Value Lies in the Eye of the Patients: The Why, What, and How of Patient-Reported Outcomes Measures

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ABSTRACT

Patient-reported outcomes (PROs) are any report of the status of a patient's health condition that comes directly from the patient (or in some cases from a caregiver or surrogate responder), without interpretation by a practitioner or anyone else. PROs are increasingly used as a valuable source of data in different domains of health care, including research, clinical practice, health care management, and decision making on the regulation, coverage, and reimbursement of new technologies. Several factors must be considered when selecting which PRO measure to use to ensure their appropriate use and interpretation as well as their relevance for decision makers. The increasing availability of PRO data, its integration with other data sources, and the improvements in data analytics offer a valuable opportunity to place the patient at the center of any health care process. However, several issues need to be addressed, including interoperability, data governance, security, privacy, and ethics, to realize an effective, integrated, standardized, real-time assessment of PROs in the health care systems. (*Clin Ther*. xxxx;xxx:xxx) © 2019 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Key words: health care decision making, health care management, patient-reported outcomes, PRO, PROM, value frameworks.

INTRODUCTION

Patient-reported outcomes (PROs) are an invaluable source of data that may inform a broad range of domains in health care, including clinical investigations, clinical practice, health care management, and decision making on regulatory, coverage, and reimbursement aspects. The imperative to include PROs in each of these domains is justified by the increasing availability of PRO data and its integration with other data sources that reduces the costs of data collection. It is also justified by the general shift to the idea that patients are the ones in the best position to evaluate to what extent the objectives of health care have been reached. The objective of this commentary is to provide an overview of what PROs are and how they are measured as well as how PROs have been used so far and, foreseeably, in the near future.

WHAT IS A PRO?

A PRO is any report of the status of a patient's health condition that comes directly from the patient or in some cases from a caregiver or surrogate responder, without interpretation by a practitioner or anyone else.[1–3] PRO is an umbrella term that classifies a range of different, patient-related concepts, including personal reports of health status (such as assessments of functional status), symptoms, and health-related quality of life.[4] Not all medical or health information collected from patients constitutes a PRO. For example, demographic characteristics, current medication lists, and personal and family medical history are all important pieces of health information that a patient may provide; however, this information

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does not represent a health outcome per se and is therefore not a PRO.[1]

There is an evolving definition of patient-generated data that reflects patient-sourced information of all types (eg, health history, information from biometric sensors, and vital signs measured and recorded by the patient or a proxy), with patient-reported outcomes representing a portion of this as information collected using formally designed questionnaires.[5] A PRO measure (PROM) is an instrument, scale, or single-item measure used to assess the PRO concept as perceived by the patient, obtained by directly asking the patient to self-report.[6] For example, the Functional Assessment of Cancer Therapy—General (FACT-G) is a widely used questionnaire to evaluate the quality of life of patients receiving cancer therapies.[7] In its latest version, the FACT-G consists of 27 items (questions) divided across 4 subscales: physical well-being, social/family well-being, emotional well-being, and functional well-being.[8]

PROMs complement existing biological, genetic, clinical information and physical examinations by providing standardized assessments of how patients function or feel with respect to their health, quality of life, mental well-being, or satisfaction with the healthcare process.[9] The vision is that combining clinical, genomic, and proteomic with PRO-mic data will provide the most complete picture of patient health status and fuel conversations between patients and practitioners to effectively result in shared decision making and individualized care.

It is important to distinguish PROMs from patient-reported experience measures, which focus on aspects of the humanity of care, such as being treated with dignity or being kept waiting,[10] and patient-reported outcome-based performance measures (PRO-PMs), which aim to include patients' direct reports about how they feel and function in health care services performance assessment programs.[6] For example, a PRO-PM is the proportion of patients with depression or dysthymia with an initial Patient Health Questionnaire 9 (PHQ-9) score >9 who after 6 months of management from mental health service have a PHQ-9 score <5. The use of PROs to assess quality of care is still in its infancy, but it is likely to increase together with the increase in the availability of PRO data and its integration with electronic health records, registries, and routine practice workflow. For example, based on a conceptual model for PRO-PM measures developed by the US National Quality Forum, Basch et al[11] proposed a specific PRO-PM measure to assess the quality of care in oncology. PRO-PMs require moving from a PROM to a PRO-based performance measure, which specifies how patient-reported outcome data are aggregated and interpreted to reflect performance of the health care service. A rationale for PRO-PM programs is that better symptom control and quality of life are associated with reduced costs and use of medical services and improved medication adherence, patient satisfaction, and survival.[12,13]

WHY PROS? THE IMPORTANCE OF CAPTURING WHAT MATTERS TO PATIENTS

Most health care aims to improve patient-relevant outcomes and tackle what matters to patients (eg, symptoms, disability, and health-related quality of life). These are aspects that only patients can assess in a way that minimizes observer bias (inevitable if asking practitioners to assess their own practice).[10] In general terms, the purpose of administration of PROMs is usually assessing the severity of symptoms,[14,15] providing information to track the effect of treatments on patient outcomes,[16] helping patients and practitioners set priorities for office visit discussions and inform treatment strategies,[17,18] monitoring general health and well-being as part of routine visits,[19] and connecting practitioners to patient-generated health data collected by patients to track their health independent of the health care encounter.[20] What is the mechanism behind the measurement of PROs that leads to better care and better outcomes? Measuring patient-reported outcomes in clinical practice may trigger several important elements: it may enhance *patient engagement*, clarifying the patient's *priorities* for care and therefore promoting *shared decision making*.[21]

This is especially important because patients and physicians do not always agree on which outcomes of care are most important. Patients welcome being involved, which may have health benefits in itself, such as increased public accountability of health services and health care professionals and satisfaction with care. The process of patient self-reporting can improve patient awareness of their conditions, their ability to communicate about symptoms, and self-efficacy to manage their own health. In turn, this may improve adherence and relatedly use of medical

services (eg, emergency department visits and hospitalizations), costs, and outpatient medication adherence.[22,23] As a result of this mechanism, patients' self-reported symptoms and health status affect patient-relevant outcomes, such as health-related quality of life and even survival[14,24] (Figure 1).

GENERIC VS DISEASE-SPECIFIC MEASURES

Different types of PROMs exist (Table I). For example, profile PROs simply provide multiple scores across a range of domains, whereas preference-based PROs also estimate an index score using a prespecified algorithm (often country specific) that reflects preferences for different combinations of health states. Other features of PROMs include using single- versus multi-item scales or static versus dynamic questionnaires (in the latter, question sets are tailored to the individual, as in computer adaptive tests).[1] In more general terms, PROMs can be categorized as disease specific or generic. Disease-specific measures are tailored to precisely represent the symptoms and effect on function of a specific condition. Generic PROMs consider instead general aspects, such as daily activities, self-care, and mobility. For example, although the FACT-G generally assesses the functional status of patients with any tumor type, more targeted measures have been developed for specific types of cancer, such as breast cancer (FACT-B),[25] colorectal cancer (FACT-C),[26] multiple myeloma (FACT-MM),[27] and other types of cancer. Often both specific and generic PROMs are used. In fact, the former may be more sensitive to specific symptoms experienced by patients but may fail to provide a general picture of patient quality of life, whereas the latter are less sensitive but may capture more commonly experienced health domains, allowing comparisons across conditions.

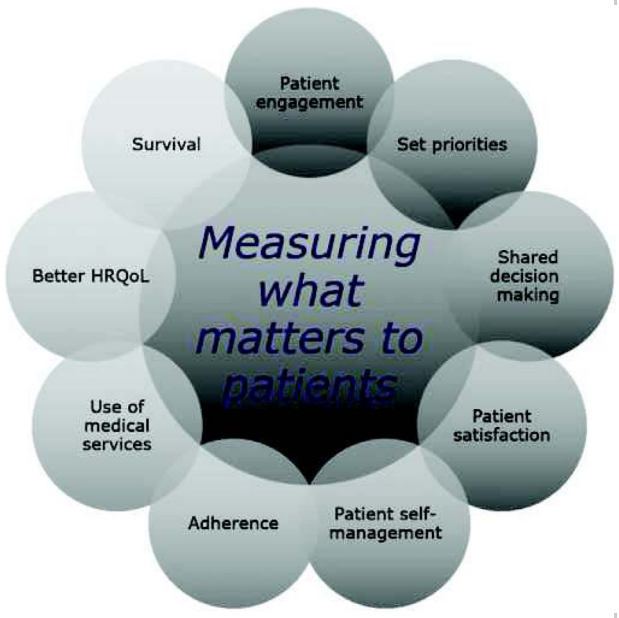

Figure 1. Effect of collecting patient-reported outcome data on patient well-being and health care management. HRQoL = health-related quality of life.

CURRENT USE OF PROMS

In recent years, use of PROs in clinical research and trials has increased substantially. Zagadilov et al[28] found approximately 85% of oncology trials registered in ClinicalTrials.gov between September 2006 and June 2012 that incorporate some form of PROs, health-related quality of life, or symptom measures. The use of PROMs in clinical practice is instead much slower and fragmented, and it is documented in few places or in pockets of excellence. In the United States, the BREAST-Q PROM has been used after mastectomy breast reconstruction with implant or autologous techniques to assess patient satisfaction and psychosocial and sexual well-being 2 years after surgery.[29] In England, the Improving Access to Psychological Therapies program monitors symptom scores before and after therapy to inform treatment planning and service delivery for patients with anxiety and depressive disorder.[30] In Denmark, the AmbuFlex telehealth system is being used to schedule outpatient appointments for chronic conditions. Patients fill in a PROM at home, which is used for decision support to evaluate the need for a consultation, thus reducing unnecessary outpatient appointments.[31]

The use of PROMs may relate to individual-, organizational- or system-level dimensions. At the individual level, some PROs may have prognostic value,[32] and completing questionnaires before clinic visits may inform the future encounters (eg, Swedish Rheumatology Quality Register[33]) or advise patient and physician decision making (eg, Mastectomy and

Table I. Features of patient-reported outcome measures. Adapted from Snyder et al[43]

Feature	Description
Generic vs disease specific	
Generic	Health states are described across a series of general health domains, such as pain, anxiety and mobility. Allow comparisons across disease areas but may be less sensitive to disease-specific health domains. Example: Quality of Well-Being Scale—Self-administered.
Disease specific	Health states are described using specific aspects of a condition or symptom. May be more sensitive to capture disease symptoms but may miss more general dimensions of patients' well- being. Example: Kansas City Cardiomyopathy Questionnaire.
Profile vs preference based	
Profile	Provide multiple scores (profile scores) across a range of patient-reported outcome domains. Example: 36-Item Short Form Survey Instrument.
Preference based	Profile scores are converted into an index using a prespecified algorithm that reflects preferences over a determined health state. Example: EuroQol 5-dimensional questionnaire
Single item vs multi-item	
Single item	Health states are measured with a single question. Easier to administer and interpret and less reliable for tracking change. Example: "Compared to 1 year ago, how would you rate your health in general now?"
Multi-item	Health states are measured with multiple questions. Generally more sensitive to differences in health interventions but may be burdensome to complete and interpret. Example: Patient Assessment for Low Back Pain—Symptoms
Static vs dynamic	
Static	Questionnaire is rigid. May require longer questionnaires to provide a reliable measure of a patient's health status. Example: Functional Assessment of Chronic Illness Therapy
Dynamic	Questions sets are tailored to the individual and adapt to individuals' responses. Can yield shorter and equally reliable measures than static forms. They require computer administration. Example: List of Common Terminology Criteria for Adverse Events presented in an adaptive way.

Breast Reconstruction Audit[34]). At the organizational level, a number of countries have launched initiatives to promote the use of PROs as a basis for performance measurement by providers.[35] In England, the principal use has been in elective surgery (hip and knee replacement, groin hernia repair, and varicose vein surgery).[10] In the United States, widespread implementation of PROMs has been restricted to spinal conditions, primary care, and depression in selected cities or states.[36] Nationwide use of PROMs commenced earlier in Sweden using the disease-specific clinical databases (quality registers) established there by the medical profession since 1975, with some systematically collecting PROMs starting in 2000.[10]

At a broader level, the use of PROMs can be extended to contracting or reimbursement mechanisms (eg, diabetes pay-for-performance PRO evaluation[37]) to licensing of pharmaceuticals and health technology assessment or coverage and reimbursement decisions. The name PROs was indeed originally introduced by the US Food and Drug Administration (FDA) within a regulatory context. Because of their increasingly significant role in the development and evaluation of new medicines, the FDA, in conjunction with industry and academic

experts, published a formal guidance entitled *Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims* in 2009 to describe how the FDA will review and evaluate the existing, modified, or newly created PRO instruments in support of the claims contained in FDA-approved drug labeling.[2] The European Medicines Agency (EMA) in 2016 released an appendix to the *Guideline on the Evaluation of Anticancer Medicinal Products in Man*, illustrating its view on the use of PROMs in oncology studies.[3] The two agencies have taken different approaches to these data over time.[38] A recent comparative study[39] revealed that they used different evidentiary standards to assess PRO data from oncology studies, with the EMA more likely to accept data from open-label studies rather than well-controlled studies and broad concepts such as health-related quality of life.

COLLECTION, ANALYSIS, REPORTING, AND INTERPRETATION OF PROMS

PRO information can be obtained in a variety of ways, including face-to-face interviews, questionnaires (via paper, telephone, interactive voice response, the web, or dedicated electronic device), and diaries. Evidence exists around the equivalence of these modes of administration that supports selection based on patients' or investigators' preference.[40–42] When selecting which PRO instruments to use, it is important to consider patient, practitioner, and decision-maker preferences regarding the types of data to collect against patient burden in filling out questionnaires. Other considerations include any physical, cognitive, demographic, or socioeconomic barrier to complete the measurement (user-centered design principles, including usability testing, may be extremely useful in this respect) and the level of psychometric evidence (face and construct validity, reliability, responsive to change, no floor or ceiling effects, and cross-culturally valid) for the questionnaire in the target population.[43] One should also consider length, assessment schedule (inappropriate assessment schedules can obscure key events pertinent to the analysis), and the reference period.[39] Shorter recall periods more accurately capture patients' actual experiences but require more frequent assessments (meaning more burden) or may miss important symptoms between less frequent assessments. Finally, it is important to obtain permission to use the questionnaire (if required) and pay any applicable user fees. Another important property of a good PRO is that it is easily scored and interpreted, actionable, and facilitative of clinical decisions.[44,45]

Reporting of PROs used in clinical research remains suboptimal across randomized clinical trials (RCTs), and these data are considered to be less accessible than outcomes such as survival or the adverse effects of treatment.[46,47] Other issues apply to the analysis of PROs, such as bias attributable to unblinding, missing data, multiple testing and cherry-picking of results, appropriate interpretation against minimally important difference estimates, cut-off scores, or clinically meaningful thresholds.[1] These patterns of PRO reporting negatively affect the effective use and dissemination of RCT PRO findings to clinical practice. To improve the reporting of RCTs in which PROs are primary or important secondary end points, an extension of the Consolidated Standards of Reporting Trials (CONSORT) checklist has been developed.[4] This extension recommends that a description of the hypothesis of the PROs and relevant domains be provided, that evidence of the PRO instrument's validity and reliability be provided or cited, that the statistical approaches for dealing with missing data be explicitly stated, and that PRO-specific limitations of study findings and generalizability of results to other populations and clinical practice be discussed.

WHAT'S NEXT? INTEGRATED, STANDARDIZED, CONTINUOUS ASSESSMENT OF PROS IN CLINICAL PRACTICE

A health and information policy agenda supporting the wide-scale collection of PROMs is critical to promote a standardized, continuous, integrated assessment of these data in clinical research and everyday care. Issues that involve interoperability, data governance, security, privacy, and ethics must be addressed so that data aggregation is possible locally, regionally, and nationally.[48] Within the big-data vision (high volume and variety of data available at a high velocity), electronic health records, administrative

data, public health records, biometric sensors, mhealth applications, and many other data sources can be integrated and used to reinforce the importance of the voice, preferences, and experience of the patient in a unified vision of health and health care. This development would also help overcoming the cost of collection, analysis, and presentation of data and logistical concerns and workflow barriers about capturing PROs, such as the increased burden on staff members and patients to ensure that patient-reported outcomes are collected, interpreted, and discussed during office visits.[9,49–51]

In a not-distant future, narrative accounts that describe encounters with practitioners in patients' own words will be automatically converted to standardized PROMs.[52] This process would become a real opportunity of progress if implemented to develop value-based care in which health services and procedures are driven by patient preferences, needs, and health outcomes.

DECLARATION OF COMPETING INTEREST

The authors have indicated that they have no conflicts of interest regarding the content of this article.

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