EDITORIAL

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Patient Reported Outcomes

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INTRODUCTION

Although traditionally, morbidity or mortality has been the main criterion of a therapy's efficacy, quantification of assessment of disease outcomes from a patient's point of view has been increasing during the last decades. A new therapy can show excellent results in the improvement of respective biomarkers involved, or even prolong life expectancy in the context of clinical trials, however, in real life patients may indicate they could not adhere to treatment due to side effects, complex dosing schemes, and reduced quality of life. Similarly, therapists seem to commonly underestimate the severity of the disease or be unable to describe the full range of clinical manifestations - the patient is experiencing [1]. The impact of a disease on patients' quality of life cannot be predicted, and by no means can be correlated with the severity of the disease itself from a medical point of view. As a result, the use of information reported by patients (patient reported outcomes - PRO) to further evaluate treatment outcomes by health professionals, is increasingly gaining ground as a way to understand and improve the quality of healthcare services [2].

A PRO is defined as modification or interpretation of the response from a health professional, or any other" [3]. The tools/instruments by which PROs are evaluated and recorded, capturing patients' perception regarding their state of health, disease and the effects of therapeutic interventions, are called PRO measures (PROMs). Many PROMs are designed to be used in a variety of diseases or, may be specific to a particular disease or population. In clinical practice, PROs can be used by patients in a self-report format, to detect various clinical manifestations that otherwise may go undetected. In addition, they can be used for monitoring treatment efficacy that common surrogate biomarkers or available indices cannot assess. Lastly, they allow patients' more active participation to their management plan, that ultimately promotes a more human-centered healthcare [4]. However, PRO should not be confused with the recording of disease symptoms from their attending physicians. These patient self-report outcomes represent a much more multi-dimensional entity, driven entirely by the patient.

PROM DESIGN

PROs have many dimensions, that can be measured with the right tools. These tools usually consist of self-completion questionnaires, which may be generic, e.g. EQ-5D (Euro Quality of life - 5 Dimension) examining quality of life, or disease-specific e.g. SGRQ (St'George's Respiratory Questionnaire) for chronic obstructive pulmonary disease [5]. Even though, PROMs are designed by the scientific community, involvement of the respective patient community that is addressed by each PROM is pivotal, before, during, and after the design and implementation of such a tool. Patients are the most suitable to develop, evaluate and review tools, recognize the need for new ones, supply with new study objects depending on community needs, and finally adopt them .

The development and evaluation of PROMs is an ongoing and detailed process that comprises content validity, reliability and responsiveness [5, 6]. Briefly, once the concept of interest is defined, patients are asked questions about this. These questions are defined as "objects". The objects are queried to determine the variation of a concept. Main concepts evaluated in PROM include quality of life, degree of patient's satisfaction, physical and social functioning, psychological state, signs and symptoms, compliance with treatment etc. Objects must be clear, valid and their number depends

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on the completeness of information they provide. They are continuously reassessed and improved based on new needs, and must be adapted to the target-population and individual level of cognitive function and linguistic preference. Each object should at the same time ensure a reasonable recall period (to what extent in the past patients are called to answer information about their condition), and adequate options of response (graphic, quantitative scale, verbal) [7]. Of note, the patient's response to the same question can be different, depending on the time of day he is called to answer, on the type of distribution of the questionnaire (electronic, telephone etc), and the results may vary depending on the questionnaire completion instructions and patient's literacy level. Clearly, the purpose of the tool, the characteristics of the disease, the duration and frequency of symptoms, the purpose and intended use of PROM determine objects. Before their final configuration, the tools are tested by patients and experts and respectively corrected if, for example, objects are not clear or relevant to the concept (not considered relevant, requiring frequent clarification), if a limited response range is noted (preventing answer variation), have little diversity (all patients give the same answer), if there is little change detection sensitivity, or redundancy is observed etc. Reliability i.e. the measurements are repeatable and stable, and distinguish between changes in the response, and validity i.e tool measures what it is intended to measure and what is important for patients, are important to structure a useful PROM.

PRO APPLICATIONS AND CHALLENGES

Initially, PROs were developed primarily for use in pharmacological and medical research [8]. However, now PRO tools seem to extend far beyond clinical research, given their ability to transform the healthcare system and improve the quality of services by placing the patient at the center of decisions. Besides assessing parameters that may not be measured by the treating physician, and complement information available from existing and measurable bio-markers, they seem to have predictive value in survival [9] and hospitalization rates [10]. Thus, they can be used from all parties involved, including patients, healthcare givers, insurance companies, healthcare systems to evaluate quality of care and reform budgets. These changes have made regulatory agencies such as the FDA (US Food and Drug Administration) and the EMA (European Medicine Agency), to recommend their use in the evaluation and promotion of new therapeutic interventions and further optimize them, as seen in a variety of products of different disciplines [11]. However, their implementation is far from an easy task. The heterogeneity of tools, the timing of the various stages of the disease that the tools are distributed, the current illiteracy levels, or the exacerbation of anxiety the tools themselves create, remain just some of the challenges [12]. After all, no one-size PRO fits all kinds of patients.

Key points

- Clinical trial endpoints often fail to be translated to meaningful clinical outcomes for patients involved.
- Patient Reported Outcomes represent patients' report of their state of health, without correction, modification, or interpretation of the response from a health professional, or any other.
- Patient Reported Outcomes can be assessed by specifically designed and constructed tools, i.e. Patient Reported Outcome Measures.
- Patient Reported Outcomes find application from clinical research, to every-day clinical practice and improvement of healthcare policies.

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