PCR139

Qualitative Approaches Using Global Assessments to Support Meaningful Within-person Change (MWPC) Estimates for Patient-reported Outcome (PRO) Questionnaires in Regulated Clinical Trials

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Objective

Understanding the meaning of change scores produced by PRO questionnaires is important to support clinical trial endpoints. While quantitative, anchor-based methods are a common method to calculate MWPC of scores from a target PRO questionnaire, the Food and Drug Administration (FDA) has demonstrated interest in collecting additional supportive qualitative evidence from patient interviews (e.g., from in-trial interviews or interviews independent from a clinical trial). This research describes ways that qualitative data associated with single-item patient global assessments (PGAs) can be collected to support MWPC estimates on PRO scores.

Methods

Published regulatory guidance and literature related to qualitative approaches for collecting data on PGAs to support MWPC estimates were summarized (including benefits and limitations of approaches) alongside recommendations for methods and data utilization.

Results

Patient interviews can support the evaluation of MWPC of PRO scores used for regulatory endpoints by documenting patients' understanding and interpretation of PGAs. These interviews can be conducted either independent from a clinical trial (e.g., cognitive interviews) or during a clinical trial (e.g., exit interviews) to answer potential research questions such as:

- >Do patients understand the global assessment (and is the PGA conceptually related to the target PRO questionnaire[s])?
- >How do patients relate the PGA response choices to disease experience (and do patients distinguish between response choices)?
- >What do patients consider a meaningful change on a PGA? What defines "improvement" and "worsening"?
- >Do patients in a clinical trial report experiencing meaningful improvement due to treatment? What global response did they select?

Table 1 below lists the benefits and limitations for each type of interview, and **Figure 1** details key recommendations.

Table 1. Benefits and limitations by interview type

	Interviews independent from clinical trial	In-trial interviews
Benefits	• Flexible study design/not limited to the trial operations (e.g., ethics review, recruitment, interview timing)[1] • Can provide data regarding expectations for changes (e.g., improvement in symptoms) without exposure to an intervention or potential to impact clinical trial results • Can inform anchor selection prior to trial initiation[4] • Provides an opportunity to revise global items before being implemented in the trial[5]	• Can be conducted under the purview of the clinical study protocol (i.e., no separate ethical review needed)[2] • May support quantitative ratings and score changes from trial (using the point-change on the global that relates to "improvement" as an anchor threshold)[1, 3] • Not based on hypothetical change; based on in-trial experiences[1] • Participants familiar with the PGAs and other PROs[1]
Limitations	• Representativeness of the sample is limited[2] • Participants not likely familiar with the PGAs and other PROs[1] • Hypothetical nature of interview and discussion of change may not align with perceptions of real change and may cause confusion discussing outside of trial context[1] • Perceived meaningful change may depend on an individual's level of disease severity[1]	• Logistical limitations including the interviews into the trial design (e.g., time, costs) [1] • Information from the interview may conflict with clinical trial data[1, 3] • Need to consider adverse event reporting and data privacy considerations[1] • Timing critical to reduce recall bias[1, 3]

Results (cont.)

Figure 1. Key recommendations by interview type

Interviews independent from clinical trial	In-trial interviews
• Debrief the PGAs to document participant understanding of the item and response options, and extent to which participants can select a response option representative of their health status • Target sample should be similar to the clinical trial sample, e.g., disease severity[1] • Provide hypothetical clinical trial context to participants to help them consider global changes that may be meaningful[1] • Gather both qualitative descriptions of what would constitute a meaningful change from the patients' perspectives, as well as a specific value or response option on the PGAs that may represent meaningful improvement and/or worsening	• Ask about changes in the concept measured by the PGA and whether change was meaningful and why • If possible, interview at multiple timepoints in the trial to reduce recall bias (i.e., before vs after treatment); if only one timepoint is possible, ask patients to remember back to experiences before and during the trial[1] • Avoid lines of questioning that ask patients to recall their PGA response from an earlier trial timepoint (i.e., focus on qualitative descriptions of change and grounding in their trial experience) • Explore the relationship between patient reports of meaningful change to their trial PRO change scores • Analyses should typically be blinded to treatment[2]

Qualitative patient reports of their experience and the meaningfulness of any change in their experience can be presented in a variety of ways.

- >For example, patients' descriptions of the level of change that they consider meaningful on a PGA evaluating disease severity (PGA-Severity) scale (e.g., that a 2-point improvement or 1-point worsening would be meaningful changes) can be summarized to support selection of anchors for quantitative, anchor-based analyses (see **Table 2** for an example).

Table 2. Example results table for qualitative data pertaining to meaningful change on a 5-level PGA-Severity

Type of change	Patient-reported meaningful change on PGA-Severity*	n (% of patients) N=20
Improvement	4-point improvement	1 (5%)
	3-point improvement	6 (30%)
	2-point improvement	8 (40%)
	1-point improvement	5 (25%)
	0-point improvement (No change)	0 (0%)
Total- mean (SD)	2.15 (0.88)	
Worsening	0-point worsening (No change)	0 (0%)
	1-point worsening	12 (60%)
	2-point worsening	7 (35%)
	3-point worsening	1 (5%)
	4-point worsening	0 (0%)
Total- mean (SD)	1.45 (0.60)	

- 5-point verbal response scale: 0-None, 1-Mild, 2-Moderate, 3-Severe, 4-Very Severe
- Note: SD=standard deviation

"Moderate to none or a 2-point change would be a meaningful improvement to my life. I would notice a difference in my ability to do my daily activities"

"Any worsening, so going from moderate to severe, would be extremely debilitating and indicate that I can no longer function normally."

Conclusions

Qualitative research on PGAs via patient interviews can help inform the selection of appropriate anchors for future clinical studies, contextualize the meaning of change scores observed on a target assessment, and further support the clinical meaning of drug efficacy by providing the patient perspective of the meaningfulness of changes.

References

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