Using Patient-Reported Outcome Measures in Cancer Clinical Trials: Perspectives For and Against a 'Modular Approach'

A Cancer Australia Quality of Life Technical Service (CQUEST) resource

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What is a modular approach to patient-reported outcome measurement?

There is growing concern among international stakeholders that the cancer clinical trial community has often relied on full-length questionnaires which may not always measure the quality of life (QoL) issues relevant for specific studies, contexts, populations, and stakeholders.

In 2021, the Food and Drug Administration (FDA) released guidance stating that

> "Assessing outcomes that patients find meaningful may reduce the collection of less important PROs, thereby limiting the unnecessary burden on patients" [1]

This has stimulated interest in customising patient-reported outcome measures (PROMs) in a more flexible manner.

In clinical trials, the modular approach has been defined as the selection and assessment of **specific patient- and clinically-relevant domains of interest**, purposefully-selected from multi-domain PROMs, which is then independently scored and interpreted [2, 3].

What are the benefits and challenges of the modular approach?

Benefits	Challenges
Promotion of scientific rigor	
• Investigators are required to justify the choice of domains (e.g., through a conceptual framework with specific hypotheses) • Enables more thorough assessment of primary PROs of more interest compared to secondary PROs	• Ensuring scientific rigor requires greater time and effort to select relevant domains • Unable to pick up unexpected effects that may otherwise be captured by full-length PROMs • Potential for bias in selecting domains to favour specific effects while minimising others
Respondent burden	
• Measurement is focused on the most clinically relevant domains, reducing respondent burden • Reduce unnecessary duplication of domains if multiple PROMs are used	• Demands certainty and justification that particular domains are irrelevant and can therefore be excluded.
Psychometric/measurement properties	
• Selected domains retain many established psychometric properties, if the domains were obtained from PROMs that have already been validated in a specific context.	• Item order effects may impact psychometric performance of domains when administered separately from the full-length PROM.
Trade-off between flexibility and comparability	
• Domains that are not available in a PROM can be appended • Flexibility in administering different domains only at timepoints when they can capture the most meaningful effects	• Limited comparability with other studies that have used full-length PROMs • Acceptability of the modular approach by health-technology assessment agencies is unclear

How do I apply the modular approach in my clinical trial?

In this exemplar case study, the modular approach can be applied in three different ways to develop a PRO strategy.

Context: Dr. Smith was developing a randomised phase II study of drug X + Y versus drug X alone for the management of symptoms in a population with disease Z.

Approach A: Using a study-specific conceptual framework, incorporating dedicated PROMs and/or domains to measure relevant QoL concepts

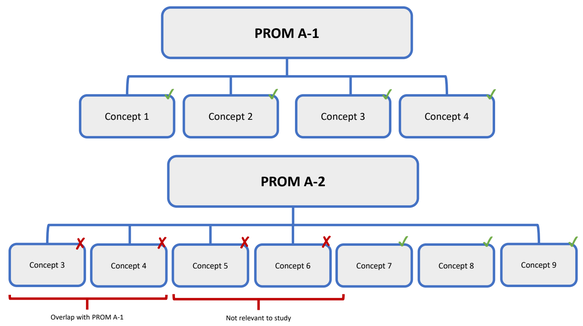
Dr. Smith identified 7 patient-reported concepts that are relevant and important to patients with disease Z, and which are expected to be affected by drug X +/- Y. He drafted a **conceptual framework** to illustrate the expected relationships between these concepts.

View our resource for instructions on how to draft a study-specific conceptual framework

After reviewing several candidate PROMs, no suitable, validated PROM that covered all 7 concepts was identified.

As a result, the team used:

- PROM A-1 (all 4 subscales assessing 4 key concepts) and
- PROM A-2 (selected 3 subscales assessing 3 key concepts).



An example of how the modular approach can improve PRO data quality:

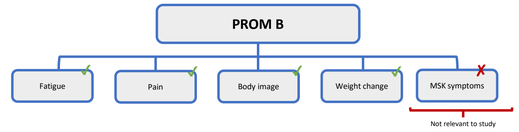
An analysis of FDA-registered trials for new immune checkpoint inhibitors found that PRO strategies **did not assess all eight adverse events** are unique to these novel immunotherapy agents [4].

Commonly used cancer-specific PROMs, such as the EORTC QLQ-C30, can be **supplemented by relevant PRO domains** (e.g., assessing rash and itching) to better inform treatment effectiveness while minimising the potential for biased assessment of toxicities.

Approach B: Using a full length PROM, removing domains less relevant to the study context

Dr. Smith planned to use PROM B in his study. PROM B is disease-Z-specific and consists of five multi-item domains. However, the literature indicates that musculoskeletal (MSK) symptoms are only relevant in patients with advanced disease Z.

Since the study includes only patients with early-stage disease Z, the team decided to use PROM B, excluding the musculoskeletal symptoms subscale.

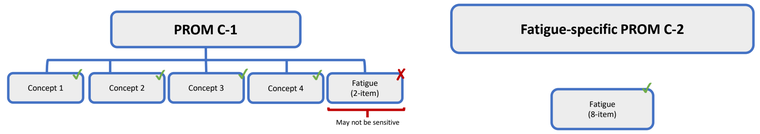


Approach C: Using a full length PROM, substituting domains that are primary/key secondary outcomes with dedicated PROMs/domains

Dr. Smith planned to use PROM C-1, which is disease-Z-specific and consists of 5 domains, all of which cover the concepts of interest that are important to his study.

Fatigue is a common symptom in patients with disease Z, and likely to be most improved by drug X + Y. However, the fatigue subscale of PROM C-1 is only two-items long, and Dr. Smith is concerned that this may not be sensitive to meaningful changes.

Thus, the team decided to use PROM C-2, which is an eight-item fatigue-specific instrument, to assess fatigue. To avoid duplication, PROM C-1 was used without its two-item fatigue subscale.



References

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2. Piccinin C, Basch E, Bhatnagar V, et al. Recommendations on the use of item libraries for patient-reported outcome measurement in oncology trials: findings from an international, multidisciplinary working group. Lancet Oncol. 2023;24(2):e86-e95.
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If you are interested in using the modular approach for PROMs in your clinical trial, please contact cquest@uts.edu.au for more information.

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