

The SISAQOL-IMI Recommendations on Standardising the Use of Thresholds for Interpretation of Patient-Reported Outcome Results in Cancer Clinical Trials

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OBJECTIVE

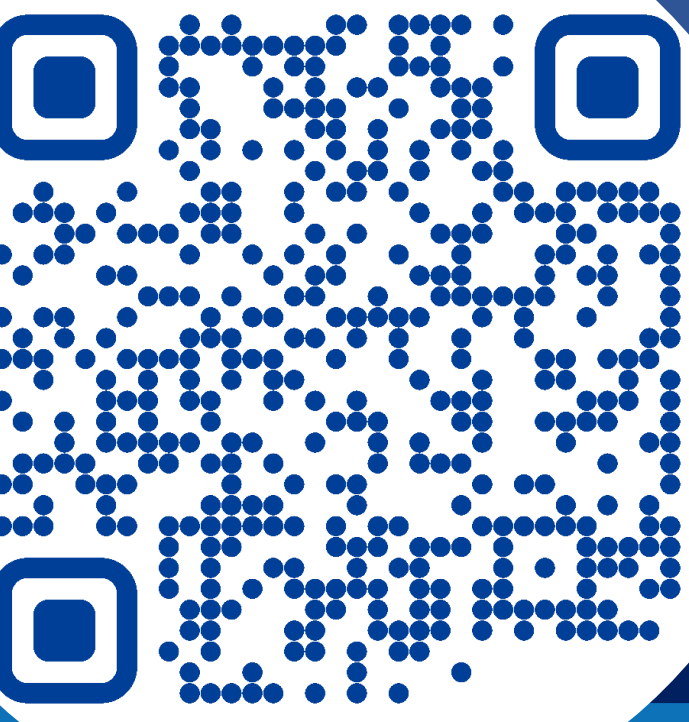
To develop international guidelines for standardisation of analysis and interpretation of patient-reported outcome (PRO) data in cancer trials, including guidance on terminology and appropriate use of PRO score interpretation thresholds

METHODS

- The SISAQOL-IMI Recommendations
- Were developed by a multi-stakeholder consortium of 41 organisations representing clinicians, patients, academics, industry, regulators, and HTA bodies
 - Were derived from a four-year consensus process including, e.g., five in-person consensus rounds, virtual meetings, a patient workshop, and stakeholder surveys
 - Built on the estimands framework
 - Are readily accessible through various resources

RESULTS

- Development of a harmonised terminology with precise definitions for PRO score interpretation thresholds
- Clarification and support of key criteria for selecting thresholds, including the use of patient-centered anchors
- Clear distinction between patient-level and group-level thresholds
- Guidance on linking specific threshold types to appropriate statistical analysis methods
 - A total of 27 recommendations concerning PRO score interpretation thresholds in cancer clinical trials
 - Detailed information available at www.sisaqol-imi.org



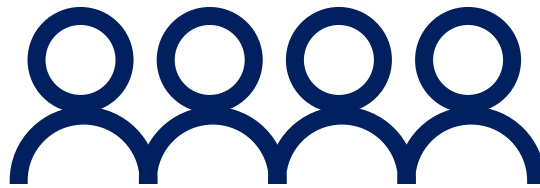
UMBRELLA TERM

‘PRO score interpretation thresholds’



PATIENT-LEVEL TERM

Threshold for
‘meaningful within-patient change’



GROUP-LEVEL TERM

Thresholds for
“meaningful within-group change”
“meaningful between-group difference”
“meaningful between-group difference in change”

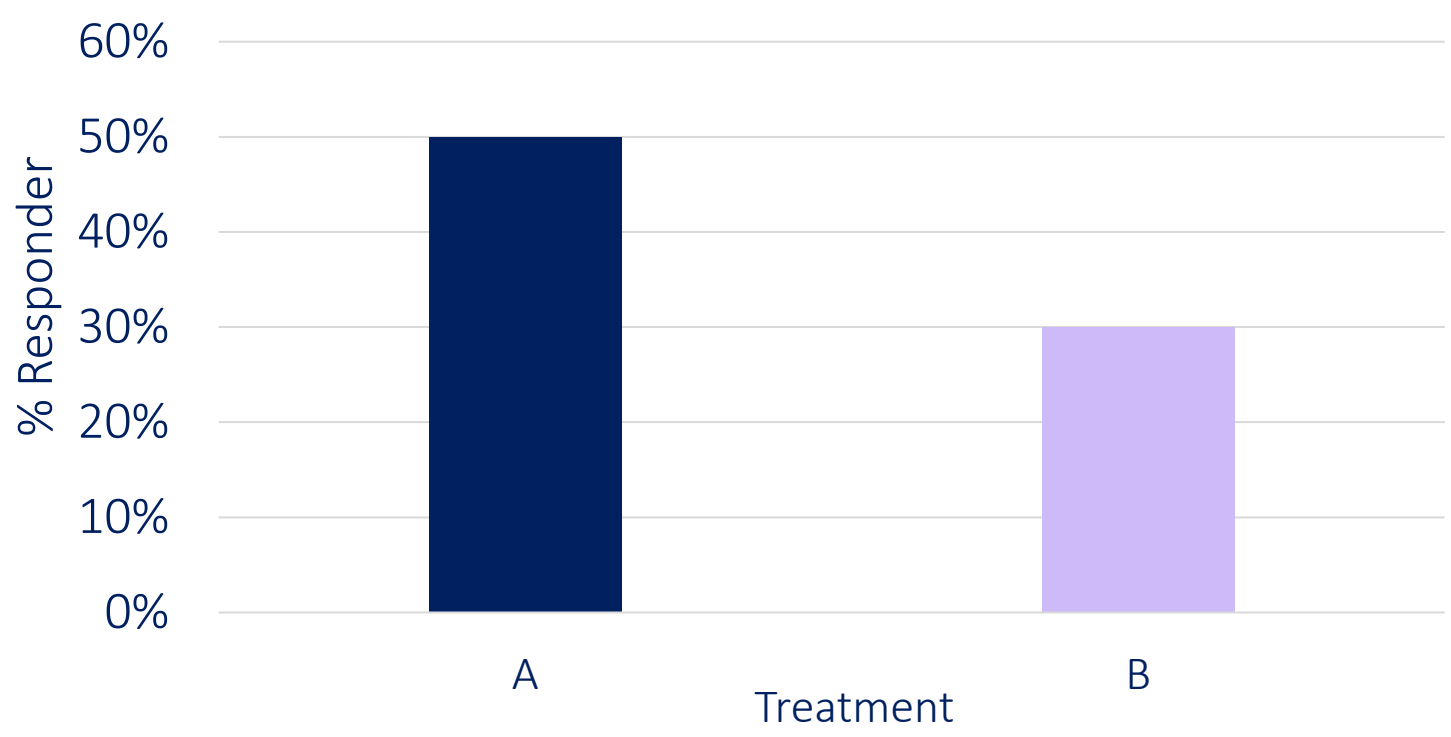
Thresholds are applied at PATIENT-level to interpret score change of individual patients

Thresholds are applied at GROUP-level to interpret mean differences

PROPORTION OF RESPONDERS

Thresholds to categorize individual patients as (non-)responders

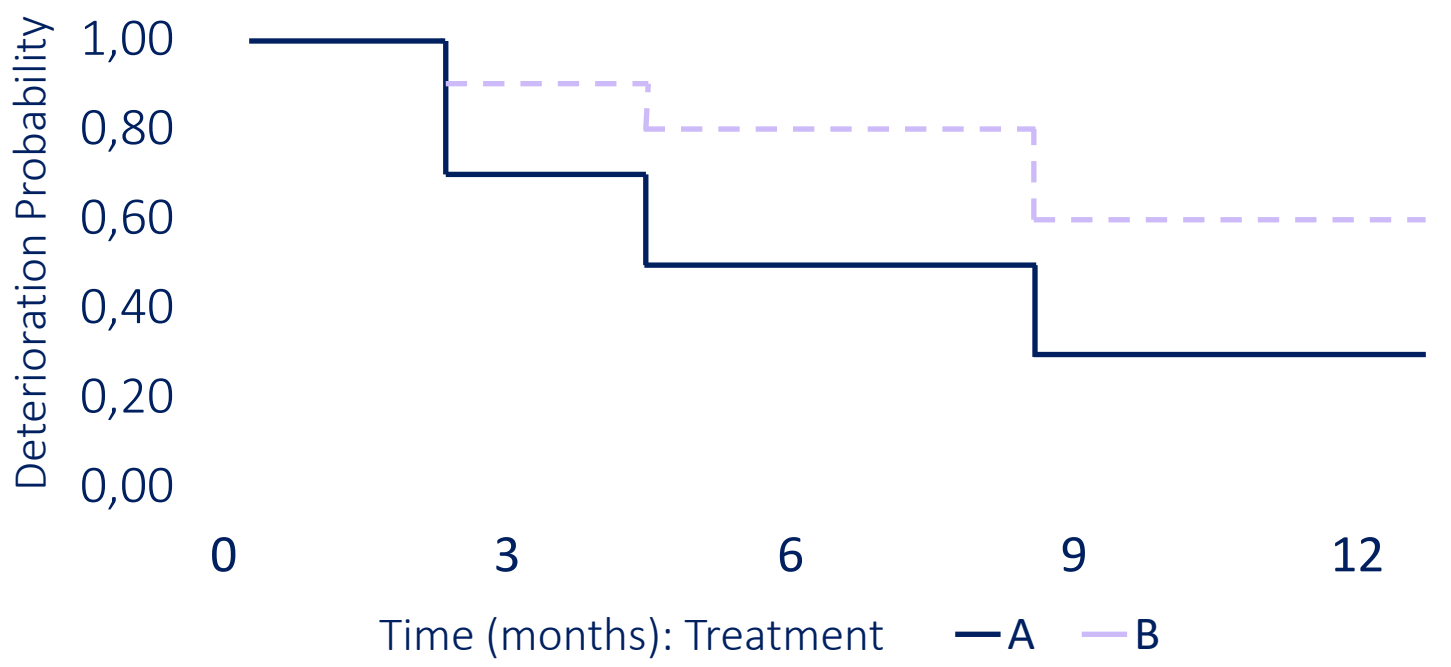
Example: Patient A has improved by +10 points since baseline – is she a responder?



TIME TO DETERIORATION/IMPROVEMENT

Thresholds to define meaningful change

Example: Patient B has deteriorated by -10 points three months after baseline – does this change reflect the event of interest?



MAGNITUDE OF DIFFERENCE/CHANGE

Within-group change:

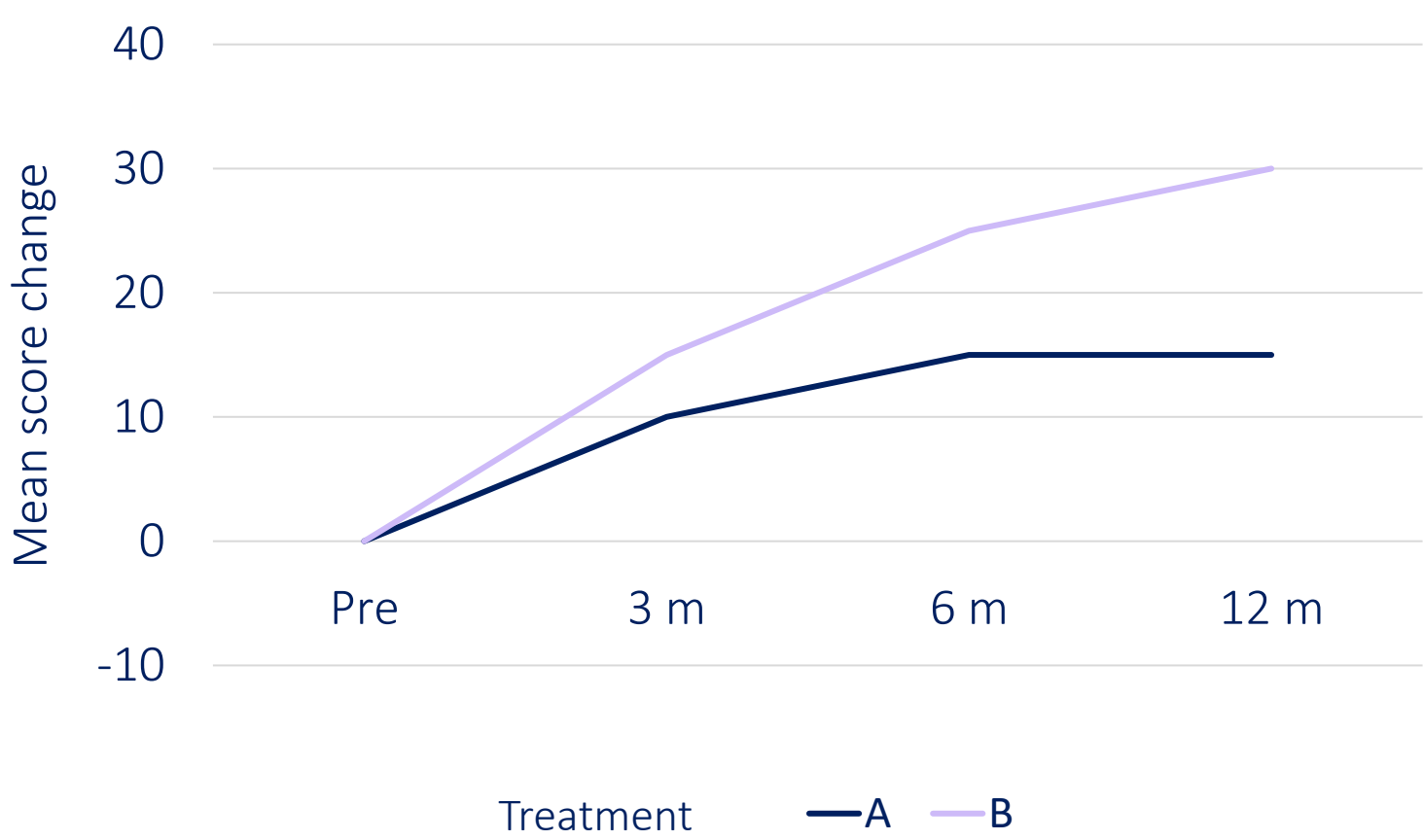
Example: Patients receiving treatment A had a mean improvement of +10.5 points since baseline – is this meaningful?

Between-group difference (Cross-sectional):

Example: At 3-month follow-up, the mean difference between treatment A and B is +5.3 points – is this meaningful?

Between-group difference in within-group change:

Example: Patients receiving treatment A have improved by +15.1 points, while patients receiving treatment B by +26.2 points – is this difference in improvement of +11.1 points meaningful?



EXAMPLE RECOMMENDATIONS ON REPORTING

THE TRIAL PROTOCOL, STATISTICAL ANALYSIS PLAN, OR TRIAL PUBLICATION SHOULD:

- > Provide a rationale for choosing a certain PRO score interpretation threshold
- > Report on what type of methodology the patient- and group-level PRO score interpretation thresholds are based on (e.g., anchor-based, or distribution-based)
- > State clearly if the PRO score interpretation thresholds are used to interpret meaningful within-patient change, meaningful within-group change, meaningful between-group difference, or meaningful between-group difference in change
- > Include a short description of the patient population in which the PRO score interpretation thresholds were established (e.g., diagnosis, or treatment type)

EXAMPLE TERMS AND DEFINITIONS

TERM:

Threshold for
‘meaningful within-patient change’

DEFINITION:

‘Thresholds for a meaningful within-patient change are reference scores for interpreting the magnitude of change of a PRO score of an individual patient that indicates what would be viewed as meaningful improvement or deterioration to an average patient.’

CONCLUSION

The SISAQOL-IMI recommendations and terminology for PRO score interpretation thresholds will support the ANALYSIS, INTERPRETATION and the REPORTING of PRO data in cancer clinical trials, leading to a more valid and critically appraisable understanding of PRO-based endpoints.

LITERATURE

Setting International Standards in Analyzing Patient-Reported Outcomes and Quality of Life Endpoints in Cancer Clinical Trials-Innovative Medicines Initiative (SISAQOL-IMI): stakeholder views, objectives, and procedures. Pe M, Alanya A, et al. Lancet Oncol. 2023 Jun;24(6):e270-e283. doi: 10.1016/S1470-2045(23)00157-2
International standards for the analysis of quality-of-life and patient-reported outcome endpoints in cancer randomised controlled trials: recommendations of the SISAQOL Consortium. Coens C, Pe M, et al. Lancet Oncol. 2020 Feb;21(2):e83-e96. doi: 10.1016/S1470-2045(19)30790-9.

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