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 that 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 Semistructured 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 members, statisticians and research nurses 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 Network; (2) NCRI Consumer Liaison Group 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-reviewed journals, patient groups and social media (@CPROR_UoB; http://www.birmingham.ac.uk/cpror).

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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 symptoms.1 The number of randomised controlled clinical trials including PROs is now substantial across all cancer disease sites, and these often include PROs as secondary endpoints.2 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. Rigorous study design and 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 validity. The use of PROs in cancer clinical trials has been exhorted by major international health policy and regulatory authorities as well as patients with cancer. PRO trial results inform clinical decision making; health technology assessment; health economic evaluations; labeling claims; healthcare policy; and commissioning when rigorously captured. PRO data can enhance clinician–patient communication relating to treatment options and contribute to complex healthcare decision making by providing information on relative benefits and side effects of new drugs or treatment options. Using this information, patient–clinician consultations may result in more informed choices, positive results and favourable experiences of care. As such, guidance included in trial protocols must ensure appropriate PRO data collection and management and results must be fully reported in resulting publications so that PRO information is readily publicly accessible to patients and integrated into clinical practice and policy.

Recent international evidence, 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 all. Our previous review of 75 National Institute for Health Research Health Technology Assessment trials 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. While there has been some qualitative research investigating PRO administration in trials, 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 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: (1) the authorship lists of the trial protocols/publications included in phase I or (2) NCRI Clinical Studies Groups and Consumer Liaison Group and the UK Clinical

AIMS
Semistructured 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-PRO 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 four groups: (1) trial chief investigators, trial management group members, statisticians and 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 multicountry cancer and quality of life research organisations, national regulatory bodies, advisory bodies and global corporations; and (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: (1) the authorship lists of the trial protocols/publications included in phase I or (2) 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-UKCTU 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 score 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 and 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 publicly 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 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 that the consent form 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 1 hour. Participants will be interviewed using a predefined topic guide (online supplementary 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.


ANALYSIS
Interview transcripts will be analysed using directed thematic analysis (AR) whereby findings from previous qualitative and review work and the analysis of included protocols and publications from phase I will be used in addition to developing an initial coding framework. Additional codes will be developed as the analysis progresses and the framework will be modified accordingly. 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 subsample of transcripts will be coded by an additional researcher (DK/MC), and differences will be discussed to ensure intercoder 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.

DISSEMINATION
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’s 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 trials have been lauded and are changing practice through their use. 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.

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Contributors The study concept and design was conceived by DK, TK, FE, JA, JMB, LC, CC, AnG, AdG, DMG, AL, RMT, GV, MB, RM-B, MKC and MC. AR prepared the first draft of the manuscript. DK, TK, TE, JA, JMB, LC, CC, AnG, AdG, DMG, AL, RMT, GV, MB, RM-B, MKC and MC provided all edited and critiqued the manuscript for intellectual content.

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Patient consent Not required.

REFERENCES


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