Patient Reported Outcomes

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An overview

SEEd

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Summary

Introduction to Patient Reported Outcomes

DEFINITIONS

Patient Reported Outcome (PRO) is an umbrella term that has become widely accepted to refer to «a measurement based on a report that comes directly from the patient (i.e. study subject) about the status of a patient's health condition without amendment or interpretation of the patient's response by a clinician or anyone else» [FDA, 2009]. Similarly, the European Medicines Agency (EMA) defines a PRO as «any outcome evaluated directly by the patient himself and based on patient's perception of a disease and its treatment(s)» [EMA, 2005]. A PRO is interchangeably referred to as a PROM (Patient Reported Outcome Measure) by some agencies (e.g. UK National Health Service, NHS). Throughout this booklet the term PRO shall be adopted.

A PRO instrument includes the standardized format for data collection, as well as all the information and documentation that

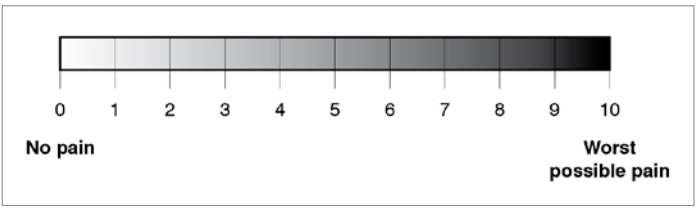

Figure 1. *Example pain Numerical Rating Scale (NRS)*

support the use of the standardized form. The standardized format could be self-report onto paper, electronic (e.g. online, tablet, mobile phone) or telephone Interactive Voice Response System (IVRS), or it could be by interview provided that the interviewer records only the patient's response without interpretation.

A PRO instrument can comprise a single question (item), such as a pain Numerical Rating Scale (NRS) shown in Figure 1. Or a PRO can have many items that are group together to form a total score and/or domain scores. For example, the EORTC QLQ-C30, a measure of Health-Related Quality of Life (HRQL) used widely in oncology comprises 30 items which are grouped together into 15 domains covering symptoms commonly reported in oncology such as pain and fatigue, as well as areas of functioning important to cancer patients such as physical function and social function.

PROs should be used to measure a *concept* that is relevant and experienced by a patient. The concept might be symptoms experienced by the patient, such as pain or fatigue. Symptoms are considered to be concepts that are proximal to the patient experience (Figure 2). The concept might be more distal to the patient experience, such as the impact of a symptom on an aspect of the

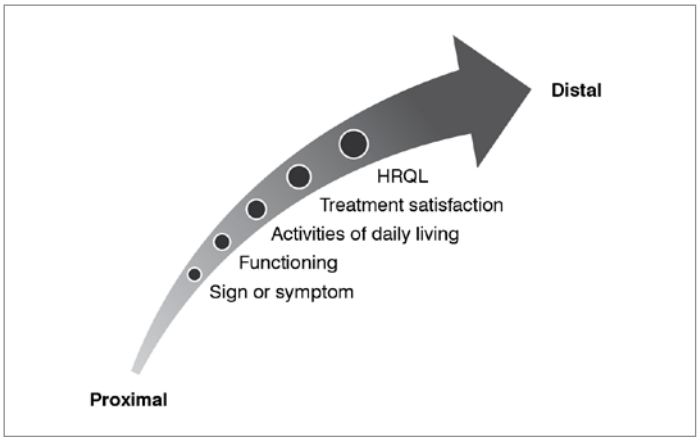

Figure 2. *Distal and proximal concept measurement using PROs*

patient's functioning such as physical function, cognitive function or sexual function. The concept might be health-related quality of life (HRQL), defined as the patient's subjective perception of the impact of his disease and it(s) treatment on daily life, physical, psychological and social functioning and well-being. The concept can be measured in either absolute terms, for example pain severity at a specified time point. Or it can be measured in terms of change from a previous measurement.

APPLICATION

PROs have several and wide reaching applications. They are used in clinical trials to measure the effect of a medical intervention on one or more concepts relevant to the patient that is expected to be influenced by the medical intervention, with PRO data being submitted to regulatory agencies such as the US Food and Drug Administration (FDA) and the Europeans Medicines Agency (EMA) to support regulatory decision making. PROs are playing an increasing role in Health Technology Assessment (HTA) decision making, particularly in the UK (National Institute for Clinical Excellence, NICE), France (Transparency Committee, TC) and Germany (Federal Joint Committee, GBA). PROs are used widely in real world evidence or observation studies in order to capture the impact of a medical intervention on patients in a real world setting. PROs are also used in clinical practice to inform discussions between the physician and the patient. In the UK NHS, all patients having hip or knee replacements, varicose vein surgery, or groin hernia surgery are invited to fill in PROs. In addition, PROs influence prescribing decision making at the clinician level, and influence patient demands for treatments, particularly in the US where there is direct-to-consumer advertising not permitted in Europe.

TAXONOMY

There is no single catalogue of all valid and reliable PRO instruments currently in use, several PRO databases exist listing several thousands of PRO instruments, and new instruments are always being developed. It is therefore important that the selection of PRO instrument(s) is carefully considered from the very many instruments that are available.

Generic vs. disease specific

Generic PRO instruments are those that can be used in the general population and/or across different diseases. This enables comparison in relation to societal norms and between disparate groups of patients. Such measures are usually multi-dimensional relating to many areas of life. Examples of the most commonly used generic measures are the Medical Outcomes Short Form 36 (SF-36) [Ware, 1992], and the EQ-5D [Brooks, 1996]. However,

	Generic	Disease-specific
Advantages	• Allows for comparison with the general population data • Allows for comparison across different diseases • Allows collection of more common health domains	• Allows greater sensitivity to the domains most pertinent to the disease
Disadvantages	• May include less relevant items or exclude relevant items • May be less sensitive to changes within the domains specific to the disease	• May fail to identify general domains which are relevant to the specific disease • Cannot be used for comparison to general population

Table I. *Generic vs. disease-specific PRO instruments*

generic measures may be uni-dimensional (e.g. Female Sexual Function Index [Rosen, 2000]); or limited by age group (e.g. PedsQL generic core scale [Varni, 1999]). The advantages and disadvantages of generic and disease-specific PRO instruments are presented in Table I.

Disease-specific PRO instruments are those that have been developed for use in specific patient populations. This may be broadly defined, e.g. the European Organisation for Research and Treatment in Cancer QLQ-C30 (core questionnaire) [Aaronson, 1993] for use with cancer patients in general. Broad disease-specific measures often also have bolt-on modules where many forms of a disease exist, e.g. EORTC lung cancer module [Bergman, 1994] and breast cancer module [Sprangers, 1996]. Additionally measures may be specified by treatment type, e.g. Urethral stricture surgery patient-reported outcome measure [Jackson, 2011], and disease stage, e.g. Needs Assessment for Advanced Cancer Patients [Rainbird, 2005]. Disease-specific PRO instruments have the advantage of being tailored to issues specific to a given condition which generic PRO instruments fail to adequately address. This can translate into increased responsiveness to clinically important changes in a patient's condition.

Examples of instruments

In Table II are summarized some examples of instruments based on the concept measured.

Concept	Descriptions	Examples
Signs and symptoms	Signs and symptoms of disease (e.g., pain, fatigue and nausea): reports of physical and psychological symptoms or sensations not directly observable and therefore only known by the patient.	A numeric rating scale to assess pain or fatigue.

Table continues >

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Concept	Descriptions	Examples
Function	Physical function: impaired physical activity and functioning (e.g., self-care, walking, mobility, sleep, sexual, disability).	The physical function domain of Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) [Bellamy, 1988].
	Psychological and emotional function: positive or negative affect and cognitive (e.g., anger, alertness, self-esteem, sense of well-being, distress, coping)	The Hospital Anxiety and Depression Scale (HADS) [Zigmond, 1983], and the Beck Depression Inventory (BDI) [Beck, 1961].
Treatment satisfac-tion	Patient satisfaction: usually an evaluation of treatments, patients' preference, health care delivery systems and professionals, patient education programs and medical devices	Treatment Satisfaction for Medication Questionnaire (TSQM) [Atkinson, 2004] [Atkinson, 2005].
Activities of Daily Living (ADLs)	Instruments measuring basic ADLs cover daily activities that are within the individual's usual environment, such as bathing, showering, bowel/bladder management, dressing, eating and personal hygiene.	The Knee Outcomes Survey Activities of Daily Living Scale [Irrgang, 1998].
	Also available are instruments that measure Instrumental ADLs which cover areas of life relating to an individual living independently within their community, such as housework, taking medications, managing money, shopping, and using transport.	

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Concept	Descriptions	Examples
HRQL	HRQL instruments are a type of PRO which attempt to capture a broader perspective on the well-being of a patient. HRQL can be defined as the patient's subjective perception of the impact of their disease and its treatment(s) on daily life, physical, psychological and social functioning and well-being [Leidy, 1999]. HRQL measures therefore assess a broad range of different concepts and are typically referred to as being *multidimensional* in nature.	The SF-36 (Ware & Sherbourne, 1992) and the EQ-5D [Brooks, 1996].

Table II. *Example of instruments*

FORMAT

Patient reported outcomes measures can be administered by self-report, interviewer-administered or proxy-report. A self-report PRO is completed by the patient directly. When possible, self-report administration is considered the gold-standard of PRO data collection because data are collected from the patient directly. Interviewer-administered PROs rely on interviewers to collect PRO data directly from the patient, without interpretation. Proxy-report involves someone other than the patient (e.g. a caregiver or healthcare provider) responding on behalf of the patient, as if he or she were the patient. Proxy-report can be used to gain the patient's perspective in situations where self-report or interview is not possible due to a limitation in the population of interest's ability to communicate and/or complete the PRO (e.g. severe symptoms, cognitive impairment, infants). Proxy-reported

PROs are at times discouraged because they require a subjective judgment to be made about the patient without patient validation. Self-report and interviewer-administered are the two most common modes of PRO administration.