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Review

Improving completion rates of patient-reported outcome measures in cancer clinical trials: Scoping review investigating the implications for trial designs

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ABSTRACT

Background: Patient-reported outcomes (PROs) play a crucial role in cancer clinical trials. Despite the availability of validated PRO measures (PROMs), challenges related to low completion rates and missing data remain, potentially affecting the trial results' validity.
This review explored strategies to improve and maintain high PROM completion rates in cancer clinical trials.
Methodology: A scoping review was performed across Medline, Embase and Scopus and regulatory guidelines. Key recommendations were synthesized into categories such as stakeholder involvement, study design, PRO assessment, mode of assessment, participant support, and monitoring.
Results: The review identified 114 recommendations from 18 papers (16 peer-reviewed articles and 2 policy documents). The recommendations included integrating comprehensive PRO information into the study protocol, enhancing patient involvement during the protocol development phase and in education, and collecting relevant PRO data at clinically meaningful time points. Electronic data collection, effective monitoring systems, and sufficient time, capacity, workforce and financial resources were highlighted.

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Discussion: Further research needs to evaluate the effectiveness of these strategies in various context and to tailor these recommendations into practical and effective strategies. This will enhance PRO completion rates and patient-centred care. However, obstacles such as patient burden, low health literacy, and conflicting recommendations may present challenges in application.

1. Introduction

The value of assessing patient-reported outcomes (PROs) in cancer clinical trials is increasingly recognized by patients, policymakers and regulatory agencies [1]. PRO measures (PROMs) enable patients to report their well-being, functioning, disease-related symptoms, treatment-induced toxicities and other issues related to health-related quality of life (HRQoL).

The implementation of PROMs in clinical trials needs improvement to ensure relevant and accurate data [2]. High-quality PRO data collection before analysis is crucial, yet low completion rates and missing data remain challenges. [1,3].

A systematic analysis revealed 95 % of trials report missing PRO data, with a median of 9 %, ranging from 0–70 %, threatening internal validity and generalizability [4,5].

While statistical handling of missing PRO data is well-researched, a preferred strategy is to prevent missing data by improving completion rates [1,6]. Completion rate refers to the ratio of PRO assessments received versus expected within a timeframe [1]. Various factors influence PROM completion rates, including trial design, logistics, administration, and patient-related issues. Implementing strategies in these areas can maintain and improve PRO completion rates [7].

This scoping review aims to provide a synopsis of published strategies to improve and maintain high PROM completion rates in cancer clinical trials, focusing on mapping evidence rather than conducting a critical appraisal of individual studies.".

2. Methodology

2.1. Literature search

A literature search on strategies to improve PROM completion rates in cancer clinical trials was conducted in Medline, Embase and Scopus. The full search strategies can be found in appendix 1. The last search was performed on January 2nd, 2024. References of eligible articles were screened. Policy documents and guidelines from leading regulatory and cancer organizations were consulted. Reporting is based on the PRISMA extension for scoping reviews [8].

2.2. Study selection

All journal articles published in English between January 2012 and December 2023 with guidance on improving PROM completion rates for adult cancer patients in clinical trial settings were included.

Policy papers with strategies to enhance completion rates of PRO data for cancer patients in clinical trial settings were also included. Cancer survivorship research referring to studies on the long-term effects of cancer and its treatment were excluded. Conference presentations, study protocols, and publications not relevant to clinical trial settings, without full-text availability, or written in a language other than English were excluded.

2.3. Study selection and data extraction

Study selection involved screening titles and abstracts by a single reviewer, with a second reviewer screening 10 % for reliability and accuracy of the findings. Given the absence of disagreements between the first and second reviewer, it was concluded that single-reviewer screening was appropriate for ensuring consistence in abstract selection. Full-text papers were assessed by two reviewers. General study characteristics and recommendations were extracted using a pilot-tested form and categorized per the structure of the Standard Protocol Items: Recommendations for Interventional Trials – PRO (SPIRIT-PRO) statement [9].

3. Results

A total of 2963 abstracts were identified and screened, and 65 papers underwent full-text review. Altogether, 16 peer-reviewed papers and 2 policy papers were included in this review. Fig. 1 provides a summary of the review process.

3.1. General description of papers included in the literature review

Eighteen papers in total were included in this review, categorised as clinical trials (n = 8; 44 %), reviews (n = 5, 28 %), guidelines (n = 2; 11 %) meta-analyses (n = 1; 6 %), qualitative study (n = 1; 6 %) and an editorial (n = 1; 6 %). Table 1. provides details of the included papers. Although only 5 (28 %) of the papers provided a definition for completion rate (see appendix for definitions of completion rate), the majority (n = 10; 56 %) provided reasons for low completion rates. These reasons included process-based [10] and administrative reasons [11–14] staff's lack of perceived value of PROMs and lack of adequate time in personnel schedule [15,16] patients' attitude [10], patients' well-being including being too unwell or tired [10,12,17] patient refusal, missed appointments [11] or patients forgetting to complete and return the PROM [13,17,18] as well as the lack of feedback regarding the PROM outcome [16]. In total, 114 different recommendations to increase completion rates have been identified. The most frequently cited recommendations included the following: using electronic PROMs (n = 7), educating participants about PROs at the study start (n = 5), collecting clinically relevant PRO data (n = 5), providing training to site personnel (n = 4), sending participant reminders (n = 4) and collecting reasons for missing data and about non-responders (n = 4). The recommendations are summarised into 8 categories in Table 2. A summary of the recommendations can be found below.

3.2. Identified recommendations

3.2.1. Stakeholders involved and study design

A committed, collaborative and trained team and site coordinator is essential throughout the study design [13,15,19–21]. Patient involvement remains critical during protocol development [19].

The study protocol should include comprehensive PRO information, such as the PRO specific endpoint, rationale for the PRO assessment, patient population, handling of missing data and data collection time points [15,20]. These time points should be practically feasible, clinically meaningful and aligned with patients' visits to the clinic and scheduled prior to medical consultations or procedures [19,22].

It is recommended to make staff require to try to obtain PRO data in study and include PRO data as an eligibility criterion as it shows the importance of PRO data collection [19,21]. PROMs should also be introduced by a trusted clinician at an appropriate time [10].

In one study, the importance of a wide enough window for back-up PRO data collection was identified [23]. The completion time of PROMs and therefore the length of the survey should be limited to avoid additional patient burden [23]. The location of PRO data collection should be private and flexible, allowing patients to complete PROMs remotely

and in the clinic [17,21,24]. Additionally, it is recommended to conduct a pilot study to assess the feasibility of collecting PROM data [21].

3.2.2. PRO assessment, PROM characteristics and mode of assessment

Careful selection of PROMs, considering the content's clinical relevance, characteristics of the target population and potential patient burden, is important [19]. The format of the PROM should be clear and professional [24].

A multi-model data collection approach, including electronic and paper-based PROM options, should be offered [25], with preference given to electronic data collection [18,22,26].

Electronic PROMs (ePROMs) should allow for automated data collection, reminders and feedback, real-time compliance monitoring, and should have an intuitive interface, include boxes for missing items and options for patients with tactile, vision or hearing disabilities [23]. The use of ePROMs should be easy without difficult passwords and software [10–13,16,18,19,23,25–27]. Display PRO results in a user-friendly manner for clinicians and patients is also deemed useful [10].

3.2.3. Participant support and education

Education of patients on the importance of PRO data and how to complete a PROM as well as automated feedback to the patient based on their outcomes also contributes to higher completion rates [13,19–23]. Providing instructions to guide patients in the completion of PROMs, identifying those who need help, offering assistance, and providing tablets with data allowance for remote completion of ePROMs are essential [10]. Encouraging patients to complete PROMs, for example with non-financial incentives, is recommended [13,17].

3.2.4. Monitoring and resources

Central and site monitoring are important, and awareness of compliance issues should be raised during site committee meetings [10,11,13,19–21,23]. Reminders for PROM completion should be implemented, with personnel contacting participants if no response is received after automatic reminders are sent [23]. However, particularly patients with advanced cancer may prefer not to receive reminders as this reminds them of their poor health [16]. Data should be collected on reasons for missing PRO data as this may provide insight on completion issues and is valuable for statistical modelling of missingness [10,11,19,23].

PRO data should be handled with the same importance as other clinical data, and sufficient resources should be allocated to support both patients and staff [21]. It is important to allocate time, capacity, workforce and financial resources to handle issues occurring outside of the clinical appointments, especially if data is electronically collected at home [10]. Additionally, PROs could be incorporated into clinical systems to ensure efficient use by health care staff [10].

4. Discussion

This scoping review highlights strategies to improve PROM completion rates in clinical trials and underscores the importance of considering clinical relevance and practical feasibility.

A multidisciplinary team including patients involved in protocol development, PROM selection and study implementation is vital [13,15,19,20].

Supporting and assisting both patients and study staff and highlighting to them the importance of PRO data collection, and providing updates on completion rates and interim results, are important during the study. Central and site-specific monitoring system coupled with adequate resources is imperative. Patient, staff and institute burden should be consistently considered in all phases of the study. While our data is applicable to the cancer clinical trial setting; it aligns with broader literature reviews [6,28,29]. These reviews stress the crucial role of staff commitment and advocate for meticulous planning and ongoing monitoring of activities. They emphasize the importance of motivating patients to complete PROMs, while considering resource and patient burden and providing technology that integrates PRO data into existing clinical workflows. Patient engagement and sharing information about the study remains essential throughout the study [6,28].

4.1. Barriers in improving completion rates in cancer clinical trials

The involvement of patients is not routinely implemented and varies greatly in current cancer clinical trials [30–32]. To include the patient's perspective and improve PRO completion rates, their involvement in PROM implementation in clinical trials is essential [6,28,31].

Patients and patient advocates offer invaluable insight regarding PROMs, appropriate recall interval, assessment time points, patient burden and strategies for engaging them [28]. Moreover, patient advocacy organisations play an important role in promoting the acceptance of PROMs, support patient education on the how to complete them and have the capacity to disseminate information and raise awareness about the importance of PROMs and PRO completion rates globally, given their representation of vast numbers of patients and caregivers worldwide.

Successful patient involvement in PRO implementation in clinical trials requires resources, education and dedicated commitment of both patients and involved staff. The challenges associated with involving

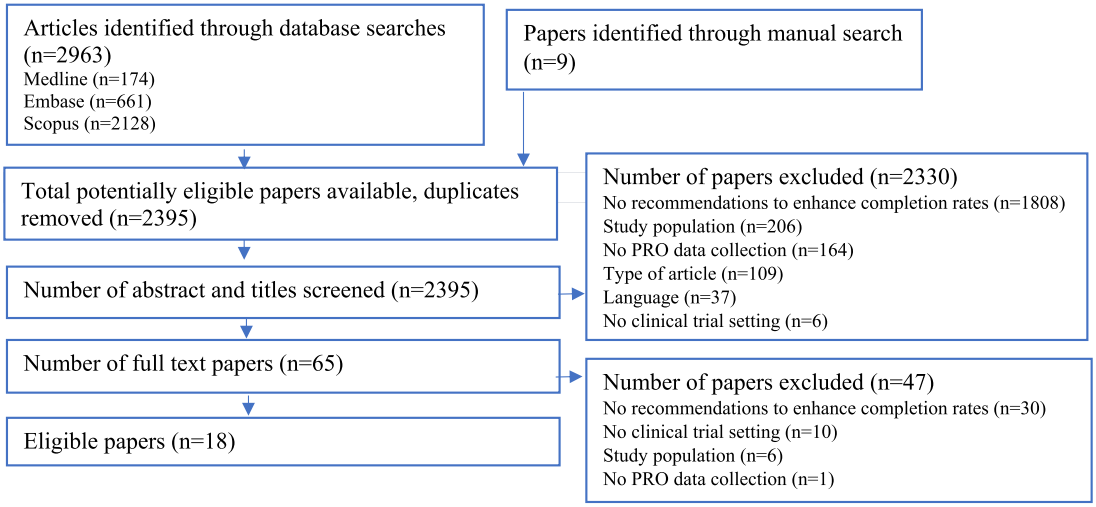

Fig. 1. Flow chart describing the selection of eligible papers.

Table 1
Details of included papers.

Reference	Type of paper	In case of clinical study, type of study	Main objective of paper	Type of cancer	PROM	Frequency of PRO assessment	Completion rate (%)	Reasons no completion
Appleyard (2021) [11]	Clinical study	Feasibility study	To explore the feasibility of collecting ePROs in older prostate cancer patients with different digital experience.	Prostate cancer	EQ−5D; EORTC QLQ-C30; PR25	Baseline, 1, 2 and 3 months	100 (n = 40) (baseline, 88 (n = 35) (3 months)	Lost to follow-up
Atherton (2016) [12]	Meta-analysis	N/A	To determine the extent of, and characteristics associated with, missing PROs.	Multiple cancer types	N/A			
Basch (2019) [13]	Editorial	N/A	To review strategies to optimize PROMs completion in clinical trials.	Any cancer	N/A			
EMA (2014) [14]	Guideline	N/A	To provide guidance on the use of PROMs in oncology studies.	Any cancer	N/A			
EORTC (2002) [15]	Guideline	N/A	To provide guidance for assessing QoL in EORTC trials.	Any cancer	N/A			
Flannery (2022) [16]	Clinical study	RCT	To determine whether and the type of assistance with PRO completion older advanced cancer adults (70 +) need.	Multiple cancer types	OARS, Fall history, GAD−7, GDS, Health Care Climate Questionnaire; Press-Ganey Patient Satisfaction Survey; FACT-G, MDASI, The Distress Thermometer; INQ-R; RDED, PEACE, PEPPI scale, Control Preferences Scale; MUIS-Complexity Subscale.	Baseline, 6 weeks, 3 months, 6 months	Not reported	Mainly due to death or hospitalization/ hospice
Friis (2020) [17]	Clinical study	Feasibility study	To design an ePROM for symptom monitoring and to evaluate the feasibility, usability and acceptability in metastatic lung cancer patients.	Lung cancer	EORTC QLQ-C30, LC13	Weekly for 4 weeks	100, 100, 94, 78	Not reported
Giordano (2020) [18]	Review	N/A	To discuss challenges of implementing ePROMs.	Not specified	N/A			
Hoque (2019) [19]	Clinical study	RCT	To compare three different methods of PROM data collection.	Prostate cancer	EPIC−26	1 time	98	Not reported
Kennedy (2021) [20]	Clinical study	Feasibility study	To explore compliance and acceptability of an ePROM on self-reported AEs and HRQoL.	Multiple cancer types	EORTC QLQ-C30; PRO-CTCAE	PRO-CTCAE: weekly, QLQ-C30: every 4 weeks for 12 weeks	QLQ-C30: 96.0, 88.5, 84.5, 79.1	Death and withdrawal (including time required to participate, being unwell, stopped treatment, computer problems)
King-Kallimani (2021) [21]	Review	N/A	To assess PROs after treatment discontinuation collected in commercial clinical trials.	Multiple cancer types	N/A			
Lidington (2022) [22]	Review	N/A	To examine the protocol content, data completeness and publication of PROs from interventional trials and explore factors associated with data missingness and PRO publication.	Multiple cancer types	N/A			
Movsas (2014) [23]	Clinical study	RCT	To test the feasibility of an electronic web-based system to improve compliance.	Prostate cancer	EPIC	Baseline, 6 and 12 months	98, 96, 82	Patient refusal, patient could not be contacted or unknown

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Table 1 (*continued*)

Reference	Type of paper	In case of clinical study, type of study	Main objective of paper	Type of cancer	PROM	Frequency of PRO assessment	Completion rate (%)	Reasons no completion
Pugh (2021) [24]	Review	N/A	To evaluate the effectiveness of email reminders and notifications on PROM submission timeliness and compliance.	Breast & prostate	N/A			
Romano (2022) [25]	Qualitative study	N/A	To characterize the experience of metastatic breast cancer patients with PROMs in a clinical trial setting to determine the importance, relevance, barriers, and facilitators for completion.	Breast	N/A			
Teixeira (2022) [26]	Review	N/A	To analyse PROs used for regulatory approval of oncology drugs within the EU.	Multiple cancer types	N/A			
Tran (2020) [27]	Clinical study	Pilot study	To explore the feasibility and acceptability of collecting ePROs using validated HRQoL PROMs for prostate cancer.	Prostate cancer	EPIC−26, EPIC-CP, FAPSI−8	Weekly for 12 weeks	Not reported	Not reported
Zivanovic (2020) [28]	Clinical study	Pilot study	To evaluate the feasibility of an electronic symptom-tracking platform for patients recovering from ambulatory surgery.	Gynaecologic cancer	PRO-CTCAE	Daily for 6 days	10, 13, 9, 11, 13, 41	Too tired, not remembering, or having technical difficulties with the computer

Abbreviations: AE, adverse event; EORTC, European Organisation for Research and Treatment of Cancer; EPIC-26, Expanded Prostate Cancer Index; EPIC-CP, Expanded Prostate Cancer Index Composite for Clinical Practice EQ-5D, EuroQol 5 Dimension; ePRO, electronic patient-reported outcome; ePROM, electronic patient-reported outcome measures; EU, European Union; FACT-G, Functional Assessment of Cancer Therapy – General; FAPSI-8 Functional Assessment of Cancer Therapy Advanced Prostate Symptom Index; FDA, Food and Drug Administration; GDS, Geriatric Depression Scale; HRQoL, health-related quality of life; INQ-R, Interpersonal Needs Questionnaire-Revised; LC, lung cancer; MUIS, measurement of uncertainty in illness; MDASI, MD Anderson Symptom Inventory; N/A, not-applicable; OARS, Older American Resources and Services; PEACE, Peace, Equanimity, and Acceptance in the Cancer Experience; PEPPI, Perceived Efficacy in Patient-Physician Interactions; PRO, patient-reported outcome; PRO-CTCAE, Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events; PROM, patient-reported outcome measure; QLQ-C30 Quality of Life Questionnaire - Core; PR, prostate cancer; RCT, randomized-controlled trial; RDED, Reluctance to Disclose Emotional Distress; QoL, quality of life

patients in clinical trial design have been extensively documented [32]. Practical guidance exists on incorporating patients' perspectives into the design of clinical trials, but no specific guidelines are currently available on the PRO part of the study [33]. This calls for more research into the engagement of patients and patient advocacy organisations in protocol development for clinical trials with PRO endpoints. This research is crucial, as their active participation aims to enhance both the study's quality and representation of patients' perspective.

A major barrier to the successful implementation of PROMs is the requirement of additional human and financial resources [34]. The recommendations in the literature review include selecting trained staff to coordinate and monitor PRO activities and appointing site staff responsible for PRO data collection and patient engagement. However, this can result in an increased workload for the staff, which is particularly challenging due to the difficulty in finding qualified healthcare staff in the current era. Hence, efficient integration of PRO data collection into the health care professionals' workflow is essential [35]. Supporting this integration requires infrastructure for data management, education materials and monitoring systems [34,35].

Despite the numerous recommendations found in our review, none directly addressed the challenges of language barriers, literacy and health literacy or digital literacy in (highly relevant for ePRO). However, a previous study showed a trend between lower PRO completion rates and patients with a primary language different from the local language [36].

Furthermore, approximately 20 % of the European population is functionally illiterate [37]. This refers to the lack of essential reading and writing skills required to function in society, presenting a significant challenge to completing PROMs. Patients with low literacy levels and health care staff have reported feeling embarrassment when faced with patients' literacy challenges. These patients may lack confidence in completing PROMs and may provide excuses to avoid completing them. Health professionals, on the other hand, may be hesitant to address suspected low literacy out of concern that labelling patients as such could discourage them from returning to the clinic.

To address these challenges, it is important to ensure that PROMs and associated PRO training materials are designed to be comprehensible to patients with varying literacy and educational backgrounds. Additionally, providing patients with PROMs in their native language, offering assistance and performing relevant readability assessments can further improve the PRO completion rates. All of these recommendations shall be amplified by an intuitive interface and adequate interaction design, in case of ePRO modality for the PRO collection, especially if conducted in the daily life environments of the patients.

Our review identified numerous recommendations for improving completion rates in cancer clinical trials. However, it remains unclear which of these recommendations are both practical and significant in enhancing completion rates. Furthermore, implementing a total of 114 recommendations presents a practical obstacle, particularly as some recommendations seem to conflict with each other. For example,

Table 2
Overview of trial design implications to improve completion of PRO assessment.

Category	Sub-category	Specific recommendations*
Stakeholders involved	**Patient involvement**	**Involve patients in PRO study design**
		Involve patients in PROM selection, study design (e.g., PRO frequency, assessment modalities), and overall study feasibility assessment
	Staff involvement	**Commitment from all staff, including physicians**
		Collaboration between study coordinator, data centre and individual organisation
		Regular contact between data manager/nurse and the study investigator
		The study coordinators need to understand the value and rationale of PROMs and need to use this data to motivate the study investigators
		Select staff to coordinate and monitor PRO activities throughout the study
		Appoint a PRO trained and qualified person responsible for PRO data collection in each study site
	Characteristics of site coordinator	Committed to the study
		Interpersonal skills, basic technical skills if ePRO are included
	Train/support staff	***Offer training at start and throughout the study to site staff, site coordinators and clinical investigators***
		Train staff on purpose and importance of PRO assessments
		Educate staff on the protocol conduct
		Ensure staff is familiar with system from patient perspective to trouble shoot issues related to ePRO
		Offer support to sites/staff (e.g., psychological support, bereavement counselling)
		Educate sponsors
		National training courses in data management could include general issues around PRO data collection
		Publish and promote PRO data if the data has contributed to the scientific validity of the study
Study design	**Protocol development**	***Comprehensive PRO information, including PRO timing, PRO assessment modalities in study protocols***
		Include/plan PRO aspects of the study carefully (e.g., PRO frequency, assessment modalities)
		Protocol adherence to SPIRIT-PRO guideline
		Use behaviour theory-informed motivational information in the protocol
		Specify the rationale for PRO assessment
		Well-defined and adequate population described in study protocol
		Specify how missing data will be handled
		Develop protocol guidance for investigators
		Publish guidelines providing recommendations and best practices on PRO strategy
	Objective	Define endpoints/hypotheses and ensure PRO endpoint is scientifically compelling
		Defined research objective for follow-up PRO data
		Make PRO a co-primary endpoint
	Eligibility criteria	**Make baseline PROM an eligibility criterion when ethically justifiable and practically feasible**
		PRO data collection should be mandatory and integral part of the study
	Pilot study	Implement local pilot study prior to the start of the main study, followed by a debriefing meeting
PRO assessment	**Time point selection**	**Specify the required PRO assessment time points**
		Select clinically meaningful time points, while considering the PRO recall period
		Timepoints when expected high levels of completion by the individual patient
		Consider patient burden
		In case of event-driven PRO assessment, only preform in a subsample rather than subjecting the entire sample
	Time window	A wide enough window for backup data collection
	Completion time	Limit estimated completion time of baseline PRO assessments to 20 minutes and 10-15 minutes completion for subsequent assessments
	Time of completion	Align PRO assessments to clinic visits to capture while the patient visits the clinic
		PROMs should be administered at the beginning of a clinic visit prior to medical interviews or procedures
	Treatment cessation	Specify procedures for contacting participants for PRO assessment after treatment cessation
	Introduction of PROM	Introduced PROM by trusted clinician
		Appropriate timing of PROM introduction
	Location of assessment	**Combine remote/home-based completions by using ePROMS**
		While in clinic, provide a private and comfortable environment for completing PROM
Characteristics of PROM	**PROM selection**	Select the most appropriate instrument
		Collect clinically relevant PRO data
		Clear/simple content and instructions of questionnaires
		Allow patients to skip irrelevant items
		Minimise patient burden
		Address feedback from patients on burdensome items or format during PROM validation process
	Length	**Should be brief (no more than 40–50 items if infrequently administered; no more than 10–20 questions if frequently administered)**
	Format	User-focused PRO design
		Clear/simple format
		Large/clear font
Mode of assessment	**Choice of MOA**	**Multi-model data collection approach (including ePROM and paper-based PROMs)**
		ePROM is encouraged
	ePROM features	Use of automated electronic data collection
		Keep it simple, without difficult passwords, soft/hardware
		Allows real-time compliance monitoring
		Allow participants to complete on their preferred electronic device
		Provision of login details on paper and via e- mail
		Intuitive interface,
		Should offer options to participants with tactile, vision, or hearing impairments (e.g., choice of web, handheld, or automated telephone system)
		Adjustable font size
		Read aloud options
		Automatic completion confirmation

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Table 2 (*continued*)

Category	Sub-category	Specific recommendations*
		E-mail PRO assessment reminders to participants
		Importance of real-time feedback to users so that they can be confident that their responses have been recorded
		Potential for family and friends to facilitate digital access
		Provide tailored advice to patients based on their responses
		User-friendly presentation of longitudinal results for clinician and patient
		Dialogue boxes for missed items
Participant support and education	**Support**	Instructions to give to participants must be specified in PRO administration guidance
		Available staff to give verbal explanation during the first time the patient is asked to complete PROM
		Provide a verbal clear explanation on the reasons for collecting. This information should be supported by a written information sheet
		Inform patients what will happen to their complete PROMs
		Provide information on when the PROMs are due
		User guide on paper and electronically
		Prospective identification of patients who are less able to completeOffer assistance to participants who need it
		Provide encouragement to participants when completing PROs
		Showing appreciation once the questionnaire is completed and expressing an interest in any concerns the patient may raise
		Provide a tablet/data allowance
	Feedback	Opportunities for the patient to make inquiries to the medical staff
		Reference to questionnaire responses by clinicians
		Feedback to the user regarding their previous answers to the questionnaire
		Feedback based on the patient-reported symptoms to act or not
		Predictive information encourages engagement and healthy behaviour change
	Education	***Educate participants about PROs at the onset of study***
	Incentives	Providing participants, a summary of trial results, include potential publication/ reports to study participants
		Offer participants non-financial incentives
	Proxy	**Proxy completion can be considered by a caregiver or family member if data is missing (for example, a brain tumour patient may have cognitive impairments which would make it difficult for the patient to complete the questionnaire).**
Monitoring	**Central monitoring**	
		Central office monitors complianceEfficient compliance management tools such as online reports and email notifications
		Staff should be contacted, engaged, and be accountable when a participant at their site is not compliant with a PRO questionnaire
		Real-time monitoring of PRO completion. This can then prompt an intervention if PRO assessments are missed
		Rapid follow up for missing data may be required due to the recall period
		Raise awareness of compliance issues through presentations, newsletter articles and leading discussions at disease site committee meetings.PRO data should be treated with the same importance as other data in monitoring clinical site performance
		Collect reasons for missing PRO data/about non-responders
	Monitoring at site level	Introduce a fixed daily work routine where nurses checked notification lists
		Prepare for upcoming assessments (e.g. have questionnaires ready)
		Document procedure of PRO data collection at each centre, including names and contacts of those involved
		Provide PRO assessment schedule for each patient to attending physician and keep in patient file
	Reminder	***Send participants PRO assessment reminders***
		After no response, including an automated reminder, a human should contact the participant
		Send site staff reminders for upcoming/overdue PRO assessments
Resources	**Resources**	Staff and patients should be provided with the necessary resources for optimal data collection
		Integrate PROs into clinical systems to allow for efficient use by clinicians
		Clinical resourcing to deal with issues reactively outside of clinical appointments

Abbreviations: EORTC, European Organisation for Research and Treatment of Cancer; ePRO, electronic patient-reported outcome; ePROM, electronic patient-reported outcome measures;MOA, mode of assessment; nr, number; SPIRIT, Standard Protocol Items: Recommendations for Interventional Trials; PROM, patient-reported outcome measure; PRO, patient-reported outcome;

*Bold recommendations indicate that the recommendation was found in 2 papers. Bold and italicized recommendations indicate that the recommendation was found in 3 or more papers.

sending reminders to patients and providing them with education improves completion rates, but may also increase patient burden [11,13,19,20,22,23]. Patient burden refers to how challenging, time-consuming, and emotionally stressful patients perceive their study participation [28]. Distress has been reported among advanced cancer patients receiving reminders as this reminds them of their poor health and HRQoL [16]. Therefore, sending reminders for the completion of PROMs may not prove beneficial for all patient populations.

Consequently, it is crucial to carefully assess the feasibility and practicality of implementing such a comprehensive set of recommendations, taking into consideration the potential burden on patients, staff and sites involved in the clinical trial process. Careful evaluation of the potential benefits and disadvantages of each recommendation before implementation is essential. Analyses of PRO completion rates of EORTC trials between 1996 and 2011 showed different completion rates (23 – 92 %) depending on the trial and population characteristics [38]. Variability in PRO completion rates have also been previously reported. Moreover, despite the availability of numerous recommendations, PRO completion rates tend to decrease over time. This raises questions about the feasibility and effectiveness of these recommendations in real-world settings. Therefore, the next phase of this research will involve conducting interviews with clinical trialists and other stakeholders engaged in PROM design study design and collection. These interviews will provide insight into the applicability and usefulness of the identified recommendations. The outcomes of this scoping review combined with the analyses of EORTC trials and the forthcoming interviews, will serve as a foundational resource for developing guidance to improving PRO completion rates in cancer clinical trials.

4.2. Limitations

This review has limitations. Only papers published in bibliographic databases or documents produced by leading cancer and public health organisations were included. This criterion was applied to guarantee the validity and methodological quality of the included literature. Furthermore, only literature published since January 2012 was included to reflect on current practices. Another limitation is that non-English papers were excluded. By doing so, we might have overlooked relevant national guidelines or regulatory aspects.

5. Conclusion

Missing PRO data in cancer clinical trials remains a challenging issue, influencing the quality of the derived results [39]. This may result in underutilization of PRO data, wasting patient time and resources or leading to erroneous conclusions regarding the patients' perspectives and the trial outcomes. This scoping review includes a plethora of recommendations for improving PROMs completion rates in cancer clinical trials. However, the practicality and effectiveness of these recommendations remain unclear. More research is needed on the feasibility and prioritization of these recommendations, as well as providing guidance on improving PRO completion rates in cancer trials.

CRediT authorship contribution statement

Roger Wilson: Writing – review & editing. **John K. Ramage:** Writing – review & editing. **Vesna Bjelic-Radisic:** Writing – review & editing. **Katarzyna Wac:** Data curation, Formal analysis, Writing – review & editing. **Susanne Singer:** Writing – review & editing. **Jolie Ringash:** Writing – review & editing. **Olga Husson:** Writing – review & editing. **Hans-Henning Flechtner:** Writing – review & editing. **Abigirl Machingura:** Conceptualization, Data curation, Formal analysis, Writing – review & editing. **Lotte Van der Weijst:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing. **Michael Koller:** Writing – review & editing. **Galina Velikova:** Writing – review & editing. **Jens Lehmann:** Writing – review & editing. **Renée Bultijnck:** Data curation, Formal analysis, Writing – review & editing. **Heike Schmidt:** Writing – review & editing. **Madeline Pe:** Conceptualization, Funding acquisition, Supervision, Writing – review & editing. **Katherine J. Taylor:** Writing – review & editing. **Winette T.A. van der Graaf:** Writing – review & editing. **Kathy Oliver:** Writing – review & editing. **Lúcia P.C. Senna:** Data curation, Formal analysis, Writing – review & editing. **Emma Lidington:** Data curation, Formal analysis, Writing – review & editing. **Lisa Wintner:** Data curation, Formal analysis, Writing – review & editing. **Ahu Alanya:** Data curation, Formal analysis, Writing – review & editing.

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Declaration of Competing Interest

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ejca.2024.114313.

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