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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Within the two reports, the task force clarifies the differences between: 1) COAs, influenced by *human* choices, judgment, or motivation compared to all-cause survival or automated or algorithmic biomarkers; 2) direct (patient-reported) and indirect measurements of treatment benefit; and 3) outcomes and how they are used to define endpoints.

All COAs, including ClinRO assessments, can be used as measurements to construct endpoints, but they are not endpoints in and of themselves. Endpoints define how a COA is used as a study result and statistically compared among treatment groups to assess the effect of treatment. This includes how the endpoint is used with other outcomes assessments, how it is analyzed (both timing and statistical methods) to determine differences between groups, and how it is interpreted to convey how observed group differences may reflect benefit on how patients feel, function, or survive. In addition, the second report helpfully illustrates how each endpoint fits within a chosen hierarchy of study objectives and how outcome assessments, singly or in combination, can be used to provide confirmatory evidence about treatment benefit.

Applying the general principles and good measurement practices outlined in both reports can increase efficiency of clinical trials while providing clarity on treatment benefit for patients. Developing valid and reliable assessments helps to: 1) better define relevant treatment benefits for patients; 2) decrease variability and error in measurements—resulting in fewer numbers of patients needed to enroll in trials to demonstrate treatment benefit; 3) provide better information for regulatory review of a treatment's benefits versus harm; 4) improve decision making for patients and clinicians in clinical practice—to evaluate benefit/risk and choose between medical interventions; and finally, 5) justify payment for new interventions. ■

Additional information:

You can access, "Clinician-Reported Outcome (ClinRO) Assessments of Treatment Benefit: Report of the ISPOR Clinical Outcome Assessment Emerging Good Practices Task Force," and other articles in this issue of Value in Health at: http://www.ispor.org/valueinhealth_index.asp

To learn more about the *Clinical Outcome Assessment Emerging Good Practices Task Force,* go to: https://www.ispor.org/TaskForces/Clinical-Outcomes-Assessment.asp