**Evaluation of Patient-Reported Outcome Protocol Content and Reporting in UK Cancer Clinical Trials: The EPiC study qualitative protocol**

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**Abstract**

**Introduction:** Patient-reported outcomes (PROs) are increasingly included within cancer clinical trials. If appropriately collected, analysed and transparently reported these data might provide invaluable evidence to inform patient care. However there is mounting indication the design and reporting of PRO data in cancer trials may be suboptimal. This programme of research will establish via three interlinked studies whether these findings are applicable to UK cancer trials, and if so, how to best enhance the way PROs are assessed, managed and reported in clinical trials. This study will explore with key stakeholders factors that influence optimal PRO protocol content, implementation and reporting; and make recommendations for training and guidance.

**Methods and analysis:** Semi-structured interviews will be conducted with members of key stakeholder groups. The purposive sample of up to 48 participants will include: (1) trial Chief Investigators, trial management group (TMG) members, statisticians and research nurses (RNs) of cancer trials including primary or secondary PRO, recruited via the National Cancer Research Institute (NCRI) Clinical Studies Group and Consumer Liaison Group and the UK Clinical Research Collaboration Registered UK Clinical Trial Unit (UKCRC-UKCTU) Network; (2) NCRI CLG members; (3) international experts in PRO oncology trial design and (4) journal editors and funding bodies. Data will be analysed using directed thematic analysis employing a coding frame and modified as analysis progresses. Formal triangulation of coding and member checking will be employed to enhance credibility.

**Ethics and dissemination:** This study was approved by the University of Birmingham Ethics Committee (Ref: ERN\_17-0085). Findings will be disseminated via conference presentations, peer-review journals, patient groups and social media (@CPROR\_UoB; <http://www.birmingham.ac.uk/cpror>).

**Strengths and limitations**

* This novel study will capture perspectives on the barriers and enablers of optimal PRO practice from a comprehensive range of stakeholders with experience of PRO data collection and reporting.
* The semi-structured interview format ensures a replicable process while allowing sufficient freedom to explore new and emerging concepts.
* The recruitment strategy involves seeking participants through networks occupied by EPiC Senior Management Group members. However, any limitation to sample representativeness and diversity will be mediated through the use of other recruitment avenues including the authorship lists of the protocols/publications included in Phase I.
* Study is at risk of self-selection and social-desirability bias. Participants are likely to take part if they have a pre-existing interest in PROs specifically and when recounting their experiences and insights are likely to wish to portray themselves in a positive manner due to the nature of this study.

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**Introduction**

Patient-Reported Outcomes (PROs) are increasingly included within cancer clinical trials to provide the patient perspective on the physical, functional and psychological consequences of treatment and the degree and impact of disease symptoms1. The number of randomized controlled clinical trials including PROs is now substantial across all cancer disease sites and these often include PROs as secondary endpoints2. PROs are typically collected using multidimensional questionnaires in electronic or paper format and are completed by patients while they are participating in clinical trials. The results provide information about the symptoms or quality of life effects of a particular therapy and may inform future treatment choices and help physicians and patients decide the most suitable treatment and care for the individual. Consistent and rigorous standardised data collection methods are required to collect the highest quality PRO data and adhering to good practice minimises errors, measurement variability, missing data and systematic bias, upholding trial validity3.

The use of PROs in cancer clinical trials has been exhorted by major international health policy and regulatory authorities as well as cancer patients4-6. PRO trial results inform clinical decision-making; health technology assessment; health economic evaluations; labelling claims; healthcare policy and commissioning7-10 when rigorously captured. PRO data can enhance clinician-patient communication relating to treatment options and contribute to complex healthcare decision-making 11-12 by providing information on relative benefits and side effects of new drugs or treatment options 13-17. Using this information, patient-clinician consultations may result in more informed choices, positive results and favourable experiences of care18-19. As such, guidance included in trial protocols must ensure appropriate PRO data collection and management20-21 and results must be fully reported in resulting publications so that PRO information is readily publically accessible to patients and integrated into clinical practice and policy21.

Recent international evidence22-25, however, suggests PRO information is often omitted from protocols, leading to impaired data collection. Such research also suggests that PRO results are poorly reported in trial publications, or may not be reported at all22. Our previous review of 75 National Institute for Health Research (NIHR) Health Technology Assessment (HTA) trials23 found that relevant PRO information is commonly omitted from trial protocols, even where a PRO is the primary outcome. As a result, PRO data may not be used effectively to inform patient-clinician decision-making at the point of diagnosis and beyond. This represents a waste of limited healthcare and research resources, devalues the contribution of trial participants providing PRO data, and has serious ethical implications.

Whilst there has been some qualitative research investigating PRO administration in trials24, 26, there has been little qualitative work investigating the factors affecting PRO trial design, protocol development and reporting.

The Evaluation of Patient-Reported Outcome (PRO) Protocol Content and Reporting in UK Cancer Clinical Trials (EPiC) study is a mixed method study investigating PRO protocol content and reporting in UK cancer clinical trials aiming to identify factors that enable and inhibit good practice. The research will take place over three stages, the methods pertaining to Phase I are presented in detail elsewhere27.

This paper provides a summary of the Phase II qualitative component, in which semi-structured interviews will be conducted to explore the potential barriers and enablers relating to optimal PRO protocol content, implementation and reporting with cancer trialists, research nurses, consumer representatives, international experts, journal editors and funders. Through the inclusion of individuals from each of these groups, the collection and reporting of PRO data can be considered by the individuals involved at every phase of the research process - including study conception and design; patients’ experiences of providing PRO data as trial participants; until the point at which results are communicated. Phase III of the study will incorporate findings and examples of best practice from both Phase I and II into our publically accessible web-based training resource ([www.birmingham.ac.uk/prolearn](http://www.birmingham.ac.uk/prolearn)).

**Aims**

Semi-structured telephone and face-to-face interviews will be conducted (AR) to explore the perspectives and experience of key stakeholders in relation to:

1. The potential barriers and enablers to optimal PRO protocol content, implementation and reporting;
2. The PRO-specific training needs of each stakeholder group;
3. The optimal methods of implementing such training and ensuring uptake of both the forthcoming SPIRIT-PRO28 and published CONSORT-PRO29 guidelines.

**Participants and setting**

The primary inclusion criteria are that participants must have experience of designing or reviewing clinical trials including PROs within a professional capacity or completion of PROs through participation in a trial. Interviewees will be sampled from 4 groups: (1) trial Chief Investigators (CIs), trial management group (TMG) members, statisticians, and research nurses (RNs) with experience of involvement in a cancer trial including primary or secondary PRO; (2) National Cancer Research Institute (NCRI) Consumer Liaison Group members with experience of involvement in the design of trials with PRO endpoints; (3) international experts in PRO oncology trial design, including members of multi-country cancer and quality of life research organisations, national regulatory bodies, advisory bodies, and global corporations; (4) journal editors and key representatives from funding bodies. Based on the experience of the research team, it is anticipated that recruitment of approximately 8-12 individuals from each group will be required to reach data saturation. Thus, up to 48 participants may be required. Individuals will be purposively selected based on having occupied a role within trials in management, data collection, as a patient partner or a participant. The categorisation of participants into the above four groups will allow the research team to attain maximum variation with regards to experience and role. Recruitment will continue for each distinct group until data saturation is achieved.

Group 1 will be identified from: (i) the authorship lists of the trial protocols/publications included in Phase I or (ii) NCRI Clinical Studies Groups and Consumer Liaison Group, and the UK Clinical Research Collaboration Registered UK Clinical Trial Unit (UKCRC-UKCTU) Network, facilitated by an EPiC study management member who is also the UKCRC-CTU Network Director. Trials from Phase I will be purposively selected to ensure representation across the following criteria: clinical area, SPIRIT-PRO and CONSORT-PRO checklist score23, 28, 29, 30, and funding source. Group 2 participants will be identified via the NCRI Consumer Liaison Group, facilitated by an EPiC study management member who is also the NCRI Psychosocial Oncology & Survivorship Clinical Studies Group Chair. Group 3 will be identified using the personal contacts of the study management group, in particular via an EPiC study Senior Management Group member who is also Director of the Centre for Patient-Reported Outcomes Research at the University of Birmingham. Group 4 will be identified using publically available information via the appropriate Journal/Funder website.

**Data collection**

Potential participants will be approached via email (either directly where contact details are in the public domain, or via the centre from which they were identified, where appropriate) and provided with a brief outline of the project aims, the consent form and information sheet, and details of how to register interest. Individuals interested in taking part will be contacted by the research fellow (AR) and will be given an opportunity to ask further questions before deciding whether or not to take part in the study. An interview date will be set for those wishing to participate. Participants will be first offered a telephone interview. In cases where the individual wishes to participate in an interview but would prefer to do so in person rather than via telephone, this will be arranged if feasible.

Participants will be sent a consent form to complete. The researcher will request this is returned prior to the interview. In cases where a consent form has not been received by the researcher in advance of the interview, verbal consent will be audio-recorded and taken via a standardised script immediately prior to the interview. If a participant would prefer their verbal consent is not audio-recorded, verbal consent will still be taken prior to interview but on the understanding that a consent form will be sent by the researcher to the participant immediately after the interview to be signed and returned.

The interviews will last for approximately one hour. Participants will be interviewed using a pre-defined topic guide (Online Appendix 1) with sufficient scope to explore novel themes where appropriate and will be audio-recorded. Interview recordings will be professionally transcribed verbatim. All participants will remain anonymous and all data will be treated as confidential.

Study dates: March 2016-September 2018.

**Analysis**

Interview transcripts will be analysed using directed thematic analysis (AR) whereby findings from previous qualitative and review work24 and the analysis of included protocols and publications from Phase I will be used in addition to developing an initial coding framework31. Additional codes will be developed as the analysis progresses and the framework will be modified accordingly31. Formal triangulation of coding will be employed to enhance the credibility of the analysis. This will be undertaken at regular intervals during analysis when a sub-sample of transcripts will be coded by an additional researcher (DK/MC) and differences will be discussed to ensure inter-coder agreement.

The findings from this phase, in combination with the Phase I findings, will be used in Phase III to highlight examples of best practice in PRO protocol design and reporting, and inform the development of an online PRO training resource.

**Ethics and dissemination**

The study was approved by the research ethics committee at the University of Birmingham (Ref: ERN\_17-0085) on 20/02/2017. The results of this study will be disseminated via presentations at local, national and international conferences, peer-reviewed journals and through social media including the Centre for Patient Reported Outcomes Research twitter account and the University of Birmingham departmental website (<http://www.birmingham.ac.uk/cpror>), as well as the NCRI (including the consumer forum), Macmillan Cancer Support and via international cancer trial groups. Participants will be anonymised and all data collected will be treated as confidential. Only anonymised, non-identifiable characteristics and quotes will be used in any arising publications/reports.

**Protocol and registration**

This study protocol for the wider programme of work is registered on PROSPERO (CRD42016036533). Registration details are available at <http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016036533>.

**Discussion**

Existing evidence and pilot data collected to demonstrate the feasibility of our approach suggests there may be substantial variation in PRO protocol content and reporting in UK cancer clinical trials. The qualitative component of the EPiC study will explore and explain the contributing factors with stakeholders and establish how clinical trial practice may be improved and supported through training and other resources. This work could benefit several groups including researchers and those involved in research dissemination and service delivery. Appropriate collection, analysis, rationale and reporting of PROs may result in comprehensive data on which treatment decisions may be based, benefiting patients, but would also promote more effective use of public and charitable funds.

This work represents the PRO component within a far wider effort to promote effective, robust and transparent practice within clinical trials. Initiatives focusing on improving practice relating to various aspects of clinical trials32-34 have been lauded and are changing practice through their use35-37. The inconsistent use of PROs in cancer clinical trials is well documented, however, the findings from this programme of research have the potential to address these shortcomings through the development of tailored PRO training and guidance for key stakeholders.

**Contributorship statement**

The study concept and design was conceived by DK, TK, FE, JA, JMB, LC, CC, AGa, AGl, DMG, AL, RMT, GV, MB, RM-B, MTK and MC. AR and KA will recruit, screen and consent participants and will undertake the interviews with input and supervision from DK and MC. AR prepared the first draft of the manuscript. DK, TK, FE, JA, JMB, LC, CC, AGa, AGl, DMG, AL, RMT, GV, MB, RM-B, MTK and MC all provided edits and critiqued the manuscript for intellectual content.

**Competing interest statement**

JA, LC, CC, AGa, AGl, DG, DK and AL are all members of the National Cancer Research Institute Psychosocial Oncology and Survivorship CSG subgroup: ‘Understanding and measuring the consequences of cancer and its treatment.’ FE receives consultancy fees from Bristol-Myers Squibb, Seattle Genetics, TEVA and Incyte; and research funding from Lundbeck, TEVA and Amgen. GV receives grants from the National Institute for Health Research and Yorkshire Cancer Research, personal fees from Roche, Genentech, Eisai and Novartis. MC has received personal fees from Astellas Pharma and Ferring and chairs the ISOQOL Best Practice for PROs in Trials Taskforce. JMB receives grants from the National Institute of Health Research, Yorkshire Cancer Research, Macmillan and Roche. JA is in receipt of grant funding from EU FP7 Framework. AGl is in receipt of grants from Candlelighters, National Institute for Health Research, Macmillan Cancer Support, Prostate Cancer UK, Yorkshire Cancer Research. MTK and RM-B have received project funding from Abbvie and Alcon. MTK co-chairs the ISOQOL Best Practice for PROs in Trials Taskforce. DK and RMB are members of the ISOQOL Best Practice for PROs in Trials Taskforce.

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**Data sharing statement**

Contact corresponding author, MC, for copies of final topic guide.

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