Enhancing Patient-Reported Outcome (PRO) Integration in Early-Phase Oncology Trials: Navigating Methodological Challenges and Opportunities

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INTRODUCTION

Background

- Patient-Reported Outcomes (PROs) provide essential insights into patients' treatment experiences, complementing traditional clinical metrics like overall survival and tumor response.
- Regulatory agencies, including the FDA, are increasingly acknowledging the value of incorporating PROs into early-phase oncology trials.

Rationale

- There is a growing recognition of the value of collecting PROs in early phases, as this information can inform clinical development and market access strategies.
- Early-phase trials (Phase I/II) present a valuable opportunity to capture data on patient tolerability, which can aid in optimizing dose selection and trial designs based on PRO experiences.

OBJECTIVE

Objectives

- **Assess the Literature**: Review existing studies to identify the advantages of integrating PROs in early-phase oncology trials, particularly in enhancing tolerability data and aiding dose-finding studies.
- **Investigate Methodological Challenges**: Analyze issues related to recruitment strategies, data interpretation, and barriers to implementation.
- **Identify Collaboration Opportunities**: Explore ways for sponsors, regulatory agencies, and other stakeholders to work together in developing a standardized approach for integrating PROs.

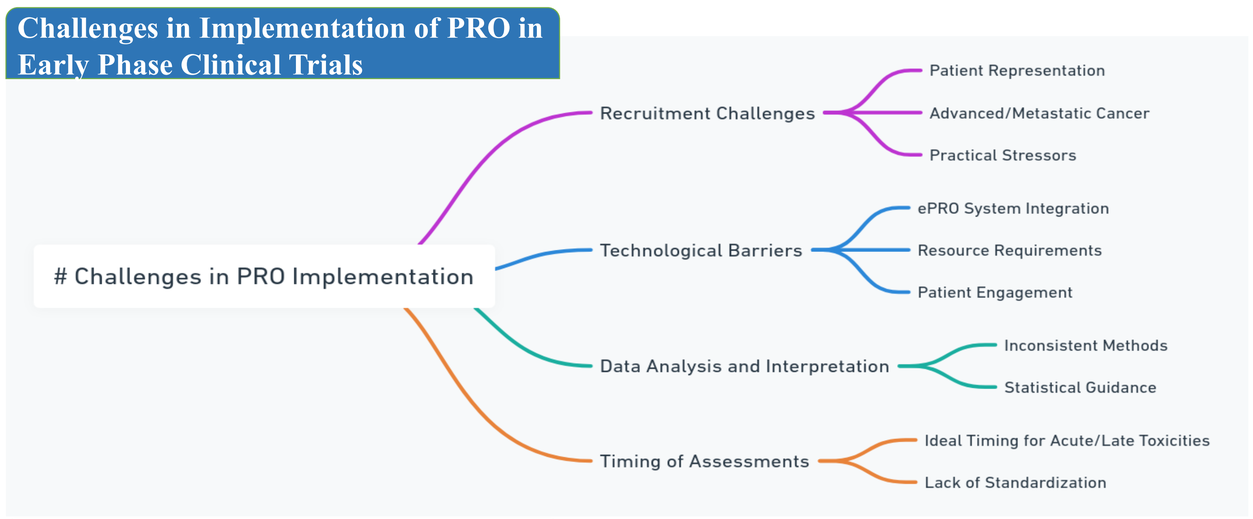
METHOD

Methods

A scoping literature review was conducted to identify relevant studies, guidelines, and grey literature on the integration of PROs in early-phase oncology trials.

RESULTS

We identified 52 early-phase clinical trials and 14 additional scientific publications that met our eligibility criteria for analysis. Common issues and challenges reported by these researchers were extracted and are presented here.



Implementation barriers

Practical barriers, such as integrating electronic PRO (ePRO) systems into early-phase trial workflows, were significant. In one Phase 1 breast cancer trial, ePROs integration required additional resources for staff training and patient support, but it ultimately streamlined data collection and improved compliance.

- A survey of 112 clinical trial stakeholders found that 66% viewed the workload associated with PRO data collection as a significant barrier, fearing it would overburden staff. In a Phase 1 hematology trial, innovative PRO collection methods - like ePRO, smartphones, and activity trackers - failed to engage patients consistently. Many participants were unwilling to provide regular PRO data, underscoring the challenges of implementing novel technology-based approaches (Douma 2020).

The timing of PRO assessments is crucial, yet no standardized approach was adopted across trials. Currently, there are no guidelines for the ideal timing of PRO data collection, which is essential for effectively capturing both acute and later toxicities.

Recruitment methodologies and representiveness of patients

When recruiting patients, it is essential to consider how their characteristics may influence later phase 3 trials.

- Phase I patients often present with more advanced or metastatic cancer and may experience physical symptoms from prior treatments (e.g., surgery, radiation, chemotherapy, targeted therapies, or immunotherapy).
- They also face considerable emotional and practical stressors, such as anxiety about disease progression and financial concerns. Due to these unique challenges, phase I populations may not accurately reflect those in later phases.

Currently, there are **no established guidelines** for optimal recruitment strategies in early-phase trials.

PRO measurement tools

Assessing PROs in early-phase clinical trials shows a significant lack of consensus on the ideal measurement tools.

Concerns about the length and specificity of these tools require careful evaluation.

- A survey of 112 clinical trial stakeholders found that 72% identified the lack of guidance on selecting appropriate PRO measures as a major barrier (Lai-Kwon et al., 2022).
- Chosen measures should be brief to minimize patient burden, as highlighted by international consensus (Aiyegbusi et al., 2024).
- For example, **Efforts are underway to develop suitable tools;** van Rensburg et al. (2023) adapted the PRO-CTCAE survey, reducing it from 128 to 58 questions. However, this tool is diseases-specific and needs further validation.

Analysis and interpretation challenges

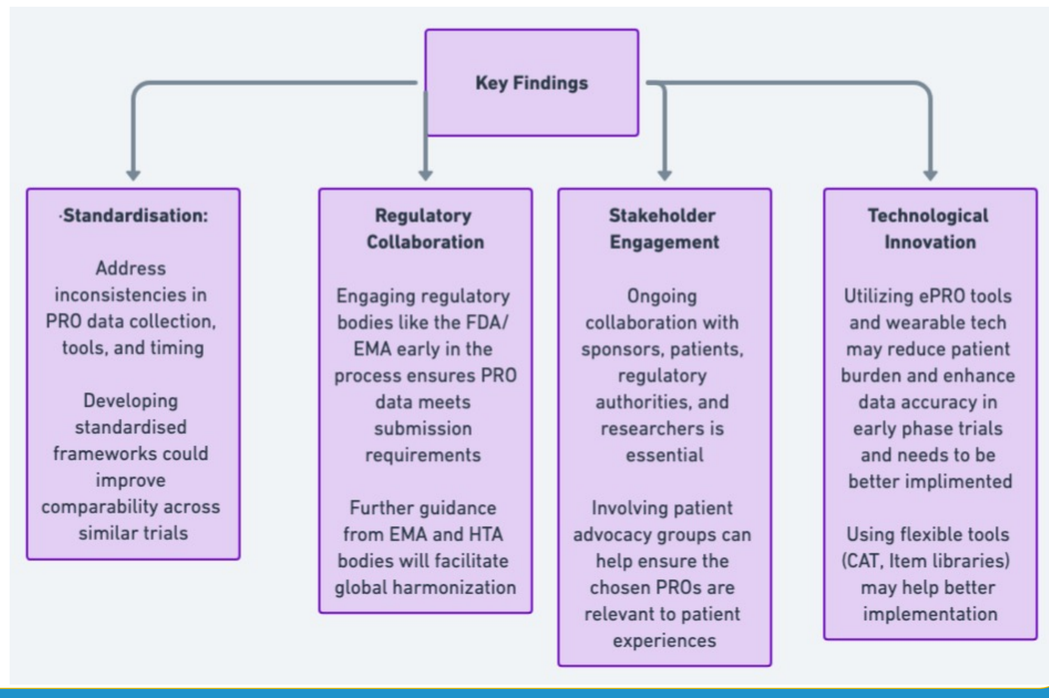
Data from phase 1 trials, similar to larger phase 3 trials, indicate **a lack of standardized methods** for analyzing and interpreting PRO data, leading to inconsist tolerability assessments.

- Alger et al. reviewed 35 early-phase trials (2015–2022) and found that statistical methods, interpriation, and reporting of PRO analyses were often inconsistent and poorly documented. This lack of standardization complicates the comparison of findings across studies, underscoring the need for improved statistical guidance and interpretation for early-phase trials.

Establishing international guidelines for interpreting PROs in early trials would be beneficial. The SISAQOL-IMI consortium is currently working on recommendations expected in 2025.

CONCLUSIONS

- Integrating PROs in early-phase oncology trials can greatly enhance our understanding of not just efficacy, but also tolerability and patient quality of life.
- However, further efforts are necessary to ensure that data from typically small-scale, single-arm open-label trials are meaningful. Key considerations include standardization, regulatory collaboration, stakeholder engagement, and technological innovation.



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