Overview of psychometrics to support the development and use of patient-reported outcome measures in migraine clinical trials

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Summary

- A variety of psychometric/statistical evidence is needed to support the development and use of patient-reported outcome measures for use in migraine clinical trials

Background

- Patient-centeredness has gained importance in migraine clinical trials
- Patient-reported outcome (PRO) measures have become increasingly critical to demonstrate that acute and preventive migraine treatments meaningfully impact outcomes that are important to patients
- Demonstrating that a PRO measure is fit-for-purpose (valid) in a given context of use (i.e., adult migraine clinical trials) is necessary for claims regarding treatment
  - e.g., Drug X improves physical functioning; Device Y reduces impact on everyday activities to be approved by regulatory bodies.
- Using current FDA guidance and personal experience in supporting the use of PROs, we provide an overview of the statistical information that is typically necessary to rigorously support a PRO as fit-for-purpose in a given context of use.

Methods

- We provide a high-level overview analyses for developing migraine related PRO measures once items have been generated from a literature review and qualitative work.
- These steps include data handling, item-level descriptives, dimensionality analyses, and validity evidence, and determining meaningful score different (MSD) / meaningful within-person change (WPMC) thresholds
- A running hypothetical, 8-item physical function (PF) PRO measure consistent with on-going work of the Migraine Clinical Outcomes Assessment System (MiCOAS) project is used, in which higher scores indicate better PF

Results

Item-Level Descriptives

- Frequency tables for the observed responses of each candidate PF item
- Item-level summaries are examined for floor effects, ceiling effects, and missing data to identify items that are performing sub-optimally
  - If many observed responses occur in the least severe [floor effect] or most severe [ceiling effect] response category, this may indicate that item is not informative/well-calibrated to the sample
  - Collapsing over response options may be necessary to avoid sparseness

Dimensionality Assessment

- In our hypothetical 8-item PF PRO measure example, a single underlying concept of interest/latent variable (that is, PF) is assumed to exist (Figure 1)

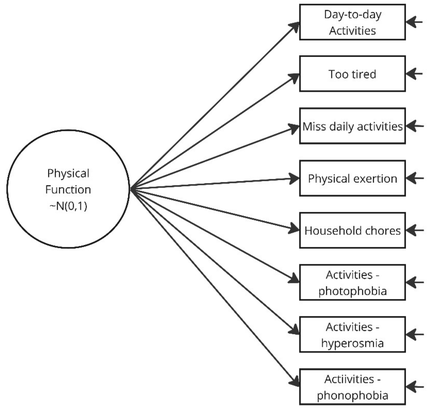
Item Factor Analysis (IFA)

- Confirmatory IFA is used to assesss the fit of the a priori model
- If the *a priori* model does not achieve good fit, exploratory IFA models may be used or items which do not load strongly on the single factor may be trimmed

Item Response Theory (IRT)

- IRT is used to examine individual items and the associated scores.
  - Item trace lines curves and test reliability functions are typically reported to visualize results

Figure 1. Example Path diagram



Reliability

- CTT analyses (i.e., coefficient alpha, alpha with item i removed, and item-total correlations) evaluate internal consistency reliability
- Test-retest reliability is evaluated using uncorrected Pearson correlations and intraclass correlation coefficients (ICCs)

Validity Evidence

- Convergent/discriminant evidence, how PF scores correlate with theoretically related constructs (stronger correlations) and more distal construct (near-zero or weak correlations)
- Known-groups evidence shows that clinically distinct groups (e.g., chronic vs episodic migraine [CM vs EM] patients) have differential PF scores (e.g., CM would be expected to have lower [worse] PF PRO measure scores than EM)
- Patient changes in PF should be reflected in PF scores (Sensitivity to Change) and PF change scores should correlate with related variables

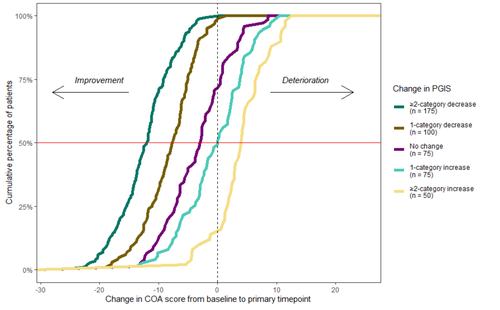
MSD / MWPC

- A single value (or range of values) to define “meaningful” change on the PF PRO measure is determined by triangulating across anchor- and distribution-based methods
- Candidate anchor variable should correlate at least 0.3 with PF scores
- Plot empirical cumulative distribution functions (eCDFs; Figure 2) and empirical probability distribution functions (ePDFs) across the levels of the anchors to support the evaluation of candidate MWPC thresholds

Conclusion

- In addition to qualitative information, extensive psychometric evidence is necessary to demonstrate that scores from a PRO measure are reliable and valid in a given context.

Figure 2. Example eCDF plot



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