Review of Patient-Reported Outcome Measures (PROMs) in Clinical Trials of Rare Diseases

Manvi Sharma, PharmD Candidate 2020; Anastasiya Voitsik, PharmD, MS; Michael Toscani, PharmD

Background

A patient-reported outcome measure (PROM) is a measurement of the status of a patient’s health conditions that come directly from the patient. PROMs include but are not limited to Health Related Quality of Life. They are most commonly used in clinical trials of products that are used for chronic, disabling conditions where the goal of the treatment is to improve symptoms, functioning and quality of life.3 PROMs have the potential to systematically incorporate patient perspectives to measure those outcomes that matter most to patients.1

PROMs are not a new idea, their uptake in the research community has been slow and laborious. Most current clinical research and practice falls short of this objective by selecting outcome measures which do not capture patient value to the fullest.1 Rare diseases pose a unique challenge to clinicians and researchers because of their low prevalence, establishing the impact of potential treatments is difficult. When sample sizes are necessarily limited, high instrument responsiveness (i.e., the ability to detect all important effects, even small) is particularly important.2

Routine PROMs have shown to improve patient satisfaction with their care, symptoms management, quality of life and survival rates. PROMs help to promote patient centered care by improving communication between clinicians and patients about disease status and progression of the patient’s disease state.2

Objective

The objective of this study is to provide a review of the value of patient-reported outcome measures in rare diseases. The study aims to identify the percentage of clinical trials which incorporate PROMs that affect patient lives the most and improve quality of life.

Method

A search of existing literature, including abstracts, published in the PubMed database from 2015 to 2019, was conducted identifying studies that show the importance of outcome measures which captured the patient perspective associated with patient reported-outcomes. Keywords used for searching included: rare disease, rare disorders, PROMs, clinical trials, quality of life.

Identification of rare diseases, defined as a disease with a global average of 40 cases/100,000 people, was evaluated in the ISPOR Rare Disease Special Interest Group. Using Orphanet Report Series, top twenty rare diseases were selected for further evaluation, such as Congenital Cytomegalovirus, 22q11.2 Deletion Syndrome and others (see Results).

Results

The number of clinical trials that use PROMs for each disease state and selected outcomes that were used to measure change in general health status, acute and chronic pain, and quality of life. PROMs have the potential to improve symptoms, functioning and quality of life.3 PROMs have the potential to improve symptoms, functioning and quality of life.3

There were a total of 612 clinical trials reviewed from the 20 rare diseases that were chosen. From 612, there were a total of 92 clinical trials that used patient-reported outcome measures as primary or secondary endpoints (Fig. 1).

- Approximately 15.03% of the clinical trials used PROMs.
- On average, 18 patient-reported outcomes were used in each clinical trials.
- Reviewed oncology studies included Neurofibromatosis Type 1, Soft Tissue Sarcoma, Polycythemia Vera, Ovarian Cancer, Follicular Lymphoma and Post-transplant lymphoproliferative disease. Evaluation of these clinical trials showed that only 14.74% of oncology clinical trials are utilizing PROMs (Fig. 3).
- Reviewed cardiology studies included Long QT syndrome, Pulmonary Valve Stenosis, Tetralogy of Fallot, Transposition of the Great Arteries. None of the cardiology studies utilized PROMs (Fig. 4).
- Approximately 32.05% of the clinical trials used PROMs.
- Approximately 32.05% of the clinical trials used PROMs.
- Approximately 32.05% of the clinical trials used PROMs.2

Limitations

- Representational research includes the whole range of clinical trial phases (I-IV). Phases I and II of clinical trials are mostly focused on safety of a new drug and designed to evaluate pharmacokinetics and pharmacodynamics of the drug, establish maximum tolerable dose and see possible adverse events. However, in this study we didn’t distinguish between phases and evaluated all primary and secondary outcomes.
- Conclusions

Rare diseases can lead to a significant reduction in quality of life for patients and their families. Ensuring the patients voice is central to clinical decision making is key to delivering, evaluating and understanding the efficacy of therapeutic interventions. Patient reported outcome measures (PROMs) are used to capture the patient’s views about their health status and facilitate our understanding of the impact of these diseases and their treatments on patients’ quality of life.

Based on the literature search and the overview of clinical trials in rare diseases, we identified that PROMs were not measured in the majority of clinical trials. Literature review demonstrated support for using PROMs in clinical trials to better understand the effect of the treatment on patient symptoms and quality of life. Previously, only measurable outcomes such as labs and mortality rates, were used. Even though such outcomes were easily quantifiable, they were not an accurate representation of the patient experience. Difficulty with technological and operational barriers may be some of the reasons hindering the incorporation of PROMs into clinical trials. It is important for healthcare systems to start integrating PROMs into patient care in order to provide better well-rounded treatment.

Only 20 rare diseases were reviewed based on their prevalence. A larger scale review of all rare diseases on a single therapeutic area would be able to provide more thorough overview of PROM utilization in clinical trials.

Resources


Author Contact Information

Manvi Sharma@Rutgers.edu