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Intensive triangulation of qualitative research and quantitative data to improve recruitment to randomized trials: The QuinteT approach

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Abstract

Randomized controlled trials (RCTs) can provide high quality evidence about the comparative effectiveness of healthcare interventions but many RCTs struggle with or fail to complete recruitment. RCTs are built on the principles of the experimental method, but their planning, conduct, and interpretation can depend on complex social, behavioral, and cultural factors that may be best understood through qualitative research. Most qualitative studies undertaken alongside RCTs involve interviews that produce data that are used in a supportive or supplicatory role, but there is potential for qualitative research to be more influential. In this article, we describe the research methods underpinning the 'QuinteT' (Qualitative Research Integrated within Trials) approach to understanding and addressing RCT recruitment difficulties. The QuinteT Recruitment Intervention (QRI) brings together multiple qualitative strategies and quantitative data and uses triangulation to understand recruitment issues rapidly. These nuanced understandings are used to inform the implementation of collaborative actions to improve recruitment.

Introduction

Randomized controlled trials (RCTs) aim to provide high quality evidence about the comparative effectiveness of health care interventions, but they can be challenging to deliver. The epistemological and methodological principles underpinning RCTs are rooted in the experimental method, but the process of generating trial evidence depends on complex social, behavioral, and cultural factors that can best be understood using qualitative research. The potential to use qualitative research to enhance RCTs has been known for some time (Sandelowski, 1996), but it is only in the most recent two decades that qualitative research is being regularly incorporated into RCT funding proposals (O'Cathain et al., 2014). Qualitative research has tended to either take the form of an independent study that runs alongside the RCT to contribute knowledge about the clinical condition/patient group, or a tool to support trial conduct and reporting – described as "enhancing evidence" from trials (Flemming, Adamson, & Atkin, 2008). A systematic review conducted between 2008 and 2010 found that over 70% of qualitative studies in RCTs focused on the content and delivery of interventions, with few examining RCT conduct or processes. Most studies were based on interview methods alone, which can be limited by recall and respondent bias and may not fully capture events/behaviors when used in isolation. The authors concluded that the 'added value' and impact of this somewhat limited qualitative research was not always explicit (O'Cathain et al., 2014).

There are well-known difficulties of delivering RCTs to time and budget (Sully, Julious, & Nicholl, 2013; Walters et al., 2017), and failure to recruit patients at the required rate is said to present the biggest threat to a trial's successful completion (Amstutz et al., 2017; Kasenda et al., 2014). Developing interventions to support recruitment has therefore been a long-standing priority in RCT methodology research (Campbell et al., 2007; Tudur Smith, Hickey, Clarke, Blazeby, & Williamson, 2014, Healy et al., 2018). Approaches informed by

qualitative research were reported to be particularly promising in a systematic review of interventions aimed at clinical professionals (Fletcher, Gheorghe, Moore, Wilson, & Damery, 2012).

The QuinteT (Qualitative research integrated within Trials) research group uses a range of qualitative strategies and quantitative analysis of trial recruitment data to investigate and understand recruitment in RCTs, particularly those with very different interventions or controversial clinical contexts (Donovan et al., 2016). The research group has developed the 'QuinteT Recruitment Intervention' (QRI): a complex intervention, designed to be integrated into an RCT's protocol to optimize recruitment and informed consent. The QRI begins with an in-depth investigation of the sources of recruitment difficulty as the RCT is underway (Phase I), and then uses this evidence to design and implement strategies to improve recruitment (Phase II). The approaches used in the QRI originated in the NIHR-funded ProtecT (Prostate Testing for Cancer and Treatment) feasibility study – a challenging and controversial RCT that initially struggled to recruit, but recently reported its 10-year primary outcomes (Donovan et al., 2016; Hamdy et al., 2016). Novel application of qualitative research was pivotal to optimizing recruitment in ProtecT (Donovan et al., 2002). The approaches were refined through subsequent application to over 15 challenging RCTs, leading to publication of the QRI protocol (Donovan et al., 2016). The ethos of the QRI is to undertake intensive and robust qualitative research to understand recruitment rates and processes (Phase I), and then translate the findings into practical solutions for improving trial conduct as the RCT continues (Phase II).

In this article, we describe the methodology underpinning Phase I of the QRI. Data are collected rapidly using several qualitative strategies (interviews, documentary analysis, audio-recordings of recruitment discussions between recruiters and patients) and compared with quantitative data about eligibility assessment and recruitment figures. Data are analyzed

using thematic, content, conversation analysis, and simple quantification techniques, and findings are triangulated to develop a comprehensive understanding of the obstacles to recruitment as the RCT is underway.

1. An overview of the QuinteT Recruitment Intervention

Origins and development

The origins and development of the QRI have been reported elsewhere (Donovan et al., 2016). In brief, the ProtecT study (described above) aimed to address uncertainties around how best to treat men with clinically localized prostate cancer by comparing surgery, radiotherapy and "active monitoring" (no immediate intervention). The primarily qualitative feasibility study evaluated the optimal design and practicability of a full-scale RCT using various approaches, including interviews with recruiters and potential trial participants, and the innovative use of audio-recordings to capture healthcare professionals' and patients' discussions about the treatments and the RCT (Donovan et al., 2002). These audio-recordings provided important insights into how the trial was being presented by recruiters and interpreted by potential participants. The findings were used to inform feedback/training and develop guidance documents for recruiters as the trial was underway. Recruitment rates improved from 40 to 70% (Donovan et al., 2002) and the approach (described as the "complex recruitment intervention" at the time) was applied throughout the main RCT (Donovan et al., 2009).

In the next project, we explored whether the "complex recruitment intervention" developed in ProtecT could be applied in five other RCTs. Practical difficulties with securing governance approvals in trials that were already underway emerged, alongside problems collecting data because of recruiters' reluctance to audio-record their consultations (de Salis, Tomlin, Toerien, & Donovan, 2008). Lessons were learned, and the methods were applied in a

bladder cancer trial that was at risk of closure. Although it was possible to elicit a detailed understanding of the sources of recruitment difficulties in this trial, these were insurmountable in the available time-frame (Paramasivan et al., 2011). These experiences highlighted the importance of rapid data collection and analysis, and the need to include the qualitative research at the funding acquisition stage to ensure optimal integration with the RCT protocol.

Qualitative data from ProtecT and the above five RCTs were extracted and synthesized to identify common themes to enable the development of a revised intervention. The synthesis identified "clear obstacles" to recruitment described readily by recruiters, such as organizational difficulties, fewer than expected eligible patients, and patients' treatment preferences. In addition, other more obscure "hidden challenges" emerged, related to recruiters' difficulties negotiating and reconciling their dual roles of 'researcher' and 'clinician' (Donovan, Paramasivan, de Salis, & Toerien, 2014). The synthesis also led to a second article which reported the discomfort and emotion recruiters experienced in relation to equipoise, and how this made recruitment a "fragile" process (Donovan, de Salis, et al., 2014). These articles led to the development of the QRI and its formalization in a protocol (Donovan et al., 2016).

The QuinteT Recruitment Intervention protocol

The QRI has two phases. It begins with an in-depth, intensive investigation of the RCT's recruitment processes (Phase 1), with the aim of identifying factors that compromise recruitment. The findings are discussed with the Chief Investigator and Trial Management Group, with a view to collaboratively producing a 'plan of action' (Phase II) to address the obstacles identified. The plan often includes multiple actions that aim to reduce missed opportunities for recruitment, including feedback and training for recruiters, written 'Tips and

Guidance' documents outlining suggestions for explaining the trial, refinements to patient-facing trial documentation (e.g. patient information leaflets), and changes to how recruitment is organized and delivered. Phase I of the QRI has evolved around the need to understand recruitment issues and act on these promptly, to allow enough time for these actions to take effect. Phase I is thus a period of intensive, focused investigation, over a relatively short period, typically lasting between 3-6 months once centers (recruiting sites) are up and running.

Epistemology and research paradigm

The methodological underpinnings of the QRI are not rooted in any single philosophy or research paradigm. Instead, techniques and approaches have been drawn from several schools of thought in sociology, anthropology, and more traditionally positivist disciplines such as epidemiology. The QRI approach is thus best described as 'pragmatic', drawing upon data sources and data collection strategies used in different methodologies, based on what is deemed most appropriate for addressing the research objectives (Seale, 1999). Data collection and analysis are informed by ethnography, phenomenology (Schutz, 1967), ethnomethodology (Garfinkel, 1967) and Grounded Theory (Glaser & Strauss, 1967). The techniques are used synergistically, with some adaptions and novel approaches to facilitate speed whilst maintaining rigor.

As the QRI was developed specifically to address the issue of poor recruitment in RCTs, the theory of 'Complex Adaptive Systems' (CAS) was informative for its development. This stems from the view that each trial is a CAS, as it follows the conventions of an RCT adapted to its clinical context, with its own culture. In the CAS, 'agents' (recruiters, trial coordinators and investigators, in the context of RCTs) can behave independently and unpredictably, based on local knowledge (Begun, Zimmerman, & Dooley, 2003). The QRI aims to understand the

'clear obstacles' and 'hidden challenges' that affect agents' behaviors and inhibit recruitment in the RCT (CAS) and uses this evidence to inform actions designed to change agents' actions.

2. QRI data collection and analysis techniques

Phase I of the QRI is designed to be flexible, driven by emerging findings, but has a set of core (mandatory) elements. Each element employs particular research strategies, providing the opportunity to examine recruitment from multiple vantage points:

- Examination of patient and study-specific documentation and resources that provide information about the RCT (e.g. patient information sheets, study protocol, websites).
- Interviews with professionals with a role in trial oversight and/or recruitment
- Audio-recordings of RCT recruitment appointments, where recruiters explain the trial to potential participants.
- Scrutiny of RCT 'recruitment screening logs', which capture primarily quantitative recruitment data collected by trial investigators from the point at which patients are screened as potentially eligible through to whether they accept/decline RCT participation.

Observation of investigator meetings can also be useful for assessing how recruitment is progressing. Written informed consent is obtained from all professionals and patients who are observed/interviewed as part of the QRI.

Data collection and analysis occur in tandem, as recruitment is underway. Findings emerging from the analyses often inform purposeful sampling for further data collection within and across the different methods. In addition, findings from each of the approaches can confirm or contradict findings from another. This triangulation provides confidence about what actions are required to optimize recruitment in Phase II of the QRI (Denzin, 1978; Patton,

1999), or inspires further sampling and data collection to deepen understandings about the issues undermining recruitment. Each of the mandatory methodological approaches used in the QRI is described below.

i. Documentary analysis

Documents produced for the RCT, such as the protocol and patient information materials, are assessed for aspects identified as problematic in previous QRI research, such as terminology that hinders equipoise communication (Donovan et al., 2002). Content analysis of documents also inform topic guides (for interviews) and provide useful contextual information when analyzing recorded appointment and/or interview data. Documents may be reviewed several times, as there is often a need to refine materials, based on insights emerging from other analyses (below).

ii. Interviews

Semi-structured interviews are undertaken with health professionals with responsibility for overseeing or undertaking recruitment. Interview schedules are developed for each RCT, covering areas that are specific to the clinical context or trial protocol, whilst incorporating generic topics in every RCT. Interviews aim to: 1) explore views about the trial's importance, relevance, and its interventions from a practitioner's point of view, and 2) understand how recruitment operates 'in practice' in each clinical center, and how recruitment processes are overseen and coordinated centrally.

Interviews are essential for examining health professionals' perceptions of equipoise and their views about the RCT's rationale. Exploring how recruitment operates in practice is important for identifying unanticipated organizational and logistical issues, particularly those related to the structure or culture of a center. Although recruitment processes are included in RCT protocols, executing these in practice often requires flexibility or adaptation, meaning

that recruitment pathways often vary between centers. Individuals tasked with delivering the RCT can offer insight into how recruitment operates, share their experiences of local recruitment challenges, and discuss any solutions they have implemented. Interviews are usually semi-structured, but more structured interviews can enable focused clarification of specific recruitment issues that emerge.

Interview data are treated in a similar way to other qualitative studies. Audio-recordings are transcribed and analyzed thematically, using inductive approaches, where previously coded data are re-examined in light of new insights using the constant comparison method (Glaser & Strauss, 1967). Data pertaining to the 'recruitment pathway' for individual centers are summarized diagrammatically, to facilitate easy comparison between centers. Producing descriptive accounts is an essential aspect of the analytical process.

Interviews provide a broad overview of how recruitment is operationalized from the recruiters' perspectives. The extent to which these views affect their behavior or influence recruitment during appointments cannot, however, be elucidated from these accounts alone; hence, there is a need to gather data from other sources.

iii. Audio-recording of recruitment appointments

Audio-recordings of recruitment discussions are a crucial component of the QRI because they enable direct observation of how the trial is actually presented by recruiters and received by patients. Recordings can provide insights into more subtle and often unanticipated practices that can facilitate or undermine recruitment. Sometimes communication issues discussed by recruiters in interviews are evident in the appointment transcripts, although not always concordantly. The true value of audio-recorded appointments lies in the opportunity to identify issues that are interpreted differently by patients than intended by recruiters, and thus would likely remain 'hidden' were it not for these data.

Audio-recordings of appointments are non-participant observations. Recordings are captured on site by trial staff following provision of written consent from all health care professionals/patients involved in the discussions. Recordings are then securely transferred to the researchers conducting the QRI. This unconventional approach to data collection is one of the factors that facilitates rapid investigation: relatively large volumes of data can be collected from multiple sites in a relatively short space of time.

All sites involved in the RCT are encouraged to routinely record appointments. A purposeful sampling strategy is implemented to distribute audio recorders where needed, in light of how recruitment progresses across centers (based on analysis of recruitment screening logs, discussed below) and findings from initial recordings and interviews. Site-specific issues emerging from the interviews may also inform decisions to target particular sites (e.g. if recruiters from a center report particularly strong views about a particular trial treatment).

Analysis focuses on the content of what is said (i.e. the meanings of the discussion) and the interactions between speakers (i.e. the 'actions' enacted by speakers' 'turns' during the conversation). Recordings are first analyzed using thematic approaches, with some adaptations. Recordings often include discussion that is not related to the research objectives. Thus, the first few recordings might be transcribed in full, but transcription and analysis then follow a more targeted approach, where the researcher listens to the recording in full whilst taking notes, and then transcribes relevant aspects of the discussion for more intensive analysis. We have also developed techniques to enhance rapid analysis of audio-recordings, such as 'Q-QAT' (Quanti-Qualitative Appointment Timing), where the time recruiters spend discussing each of the trial arms is quantified to provide a crude sense of how balanced the discussion is, followed by more in-depth qualitative analysis to understand reasons for discrepancies (Paramasivan et al., 2015).

Some aspects of the RCT discussion are examined from an interactional perspective, looking at the structure and sequencing of talk using techniques adapted from conversation analysis (CA) (Sidnell & Stivers, 2012). The focus here is on what 'actions' speakers accomplish through their turns at talk. These techniques are used selectively for parts of the discussion that appear 'troubled' (e.g. indicating confusing/conflicting ideas), or around decisions about RCT randomization. Relevant sections of the recordings are transcribed in more depth, using elements of CA notation to indicate details such as overlapping speech, length of pauses, and intonation. These approaches can provide insight into factors that may impede a patient's potential to fully comprehend or engage with discussion about the RCT, including how they react to the information provided.

Researcher judgment is used to determine how many appointments to analyze. As recruiters tend to adopt a consistent approach to structuring their recruitment consultations, data saturation can occur quite quickly. As with interview data analysis, established approaches to safeguard rigor, such as double-coding and sustained joint discussion of analysis are used (Denzin, 1978). The emergence of 'negative cases' in recorded appointments often requires seeking out data from other sources to try to understand deviations from emerging patterns (e.g. in how a recruiter explains an RCT, or how patients respond to particular ways of conveying information). This triangulation of findings from thematic and conversation analysis approaches can also provide confirmatory evidence about key communication issues that appear to be undermining recruitment and illuminate issues that might not have emerged had one approach been used alone (Seale & Silverman, 1997).

Findings emerging from the audio-recorded analyses are added to the descriptive account of interview findings to enable comparison. For example, recruiters' intentions in relation to presenting equipoise elicited in interviews can be compared/contrasted with what they say to patients in audio-recordings of recruitment appointments (Rooshenas et al., 2016).

iv. Recruitment screening logs

Most RCTs collect some quantitative data about the numbers of patients who might be suitable to be approached about the RCT, and those actually recruited. These data can be recorded in 'screening logs' (also referred to as 'recruitment logs'). We have developed the 'SEAR' (Screened, Eligible, Approached, Randomized) framework to encourage documentation of site-specific quantitative documentation about these aspects of recruitment (Wilson et al., 2018).

Data obtained from the RCT's logs are routinely reviewed to produce summaries of the numbers and proportions of patients who are eligible, approached, and randomized in each center. Regular monitoring of screening log data can provide a broad picture of how recruitment is progressing and the types of issues that are likely to be affecting it across (or within) centers. These quantitative data can be compared with qualitative interview and audio-recorded appointment analyses and vice versa, to triangulate emerging understandings of recruitment issues. For example, large proportions of patients declining RCT participation in a given center may be indicative of issues with how recruiters are presenting the RCT, which can be supported (or refuted) through analysis of audio-recorded appointments and interviews. Likewise, qualitative analyses of appointment data indicating a lack of equipoise can be triangulated with screening log data, to lend confidence to suggestions for prioritizing feedback on recruiters' communication. Screening log analysis also plays an essential role in purposeful sampling for qualitative data collection – particularly in large multi-center RCTs. This further enhances the efficiency and robustness of the QRI.

Triangulation of evidence to inform the Phase II plan of action

The findings from the research undertaken during Phase I of the QRI – the qualitative interviews, documentary analysis, audio-recordings of appointments, and analysis of

quantitative recruitment log data – are brought together to inform the QRI Phase II plan of action to improve recruitment.

The researcher crystallizes the findings from Phase I into a key set of recruitment issues that can be easily shared and discussed with the Chief Investigator and Trial Management Group. Each key issue brings together evidence from the different methods, synthesized iteratively until the researcher is confident that they have accounted for all data described in their account. This process is an important step for ensuring rigor in the Phase I outcomes, in that the researcher is triangulating the major findings with data from different sources (i.e. methodological triangulation) and creating a clear audit trail of evidence to support findings. In some cases, the process may suggest the need for further data collection (e.g. where there is insufficient evidence to be confident about whether an observed phenomenon is a 'key issue').

The major sources of recruitment difficulty are presented to the Chief Investigator and (with permission) the Trial Management Group/trials unit. Strategies to improve recruitment– referred to as 'QuinteT Recruitment Intervention (QRI)-actions' – are discussed and then delivered collaboratively in Phase II. The nature of the actions depends on the types of issues identified. For example, widespread issues relating to how to explain the trial design, interventions, and RCT concepts can be addressed through dissemination of written guidance. Specific issues within centers or individual recruiters' appointments can be addressed through center-specific or individual confidential feedback. Topics such as conveying equipoise and addressing patient preferences may require feedback and training sessions, providing opportunity for group discussion and reflection.

Box 1 describes two examples of RCTs that integrated the QRI, to illustrate the methods in context. The RCTs selected were different in size, scales and point at which they integrated the QRI, to demonstrate the flexibility of the QRI and its methods.

[Box 1 to be inserted here – included as Supplementary file]

Discussion

In this article, we have presented the first detailed account of the QuinteT methodology – an intensive, focused approach, triangulating qualitative and quantitative evidence from several sources to optimize RCT recruitment and informed consent. The QRI methods evolved through efforts to support recruitment in specific challenging RCTs. Methodological triangulation (Denzin, 1978; Patton, 1999) is key to the QRI's rapid and dynamic approach, enabling investigation of recruitment processes from different vantage points. Observations examine naturalistic behaviors, interactions, and events; interviews investigate informants' perspectives and experiences; quantitative recruitment data capture when patients enter/exit recruitment pathways; and content analysis of trial documentation provides essential contextual information. Convergence of findings from these different methods facilitates rapid, plausible explanations for recruitment difficulties, while discordant or unique findings inform further sampling and investigation to stimulate a more comprehensive understanding of recruitment issues. 'Source triangulation', demonstrated through sampling across different centers and professional roles, and 'investigator triangulation' (i.e. multiple analysts) are also fundamental to ensuring credibility and confidence in the findings.

The novelty of the QRI is the way in which established techniques for enhancing rigor have fused into a flexible framework, specifically developed for investigating the perennial problem of RCT recruitment. Experienced researchers' theoretical and practical insights from previous QRIs facilitate rapid investigation of recruitment issues in subsequent trials. The

intensity of data collection and analysis over a short period of time is fundamental to the successful delivery of the QRI.

Despite its successful integration in a growing number of RCTs (Rooshenas et al., 2018), the QRI has some limitations. A QRI's success is highly dependent on engagement from the RCT investigators and recruiters. This can lead to restricted sampling, with the risk that those who agree to participate have a particular interest or sense of commitment to the research (or RCT); as such, the full range of practices that may be compromising recruitment may not be included. Engagement is a particular concern in relation to audio-recording recruitment appointments. Some reluctance or discomfort about the recording process persists, despite audio-recording of conversations becoming more common-place in everyday life.

The remote recording of recruitment appointments is a key part of the QRI. One of the principle advantages of this approach that distinguishes it from traditional observational methods is the researcher's relative unobtrusiveness. Although the lack of visual observation means non-verbal communication cannot be accessed, there is a low risk of the researcher influencing the interactions. Knowledge of the recorder could still affect the interactions, but recruiters settle into their usual practices relatively quickly.

The time-limited nature of the QRI can be effective for addressing the focused objective of optimizing recruitment but may limit the potential to pursue new lines of enquiry. However, there is the potential to pool data from ongoing and completed QRIs to conduct investigations of issues across several RCTs. Such analyses have led to greater understanding of some of the key issues in RCT recruitment, such as equipoise communication (Donovan, de Salis, et al., 2014; Rooshenas et al., 2016), patient preferences (Mills et al., 2011), recruitment logs (Wilson et al., 2018), and explanations of common trial concepts (Jepson et al., 2018).

Working with secondary data can limit opportunities to test emerging theories through new data collection, although this can be pursued in new QRIs.

The QRI was developed with the focused objective of optimizing recruitment to RCTs, but there are opportunities to apply the QRI approach to address other RCT-related issues, such as participant retention or intervention fidelity. There is also the potential to explore the approach in other areas of problematic communication in applied health research.

Conclusion

In this article we have presented a detailed description of the QuinteT Recruitment Intervention approach and its underpinning research methods. The QRI achieves intensive and robust investigation through the triangulation of findings from several established qualitative strategies and quantitative recruitment data. The combination of these approaches has resulted in a flexible framework, which has been used in a growing number of RCTs to identify and address social, cultural, and behavioral factors that can affect recruitment and informed consent. In this way, the QRI is not a qualitative study undertaken independently or alongside an RCT. Instead, it is fully integrated with the RCT, and its leadership and personnel, providing nuanced understandings that can drive changes to the way the RCT is delivered.

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