
- Patient Satisfaction
- Activity limitations (Disability)

2. Pro Instruments
A PRO instrument (i.e., a questionnaire plus the information and documentation that support its use) is a means to capture PRO data used to measure treatment benefit or risk in medical product clinical trials [4]. PRO instruments are the means to gather the data obtained from PRO and to measure treatment benefits by capturing concepts related to how a patient feels or functions with respect to his or her health or condition. PRO instruments measure concepts like the state of discrete signs or symptoms (e.g., pain severity or seizure frequency) and the overall state of a condition (e.g. heart failure, depression, angina, asthma or rheumatoid arthritis).

2.1 Type of PRO instruments [10];
- Disease-specific
- Site or region-specific
- Dimension-specific
- Generic Summary items
- Individualized
- Utility measures
- Disease-Specific:
  Disease-specific instruments have been developed to measure the patient's perceptions of a specific disease or health problem. Nowadays multiple instruments are available for common health problems. Example: Diabetes Self Management Questionnaire
- Site-specific:
  Site-specific instruments have been designed to assess health problems in a more specific part of the body. Example: The Oxford Hip Score, the Shoulder Disability Questionnaire
- Dimension-specific:
  Dimension-specific instruments are the type of PRO instrument designed to assess one particular aspect of health status (Physical function, Symptoms, Global judgments of health, Psychological well-being, Social well-being, Cognitive functioning, Satisfaction with care, etc.). Example: Beck Depression Inventory, McGill Pain Questionnaire
- Generic:
  Generic instruments are designed to measure broad aspects of health, therefore potentially suitable for a wide range of patients and the general population. Example: SF-36, FLP
- Summary items:
  In summary items respondents are asked to summarize diverse aspects of their health status using a single item or a very small number of items. Example: General Household Survey
- Individualized
  Individualized instrument are developed for respondents to select the content of items and/or rate the importance of individual items. In this type of instrument respondents are asked to list most important areas of their lives affected by a disease or health problem and then to rate how badly affected they are in each area, and in the rest of their lives. Example: MACTAR, SEIQoL
- Utility measures:
  Utility measures include values or preferences attached to individual health states and express health states as a single index. This type of instrument produces evidence for the overall value of health states and can be used in cost-utility analysis. Example: EuroQoL EQ-5D, Health Utility Index (HUI)

3. Selection criteria of instruments
Instruments are selected on the basis of following parameters:
- Appropriateness
- Acceptability
- Feasibility
• Interpretabilitability
• Precision
• Reliability
• Validity
• Responsiveness

• Appropriateness
It is a property which represents that how much the content of any instrument is appropriate to the particular application. To give general recommendations that makes an instrument appropriate for a given application is a difficult task because this ultimately depends on the users' specific questions and the content of instruments.

• Acceptability
Acceptability is the property which show the extent to which an instrument is acceptable to patients. Parameters for acceptability include response rates, administration time and levels of missing data [11]. There are many factors that can influence acceptability including the questionnaire design, mode of administration and the health status of respondents. The format of patient-reported instruments can also influence acceptability. In addition general features of appearance, layout and legibility are thought to be important influences on acceptability. The instrument must be presented in a language which is familiar to respondents this makes the instrument more acceptable. To ensure a high standard of translation few guidelines are available [12, 13].

• Interpretabilitability
Interpretabilitability is the property which concerns about the meaningfulness of scores generated by an instrument. The lack of familiarity in the use of instruments may be a hindrance to interpretation. For interpretation three approaches have been proposed. First, change in scores of instrument have been compared with the previously documented change in scores produced by the same instrument for major life events such as loss of a job [14]. Secondly, the minimal clinically important difference (MCID), which is equal to the smallest change in scores of instrument that is perceived as beneficial by patients [15, 16]. Thirdly, normative data from the general population can also be used to interpret scores from generic instruments [17, 18].

• Precision
Precision is one of the important parameters which concerns about the accuracy and number of distinctions made by an instrument. For the issue of precision there are a number of aspects, which relate to methods of scaling and scoring items, and the distribution of items over the range of the construct being measured. One of the important implications for precision is scaling of items within instruments. Item Response Theory (IRT) help in determining the precision of an instrument. As per the IRT the measurement construct such as physical disability, can be represented by a hierarchy that ranges from the minimum to maximum level of disability [19]. IRT represents that a number of instruments have items concentrated around the middle of the hierarchy with relatively fewer items positioned at the ends [20, 21]. Furthermore the scores produced by such instruments represent the function of the health status of patients and also show the imprecision of measurement.

• Reliability
Reliability is the property which concerns about whether an instrument is internally reproducible or consistent or/and it assesses the extent to which an instrument is free from measurement error. Reproducibility determines whether an instrument produces the same results on repeated administrations when respondents have not changed. This is determined by test-retest reliability. By correlating instrument scores for the two administrations, the reliability coefficient can be calculated. Reliability estimates of 0.7 and 0.9 are usually recommended for the instruments that are to be used in groups and individual patients respectively [8]. In addition reliability is not a fixed property and must be assessed in relation to the specific population and context [22].

• Validity
Validity is the property which concern about the extent to which an instrument measures what is intended. Validity can be assessed qualitatively as well as quantitatively through an examination of instrument content and through factor analysis respectively. Face validity and content validity determine whether items adequately address the domain of interest. Face validity is concerned about whether an instrument appears to be measuring the domain of interest. Content validity assess whether instrument content adequately covers the domain of interest.

• Responsiveness
Responsiveness is that property which concerned about the measurement of important changes in health and is therefore relevant when instruments are to be used in an evaluative context for the measurement of health outcomes. Moreover estimates of responsiveness are related to applications within specific populations and are not an inherent or fixed property of an instrument. Responsiveness is determined by examining changes in instrument scores for groups of patients whose health is known to have changed. Besides it a number of statistical techniques are used for quantifying responsiveness.

4. Ideal Properties of pro instrument [23]
• PRO instrument should be specific to the concept being measured.
• PRO instrument should have conceptual equivalence.
• PRO instrument should be based on the conceptual framework.
• PRO instrument should be based on end-point model.
• PRO instrument should have optimum number of items.
• PRO instrument should have proper evidences for the conceptual framework.
• PRO instrument should maintain the confidentiality of the subject (patient).
• PRO instrument should be reproducible.
• PRO instrument should have specific and easy measurement properties.

5. Development of pro instrument
According to the US FDA Guidance on PRO measurement, five steps of PRO development are as follows [24]:
1. Hypothesize Conceptual Framework
2. Adjust Conceptual Framework And Draft Instrument
3. Confirm Conceptual Framework And Assess Other Measurement Properties
4. Collect, Analyze And Interpret Data
5. Modify Instrument

1. Hypothesize conceptual framework
This is the first step for the development of PRO instrument. This step include outlining of hypothesized concepts and potential claims, determination of intended population and application i.e. mode and frequency of administration, scores, performance of expert/literature review, development of the framework, assignment of PROs in preliminary endpoint model and documentation of the preliminary instrument.

2. Adjust conceptual framework and draft instrument
In the second step, finding of the patient inputs, assortment of recall period, response options, making of new items and format, selection of mode of administration and data collection, conduction of patient cognitive discussion, pilot testing of the outlined instrument and documentation of content validity are included.

3. Confirm conceptual framework and assess other measurement properties
This step may include the following-confirmation, assessment and finalization of the instrument documentation of the measurement progress and the assessment of measurement properties.

4. Collect, analyze and interpret data
Fourth step may contain- preparation of SAP (statistical analysis plan) and protocol, compilation and analysis of data, assessment of treatment response (by means of responder definition and cumulative distribution), documentation of interpretation of treatment advantage (in relation to claim).

5. Modify instrument
Last step in the development of the instrument is modification of instrument which include- phrasing and altering of items, population response options and mode of administration, translation and culturally adaptation of the instrument, evaluation and documentation of the changes.

6. Administration of pro instrument and data collection
Number of options for mode of administration and mode of data capture are mentioned below [25].

A. Self-Administered: In Clinic
For this mode of administration resources needed are personnel to supervise and assist, where necessary and administrative personnel for data entry. This is relatively more economical than other modes and also requires less technology. It is difficult to administer this mode in patient with low literacy and with visual handicap.

B. Interview administered: In-clinic
Skilled interviewer and an administrative personnel for data entry are required for this mode. This mode circumvents literacy problem and/or visual handicap. This method is relatively expensive and may create problems with social desirability.

C. Computer-assisted: In-clinic (including portable devices)
In this mode of administration a software is required to collect and report the PRO data. In this efficient data capture with simultaneous data entry is possible.

D. Telephone administration: live interview
Skilled interviewer is required for this mode. This way of collecting data is more convenient to the patient and more personal also.

7. Ways to present pro results: [25]
There are various ways to present the PRO score results, mentioned below:
- Numeric Presentation
- Graphical Presentation
- Presentation Of Trends Over Time

8. Barriers to patient-reported outcomes measurement [5]
There are following barriers in PROM:-
- Vulnerable Populations
- Literacy
- Language And Cultural Differences
- Differences In Functional Abilities
- Response Shift
- Use Of Different Methods And Modes Of Administration
- The Impact Of Non-Responders To Items And Questionnaires

References


