Q&A with John Powers

Clinician Reported Outcome Assessments of Treatment Benefit: An Interview with John Powers, PhD, Chair, Clinical Outcome Assessment Emerging Good Practices Task Force

ISPOR TASK FORCES

Value & Outcomes Spotlight was fortunate to meet with John Powers, PhD, on the recent article, "Clinician-Reported Outcome Assessments of Treatment Benefit: Report of the ISPOR Clinical Outcome Assessment Emerging Good Practices Task Force," that appeared in the January 2017 issue of *Value in Health*. What follows are some of the highlights from our conversation about the important implications for clinician-reported outcomes.

Powers III, JH, Patrick DL, Walton MK, et al. Clinician-Reported Outcome (ClinRO) Assessments of Treatment Benefit: Report of the ISPOR Clinical Outcome Assessment Emerging Good Practices Task Force. Value Health 2017;20(1):2-14.

***Value & Outcomes Spotlight*:** The ISPOR Clinical Outcomes Assessment Task Force wrote two reports. Who is the audience for these reports?

Powers: While the first report, Clinical Outcome Assessments: A Conceptual Foundation Task Force Report (2015) (https://www.ispor.org/clinical-outcomes-assessment-guidelines.pdf) and the ClinRO Assessments of Treatment Benefit Task Force Report (2017) (https://www.ispor.org/Clinician-Reported-Outcome-Assessments-Treatment-Benefit-guideline.pdf) have a regulatory focus, the audience is anyone interested in outcome assessments in clinical research – investigator, sponsor, research staff, patient or consumer. These task force reports would also be of interest to third party payers who want to understand how outcome assessments define endpoints that can be used to demonstrate added benefits for patients consequently, justifying payment.

ISPOR has published eight ISPOR Patient Reported Outcome (PRO) Good Research Practices Task Force Reports (https://www.ispor.org/workpaper/practices_index.asp) since 2009, based in part on the US Food & Drug Administration's Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims (http://www.fda.gov/downloads/drugs/guidances/ucm193282.pdf). When the FDA PRO guidance was first developed, there was discussion on how the same principles could apply to other outcome assessments, like the clinician-reported outcome (ClinRO) assessments commonly used in clinical trials. Because the previous task force reports focused only on PRO assessments, this task force undertook addressing the gap in research guidance for using clinician-reported outcome (ClinRO) assessments.

While there are similarities in the development and evaluation of PRO and ClinRO assessments, there are differences, too. ClinRO assessments can be subdivided into readings, ratings or clinician global assessments. With a ClinRO assessment, a trained health care professional (clinician) implements the evaluation of patients' health status, makes judgments on the measurement, and interprets and reports the assessment.

Because someone other than the patient is conducting the evaluation, ClinRO assessments are usually *indirectly* related to how patients feel or function in their daily lives. Clinicians cannot know exactly how patients feel or experience feelings or symptoms. However, the observations and judgements of clinicians should reflect some aspect of how patients feel or function in their daily lives.

***VOS*:** Were there any surprises that came up during the manuscript development process?

Powers: Initially, we were not expecting to write two reports. We quickly realized that before we could explain the differences and similarities between PRO and ClinRO assessments, we would have to write an introductory report that defined basic principles related to clinical outcomes terms and concepts.

For example, we encountered a lot of confusion over the difference between outcome assessments and how those outcomes assessments are used – either alone or with other outcome assessments - to define endpoints. The endpoint is *how* an assessment is: 1) used to evaluate treatment benefit; 2) analyzed to detect differences between groups including timing of when measurements are performed and the statistical analysis of the difference between groups in clinical trials, and 3) interpreted to reflect how group differences reflect benefit to how patients feel, function or survive.

In plain language, the ClinRO report clarifies these important points: 1) *what* you are actually measuring; 2) whether you are measuring the *right* concept(s), 3) *how* to measure the concept in a standardized way that minimizes error, and finally, 4) *what this measurement means* to patients in terms of their own lives.

VOS: For those with little understanding of clinical trials, what are two simple messages that you would like them to remember?

Powers: I would say the first is understanding the terminology. If we don't define concepts and have a common understanding of them, we aren't speaking the same language. The second is understanding the three general types of outcome assessments (OAs) – all-cause survival, biomarkers and clinical outcome assessments (COAs). All-cause survival is clear by itself and obviously relevant to patients. *Biomarkers rely completely on automated processes or algorithms*, i.e., no human influence. However, their relationship to how patients feel, function or survive may or may not be clear or have been evaluated previously. This is an empirical question.

Clinical outcome assessments, whether a PRO, ClinRO, observer-reported outcome (ObsRO) or a performance outcome (PerfO) assessment, *are evaluations influenced by human choices, judgment, or motivation* depending on who conducts the evaluation, judges and interprets it. PRO assessments, are almost always *direct* measurements of patient benefit because the patient evaluates and reports his/her symptoms and functioning. In contrast, most ClinRO, ObsRO and PerfO assessments are observations, examinations or scores that *indirectly* reflect how patients feel or function in their daily lives.

VOS: The second report is focused on Good Measurement Practices. Can you tell us more about that?

Powers: I am a physician who sees patients, a clinical trialist and a study investigator. I want to make the most accurate assessment of any patient I see, whether it is in clinical practice or clinical research, and I want patients to receive the most effective treatment with the fewest side effects. By applying good measurement practices to ClinRO assessment development and evaluation, we will increase the efficiency and accuracy in the measurement of treatment effects.

Furthermore, standardizing outcome measures in clinical trials can advance the development of medical interventions, make it more relevant to the "real world" and make it more patient-centered. It also makes new interventions worth paying for if they have clear added benefits as they are used in practice. ■

Clinician-Reported Outcome Assessments of Treatment Benefit: Report of the ISPOR Clinical Outcome Assessment Emerging Good Practices Task Force

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Have you ever wondered why it is so difficult to demonstrate differences between interventions on patient-centered outcomes? Alternatively, why does it take so long to detect the benefit of an intervention to improve health or prevent health decline? Perhaps it is because the study is measuring the wrong outcome, or conversely, because the right outcome is measured poorly.

The ISPOR Clinical Outcomes Task Force Assessment addressed these issues in two reports on various types of outcomes used to define endpoints in clinical research trials. The first, Clinical Outcome Assessments: A Conceptual Foundation, (https://www.ispor.org/Clinician-Reported-Outcome-Assessments-Treatment-Benefit-guideline.asp), published in 2015, contains general principles for the definitions, development, and use of all clinical outcomes assessments (COAs), whether patient-, clinician-, or observer-reported or performance outcome assessments. These questionnaires, instruments, examinations, or observations are used to measure patients' health status and define endpoints that can be interpreted to reflect treatment benefits of medical interventions on how patients feel, function, or survive in clinical trials.

The second report focused on one type of COA, clinician-reported outcome (ClinRO) assessments. ClinRO assessments are outcome measurements that require professional training to make and/or interpret the assessment, unlike patient-reported outcome (PRO), in which the assessment comes from patients without anyone else's interpretation. The task force defined three types of ClinRO assessments: readings, ratings, and clinician global assessments and then described good measurement practices for their development and evaluation.

The task force outlined good measurement practices. While general principles of good measurement practices for ClinRO assessments are similar to those for other clinical outcomes assessments (e.g., PRO), there are also important differences in the methods and approaches, as well as certain areas requiring increased attention.

Good Measurement Practices

1) Defining the context of use

2) Identifying the concept of interest measured

3) Defining the intended treatment benefit on how patients feel, function, or survive reflected by the ClinRO assessment and evaluating the relationship between that intended treatment benefit and the concept of interest

4) Documenting content validity

5) Evaluating other measurement properties once content validity is established (including intra- and inter-rater reliability)

6) Defining study objectives and endpoint(s) objectives, defining study endpoints, and placing study endpoints within the hierarchy of endpoints

7) Establishing interpretability in trial results

8) Evaluating operational considerations for the implementation of ClinRO assessments used as endpoints in clinical trials

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