Patient-reported outcomes (PROs) assessment

Introduction

Measures of clinical effectiveness typically reflect outcomes that are important to patients, such as symptoms, morbidity, or mortality.

Sometimes, outcomes – such as a heart attack, a malignant growth (cancer), or death – can be identified and measured using a clinical definition by someone other than the patient. However, there is increasing awareness that treatments should not just be clinically effective and economically efficient, but should also be acceptable and indeed desirable to patients. Clinical effectiveness measures cannot tell us how a patient feels or functions, or what they want to achieve from a treatment. Measuring this element of acceptability requires patient-based evidence that includes measures of well-being.

To this end, an increasing focus has been placed on the development of patient-reported outcomes (PROs), which are based on a patient's perception of a disease and its treatment (adapted from the European Medicines Agency (EMA)'s definition). Patient-reported outcome measures (PROMs) are the tools used to measure and collect data on PROs.

Why are patient-reported outcomes important?

Patient-reported outcomes are important because they provide a patient perspective on a disease/treatment that might not be captured by a clinical measurement but may be as important to the patient (and their adherence to the treatment) as a

clinical measurement. For example, imagine a scenario in which a patient is diagnosed with chronic obstructive pulmonary disease (COPD). A quick look for a review of clinical studies for treatments of COPD reveals the following finding:

Tiotropium reduced the number of participants experiencing one or more exacerbations compared with [long-acting beta agonists] (odds ratio (OR) 0.86; 95% confidence interval (CI) 0.79 to 0.93)… There was no statistically significant difference in forced expiratory volume in one second (FEV(1)) or symptom score between tiotropium and LABA-treated participants.

What do these findings say about how the patient felt about the new treatment? What about how they were able to perform their daily activities? Further understanding about what these outcomes mean for the patient is needed. For example:

- Is an exacerbation something that leads to hospitalisation? Or is it a coughing spell that can take place at home?
- Is the laboratory test FEV(1) something that directly affects how patients function?
- Does the symptom score capture how the patient felt or is it an 'objective' measure of symptoms?

Unlike standard clinical outcomes, PROs give us unique insights into how a therapy can affect a patient. Individuals with the exact same health status, diagnosis, or disease may have different perceptions about how they feel and function, as their ability to cope with limitations and disability and other factors can alter perception about satisfaction with life. PRO measures are important as they can lead to a medical science that is more focused on real benefits achievable for the patients.

The ability to measure well-being as an outcome becomes especially important in clinical situations where the primary

goal of treatment is patient well-being rather than prolonging life or reducing disease events. For example, patients diagnosed with a chronic disease that is not immediately life-threatening may be most concerned with their emotional state and their ability to live a full life. A patient with a terminal illness may be more concerned with their level of comfort, their ability to live longer, and the impact of their illness on loved ones.

What outcomes are important? How are they measured?

PROs must be carefully defined so that they capture information that is important to patients. This information must also be measured accurately and – as much as possible – in a way that makes it comparable with other measurements. Poor development of concepts will result in the measurement of outcomes that are not important to patients (however accurately measured), while poor measurement methods will identify an outcome that is important to patients, but which is difficult to interpret.

This means that how a question is formulated is very important – vague questions may provide vague information that is not useful. For instance, a patient may be asked, 'How are you feeling on a scale of 1 to 10?' (1 being poorly and 10 being extremely well). This is very imprecise. More specific questions relating to emotional wellbeing influenced by mobility, breathing, etc., will provide more detailed and specific information. Deciding precisely what to measure and how detailed the question formulation must be is therefore critical.

In PROs, a 'concept' is the object of measurement, such as:

- a symptom or group of symptoms
- effects on a particular function or group of functions,

or

- a group of symptoms or functions shown to measure the severity of a health condition.

Once the ‘concept’ is agreed, patients are asked questions relating to it. These questions are known as ‘items’. Items are asked in order to understand the change in the concept.

For example, investigators researching the response of patients with COPD to a therapy may recognise that these patients may find performing tasks more difficult in the morning. The concept that they decide to measure is the burden and extent of morning symptoms and the ability of patients to perform activities at that time of day. The items to capture this concept may be questions such as:

- Did you wash yourself this morning other than your face, i.e. body wash, shower, bathe?
- Did you get dressed this morning?
- Did you walk around your home early this morning after taking your medicine?

The optional answers that patients are given to these questions may include a range of responses, such as:

- Yes, I did it myself
- Yes, but I needed help
- No, I was unable to
- No, I did not for other reasons

Patients may also be given an option to respond to a follow up question, such as ‘How difficult was it for you to perform this task?’

In some cases, caregivers or doctors have developed the concept attached to a disease and patient group. However, the need for patients themselves to help identify and develop concepts has become increasingly recognised.

Major concepts measured in PROs

- **Health-related Quality of Life (HRQoL)**
  HRQoL is multi-dimensional; it represents the patient's evaluation of a health condition, and its treatment, on their daily life, including: physical function, psychological function, social function, role function, emotional function, well-being, vitality, health status, etc.
- **Patient satisfaction**
  Evaluation of treatments, patient's preference, healthcare delivery systems and professionals, patient education programs, and medical devices.
- **Physical functioning**
  Physical limitations and activity restrictions, including: self-care, walking, mobility, sleep, sex, disability.
- **Psychological state**
  Positive or negative affect and cognitive functioning, including: anger, alertness, self-esteem, sense of well-being, distress, coping.
- **Signs and symptoms**
  Reports of physical and psychological symptoms or sensations not directly observable, including: energy and fatigue, nausea, irritability.
- **Social functioning**
  Limitations in work or school, participation in community.
- **Treatment adherence**
  Reports or observations of actual use of treatments.
- **Utility**
  Utility, or usefulness, is the (perceived) ability of something to satisfy needs or wants. In health economics, utilities measure the strength of patient preferences. For example, how important various factors are to patients, such as symptoms, pain, and psychological health. The impact of new treatments on

those factors, and therefore on quality of life (QoL), can then be calculated. This is a common approach used by health technology assessment (HTA) bodies, which advise on whether treatments should be funded by (for example) government health departments.[1]

How to measure and interpret?

Measurement methodology is very important in PRO research. Once the concept and the items are identified and set out, careful decisions also need to be made about:

- how the questions are delivered to patients,
- when the questions are delivered to patients,
- how answers are recorded, **and**
- how the data is interpreted.

Typically, PROs are measured with questionnaires or surveys that are either:

- completed by the patients themselves,
- completed by the patient in the presence of the researcher, **or**
- completed by the researcher through face-to-face interview or by telephone interview.

There are strengths and weaknesses to the different approaches to collecting information. For example, while the use of trained interviewers reduces errors and ensures surveys are completed, trial/treatment resources may not allow for this.

It is crucial that approaches and methods used address patients' perceptions and the actual concepts being measured rather than focusing on the interviewer and on the way questions are asked. In the example of COPD given in the section above, morning symptoms can more reliably be ascertained if the questionnaire is administered in the morning than if the questionnaire is completed later in the

day.

The researchers who develop these tools/instruments must make every attempt to ensure that they are measuring concepts important to patients in a way that is repeatable and understandable. Table 1 below provides an overview of important aspects to be considered in PROMs.

Aspects to be considered in PROMs.

Property	Description
Reliability	Measurements are repeatable and consistent, and must distinguish between changes in response and changes due to errors in administration
Validity	
Face validity	Measures what it is intended to measure
Criterion validity	Measurements of aspects that are actually important to patients
Content validity	The extent to which an instrument covers all key dimensions of relevance
Construct Validity	Measurements reflect what is happening in reality
Responsiveness	Change in measures in response to change in HRQoL
Practicality	Measurements are easily obtained, and the instrument is easy to administer.
Interpretability	Significance of measurements are understood by clinicians or researchers rather than patients and others

Patient-reported outcomes, Health Technology Assessment, and patient

involvement

Many health technology assessment (HTA) bodies rely on the synthesis of evidence to make recommendations regarding access to new therapies. HTA relies largely on **quantitative** research from clinical data and patient experience, as provided by PROMs.

Clearly, an important part of patient involvement in the use of PROs should occur during the stages of clinical development. However, once a submission is already made for a marketing authorisation, it can be too challenging for this kind of involvement.

Many PROMs have not been developed with the extensive participation of patients.[2]

This means that PROMs are not necessarily measuring concepts important to patients. There are a number of things patient groups can do to address this gap, before, during, and after PROM development:

- **Evaluating and reviewing PROMs** – Patients and patient groups can learn to appraise the quality of PROMs. They can then use the information they gain to inform similar patient groups about what scales are and are not relevant. This may be particularly important for patients consenting to participation in clinical trials.
- **Identifying the need for PROMs** – There are some initiatives that are engaging with patients who identify the need for PROMs. This is of particular importance to companies, who must identify measures very early in medicines development. The FDA has also taken some leadership in this area (for more information, see https://www.fda.gov/patients)
- **Developing and evaluating conceptual and/or theoretical frameworks** – Validating these tools requires qualitative

research with patients. Although patients have been consulted in the past, there is an identified need for collaboration with patients and giving them more influence in the development of PROMs.

- **Providing concepts through PRO awareness** – When patients describe experiences about what having a disease is like, they indirectly identify concepts of health that are most important to them. HTA bodies often try to find PROMs that capture these concepts. Some awareness of which PROs already exist might help patients to better describe experiences and concepts to HTA bodies to ensure PROs are captured.
- **Endorsing PROMs** – Patient groups that have reviewed PROMs may also consider endorsing them as part of patient input processes to HTA.
- **Highlighting needs** – Patients may also want to flag PROMs that were not validated with patient involvement or concepts that require development of a PRO.
- **Reviewing HTA outputs –** Many HTA decisions consider economic evidence that is based on measurements of health-related quality of life (HRQoL). HRQoL measures should make sense to patients, as these measures may make the difference between positive and negative listing decisions.

Further Resources

- Food and Drug Association (2009). *Guidance for industry. Patient-reported outcome measures: Use in medicinal product development to support labelling claims.* Retrieved 6 January, 2016, from http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm193282.pdf

References

1. PROQOLID (2015). ‘Free access level: Concept of interest’. Retrieved 4 July 2021, from https://web.archive.org/web/20160215162922/http://www.proqolid.org/about_proqolid
2. Staniszewska, S., Haywood, K.L., Brett, J., Tutton, L. (2012). ‘Patient and public involvement in patient-reported outcome measures: Evolution not revolution’. *The Patient*, 5(2), 79-87.

Articles

- Presentation: Patient-Reported Outcomes (PROs) Assessment

  Size: 408,285 bytes, Format: .pptx

  A presentation describing the Patient-Reported Outcomes (PROs) Assessment process, which can be adapted for own use.

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