Exploring the conduct and reporting of qualitative research in trials using mixed methods

Short title: Evaluating QUalitative research In Trials and their Yields. (EQUITY)

by

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Summary

Background

The benefits of using qualitative research in trials (QRT) have been demonstrated and it is commonly used. However, the prevalence of QRT and issues with its conduct have been highlighted. Underpinned by a pragmatic approach, this study aimed to explore the use of QRT and identify factors that influence its implementation and reporting.

Methods

A convergent mixed methods design which included five components 1) a systematic review of 1,492 registered trials that report using qualitative research (1999-2016), 2) a critical review of 2,343 publications reporting QRT (2011-2017), 3) a narrative synthesis which involved the thematic analysis of 23 publications (2011-2020), 4) a case study of three trials which used qualitative research. The case study included nine interviews with members of the case study trial teams as well as 149 trial documents, and 5) the development and piloting of two quality appraisal checklists for QRT reporting.

Findings

The use of QRT has increased over time, but overall usage remains low. Use is limited to trials investigating behavioural interventions, those conducted in rich Western countries and in trials in co-morbidity conditions, oncology, and mental health. Overall reporting quality for QRT appears to be good but is variable with some areas of reporting being poorer. Engagement with QRT depends on people understanding it and seeing its value. Embedding qualitative researchers within the trial team, good collaborative relationships, consideration of the needs of all trial components and how these relate to each other and being flexible can help to overcome methodological tensions and ensure successful QRT.

Conclusion

Researchers and other stakeholders involved in trials need to recognise the benefits that QRT can bring and consider its use in a wide range of health areas, countries and in trials evaluating all forms of interventions. Further recommendations for the planning, conduct and reporting QRT are provided.

Declarations

This work has not previously been accepted in substance for any degree and is not being concurrently submitted in candidature for any degree.

…… [redacted]……(candidate)

……1.11.2022……(date)

This thesis is the result of my own investigations, except where otherwise stated and other sources are acknowledged by footnotes giving explicit references and a bibliography is appended.

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I hereby give consent for my thesis, if accepted, to be available for photocopying and for inter-library loan, and for the title and summary to be made available to outside organisations.

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……1.11.2022……(date)

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For Nathan - "Get it done."

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Content

List of Tables

List of Figures

Abbreviations

ASSIA	Applied Social Sciences Index and Abstracts
BMJ	British Medical Journal
CASP	Critical Appraisal Skills Programme
CDSS	Clinical Decision Support System
CENTRAL	Central Register of Controlled Trials
CI	Chief Investigator
COREQ	Consolidated Criteria for Reporting Qualitative Research
CTU	Clinical Trials Unit
DMC	Data Monitoring Committee
FDAM	Food and Drug Administration Modernization
GDP	Gross Domestic Product
GP	General Practitioner
HTA	Health Technology Assessment
HRA	Health Research Authority
ICMJE	International Committee of Medical Journal Editors
ICTRP	International Clinical Trial Registry Platform
IRIS	Identification and Referral to Improve Safety
IS	Information Science
ISRCTN	International Standard Randomised Controlled Trial Number
MRC	Medical Research Council
NAC	N-Acetylocysteine
NHS	National Health Service

NIH	National Institutes of Health
NIHR	National Institute for Health Research
NPT	Normalised Process Theory
OMA	Optimising Management of Angina
PGT	Pressure Garment Therapy
PPI	Patient and Public Involvement
QRI	QuinteT Recruitment Intervention
QRT	Qualitative Research in Trials
RATS	Qualitative research review guidelines
RCT	Randomised Controlled Trial
RE-AIM	Reach, Effectiveness, Adoption, Implementation, and Maintenance
REF	Research Excellence Framework
SIV	Site Initiation Visit
STEPS	Strategies for Trial Enrolment and Participant Study
TCA	Traditional Chinese Acupuncture
TMG	Trial Management Group
TMRP	Trials Methodology Partnership
TQR	Trial Qualitative Researcher
TSC	Trial Steering Committee
UK	United Kingdom
US	United States
WHO	World Health Organisation

Chapter 1 Introduction

An introduction to the study

To ensure healthcare practice is appropriate and patients receive the highest standards of care, healthcare decisions should be informed by the best available evidence (1, 2). The Randomised Controlled Trial (RCT) (referred to as a trial or trials from here onwards) is widely considered to be a robust and reliable approach to determine the effectiveness of healthcare interventions (1, 3). Trial findings have made important contributions to changes in treatment guidelines, (4) clinical practice, (5) healthcare policy (6) and associated positive health outcomes (7). However, trials can be challenging to conduct and issues with recruitment, (8, 9) retention, (10, 11) equipoise (12, 13) and fidelity to the intervention (11, 14) have been reported. These issues can threaten the validity and reliability of findings (10, 15) and limit the degree that they can inform clinical decision making (16). Poor recruitment can also lead to requests for funding extensions (8) or trials being prematurely terminated (17). Researchers designing and conducting trials can also face challenges when defining and implementing the interventions being assessed (18). This can lead to problems selecting appropriate outcome measures (19) and interpreting findings from the trial (15, 19). Translating trial findings into practice can also be challenging as the environment the trial is conducted in and the processes involved may be different to those 'in the real world' (15, 20, 21).

The potential benefits and utility of qualitative research to address these issues, to improve the conduct and efficiency of trials, and enhance the evidence produced from trials have been outlined (15, 19, 22-27). This has led researchers to adopt a mixed-methods experimental design when conducting trials (28). Within these designs, qualitative research is embedded or nested as a secondary component within the framework of the primary quantitative experimental design (the trial) (28, 29). Both quantitative and qualitative data are collected and integrated within a trial. I refer to this throughout the thesis as qualitative research in trials (QRT) or trials using qualitative research/methods. Qualitative research seeks to answer 'how' and 'why'

questions and can provide insights about personal views and experiences, behaviour, the setting, the culture within which an intervention is delivered or the processes involved (28, 30). Qualitative research can be used to help develop, optimise, and evaluate interventions being evaluated in trials (19, 25). It can help identify and address recruitment issues (31) and whether trial processes are acceptable and ethical (32, 33). Thus, qualitative research can help ensure the trial is feasible and conducted efficiently and ethically (23). Qualitative research can also help ensure outcomes to be measured in the trial are relevant to patients, (34) develop outcome measures, (35) and interpret quantitative outcome data (36).

Although undertaking QRT has been increasingly advocated and accepted by a range of stakeholders, (22, 37, 38) the approach has not gone uncontested and resistance to its use has been indicated (39). The prevalence of QRT is low in comparison to the number of trials being conducted (15, 26, 40). The use of qualitative research also appears to be largely limited to trials evaluating complex interventions (23) and those conducted in high-income countries such as the United States (US) and the United Kingdom (UK) (23, 26). Issues have also been raised about the way QRT is conducted and reported, resulting in its potential value not being realised (22). Qualitative research has not always been integrated well with trial designs, and a lack of integration of qualitative and quantitative data sets and reporting findings has been highlighted (22, 26). This can lead to issues with transparency and reduce study rigour (41). Concerns have also been raised about the visibility of qualitative findings within reports and publications and poor reporting of qualitative methods and findings (22, 26, 37).

Useful guidance and recommendations have been published to help overcome some of these challenges and help maximise the value and impact of qualitative research in trials (22, 28, 37, 38, 41-43). These include:

- Comprehensive recommendations for what qualitative research can do for trials and how to maximise the value of QRT for a range of stakeholders (22, 43);
- A standard operating procedure (SOP) for a Clinical Trials Unit (CTU) to inform good practice when designing and implementing QRT. The SOP outlines recommended standard procedures and the roles and responsibilities of key stakeholders in conducting QRT within a CTU (37);

- Guidelines and recommendations for improving the management of QRT within CTUs (38);
- Guidance for the design and conduct of qualitative research in feasibility studies (42).
- Recommendations for procedures to use when implementing a mixed methods experimental design (28, 43);
- Guidance for writing research proposals that include QRT (22, 43);
- Guidance and examples of how to integrate qualitative and quantitative data and findings in trials (41, 43).

However, undertaking QRT has been described as a *"dynamic and evolving field"* (24) and a *"rapidly evolving field"* (22). It is important for researchers conducting QRT to be able to develop and use strategies to ensure it is planned, conducted rigorously, and reported well. Updating current knowledge and providing insight into processes and procedures involved in the successful implementation and integration of QRT can help inform these strategies. Previous research has illustrated the benefits and provided recommendations for maximising the impact of QRT but has also highlighted some of the barriers to its use.

At the start of this study there was limited research in the following areas: exploring the process and procedures involved in planning, conducting, and reporting QRT; the roles of the people in QRT; how qualitative and quantitative methods, data sets and findings could be meaningfully integrated; how QRT could be more visible in reports and publications; and how reporting of qualitative findings could be assessed and improved. Assessing the use of QRT over time and exploring the characteristics of trials using qualitative research could also help identify areas for improvement.

To address this, I conducted the study described in this thesis. In the study, I sought to build on previous research and to add to the knowledge regarding the use and conduct of QRT. I focused on providing practical recommendations for the planning, conduct and reporting of QRT.

Aims and objectives

This study aimed to explore current knowledge about whether trials are using qualitative research, how QRT is organised, carried out and reported and to identify what influences implementation and reporting of QRT.

The study had six objectives:

1. To assess the prevalence of use of QRT over time.
2. To describe the characteristics of trials that report using qualitative research.
3. To describe the characteristics of the qualitative research carried out in trials.
4. To develop a tool to assess the quality of reporting of QRT.
5. To explore how factors influence the planning, conduct, and reporting of QRT.
6. To develop recommendations for good practice in the conduct and reporting of QRT.

Design and methods

Design

To address the aim and objectives, I conducted a convergent mixed-method design which was informed by pragmatism. This design involved collecting and analysing multiple quantitative and qualitative data sets separately and then combining the results to obtain a more complete understanding. The intent of using this design was to collect different but complementary data to inform the different objectives. In some cases, different data were used to inform the same objective (see table 1). A convergent design usually involves concurrently collecting and analysing independent datasets. However, this study deviates from this standard design. Within this study the narrative synthesis and case study (both qualitative data) were conducted sequentially with findings from the narrative synthesis informing proposition development for the case study. Results from both the narrative synthesis and case study (individual datasets) were then combined with the other datasets during the triangulation stage.

The study was made up of five components:

1. A systematic review of registered trials in trial registries reporting the use of qualitative methods.
2. A critical review of literature reporting on the use of QRT.
3. The development of reporting checklists for publications reporting on QRT.
4. A narrative synthesis of publications reporting on the use of QRT.
5. A case study of three trials that used qualitative research.

Findings from each of the five components were then brought together using a triangulation protocol approach. Table 1 outlines which objectives each study component addressed.

Table 1 Study objectives addressed by each study component

Objective	Systematic review of trial registries	Critical review of published literature	Quality checklists	Narrative synthesis	Case study	Triangulation of findings
1	✓	✓				
2	✓	✓				
3		✓				
4			✓			
5				✓	✓	
6						✓

I chose a mixed method design for this study as combining quantitative and qualitative methods drew on the strengths of both approaches and could overcome some of the potential limitations with each individual approach. The different methods were used to supplement and inform each other and addressed different aspects of the study as a way of building on and developing initial findings. This would provide a more

comprehensive understanding of QRT and more useful knowledge to inform practical recommendations for its conduct (28).

Pragmatism

Pragmatism emerged in the late nineteenth and early twentieth century from the writings of classical pragmatists Charles Pierce, Williams James, and John Dewey (44, 45). Pragmatism for the purposes of this study is defined as a philosophical and epistemological framework in which the meaning of actions and beliefs are evaluated in terms of their practical consequences (46-48). As a research paradigm, *"Pragmatism offers experience-based, action-orientated framework whereby the purpose of research is to help us address the issues of dealing with how we experience and come to know the world in a practical sense" (49).* (p.10)

This study drew on the following elements of classical pragmatism.

Knowledge, experience, and action are interconnected

Within pragmatism, the meaning of any concept or idea is inextricably linked with its practical consequences (44, 50). Knowledge is considered in terms of its usefulness, or as James (45) termed its *'cash value',* for informing appropriate action. Knowledge is formed from our experiences of what happens when we apply existing values and beliefs to a given situation. As repeated action in similar situations leads to repeated consequences, we learn what the likely consequences of those actions in those circumstances will be. This leads to warranted beliefs (46, 51, 52). Warranted beliefs are constantly evolving because of ongoing experience in a cyclical manner and are open to change. As Morgan (46) states *"Experiences create meaning by bringing beliefs and actions in contact with each other." (p.2)* It is therefore important to examine what the sources of beliefs and meanings of our actions are and recognise they are interconnected with experience.

Knowledge, experience, and action are context dependent

Experience will always occur within a specific context and actions cannot be separated from the situations in which they occur (46, 47). As situations change so do the criteria for determining how useful knowledge is (47, 50). Context dependency means knowledge is relative and cannot be absolute. Our ability to use prior experience to predict outcomes of a current situation can be fallible and the knowledge we have may not be sufficient to inform actions in that given situation (46, 53). However, even though knowledge is context dependent and is not completely generalisable (nor does it need to be), it can be transferrable. Imported knowledge can still be useful and collective learning adds to shared learning and understanding (49, 50).

Knowledge is both individually and socially constructed and actions are informed by a set of socially shared beliefs

Knowledge is constructed at both the individual and social levels (46, 47, 53, 54). At the individual level, people will have different experiences which will lead to different worldviews. However, varying levels of shared experience can lead to different degrees of shared beliefs. This can lead to people assigning similar meanings to experiences and lead them to behave in similar ways. Worldviews can therefore be individually unique and socially shared at a broader level (46, 52). From a pragmatist perspective, all experiences will be social in nature and influenced to an extent by others (47). Concepts and settings such as culture, language, organisations, and human institutions can play a role in shaping our worldviews and influence how we think and act (46, 47, 54). Pragmatism therefore, accepts that there can be single or multiple realities that are open to empirical inquiry (55).

Dewey's Model of Inquiry

According to Dewey (56) inquiry is a form of experience that helps resolve uncertainty and adapt to new situations. Action and beliefs are linked through a continual decision-making process of belief, doubt, inquiry, modified belief, new doubt, new inquiry etcetera (46, 47, 52).

Dewey's systematic approach to inquiry involves 5 steps (46, 52)

1. A situation is determined to be problematic as it is outside current experience and known appropriate action.
2. The problem is thought through and the different ways of addressing the problem are considered using existing beliefs. What difference it would make to act one way, or another is considered.
3. Possible lines of action are developed to respond to the problem. This involves a process called abductive reasoning. Abductive reasoning involves deciding what the most likely outcome of our actions will be based on a set of observations or assumptions. This may include generating 'if-then' formulations to inform possible lines of action.
4. Existing beliefs are used to think about likely outcomes within the given circumstances.
5. Actions believed to be likely to address the problematic situation are taken.

As in other forms of experience, inquiry takes place within a given context and is subject to social influences (46, 51). The primary purpose of inquiry is to create knowledge in the interest of change and improvement (57).

Pragmatism and research

Pragmatists view research as one form of inquiry that is performed more rigorously and with more self-awareness than other ways of responding to a problematic situation (46, 52). Pragmatism indicates that research contexts are complex and require the investigation of multiple perspectives using a variety of approaches. Research processes may appear as tangible activities but can be influenced by variable factors when being implemented (47). These factors can affect how research is viewed and how it is used in practice.

Pragmatism indicates that researchers' beliefs and actions are interconnected within a given set of circumstances (46, 58). To understand and improve research methodology it is important to capture and understand how researchers make choices about which research approach to use when addressing research questions, why they make these choices and the impact these choices have (46).

Pragmatism also indicates that research processes occur at both the individual and social levels (46, 50). At an individual level, researchers will draw on their personal beliefs and experiences and preferences for methods to address research questions (46). Individuals can also experience action and change differently which influences how they apply data collection and analysis techniques (54). However, researchers will also draw on other researchers' experiences and wider shared belief systems through research networks, training, and publications (46, 58). The knowledge provided by research is considered within communities of practice (59). For products arising from research to be understood, accepted and acted upon, they would need to be evaluated by peers and the people who will use them (52). There also needs to be a consensus within and across communities (58).

Pragmatism encourages pluralism and analytic eclecticism to explore multiple perspectives and the use of different and multiple methods in different ways to build a better understanding of the phenomenon being investigated (54, 60).

The basis for using a pragmatic approach to this study

Pragmatism was chosen to inform this study as I wanted to contribute useful and actionable knowledge based on the experience of those involved in QRT which would have practical relevance to those conducting QRT. Pragmatism is a useful paradigm for both understanding research methodology (46) and informing how a study is designed (46, 51, 52, 54). Pragmatism was valuable for investigating QRT as it views people's beliefs and experiences as tools for problem solving and action and encourages the production of knowledge.

Application of pragmatism to this study

The principles of pragmatism described above informed:

- how the study was designed,
- how QRT was conceptualised for the purposes of the study,
- approaches to the analysis of data (e.g., when using reflexive thematic analysis in the narrative synthesis and proposition testing in the case study), and

- how the findings were interpreted and disseminated.

I used Dewey's model of inquiry to inform the design and conduct of the study. The start of the inquiry process was the identification of a problem. This was a recognition of the need for further knowledge and guidance in the field of QRT. Next, I framed the research problem to formulate the research aims and objectives using existing beliefs. To do this I used existing literature and my professional experience of QRT.

As part of framing the research problem, I conceptualised QRT as a research approach that seeks to provide 'useful' knowledge to help inform action within healthcare research and practice. QRT is often considered in terms of its' 'value' in optimising trials or improving understanding from trials research (22, 26, 39, 42). When considering using QRT, researchers will assess whether it is appropriate to address problems and how evidence produced from it will be assessed. The use of QRT can be influenced by both social processes and individual and shared beliefs that could produce consensus or conflict within the field (52, 58). Whether and how researchers have previously conducted QRT, used findings from QRT in practice or how the wider research community perceives QRT for example, may influence how QRT is perceived and conducted. QRT is conducted within complex research contexts which can influence how it is implemented.

Next, I developed a research design which could address the objectives. I focussed on how useful knowledge could be gained to inform action in the field of QRT. The most important determinant of the research design was the study aim and objectives and how best these could be addressed (51, 54). The research objectives for this study focussed on building actionable knowledge and understanding about whether and how QRT is used in practice, how this is influenced by researchers' beliefs and experiences and how these relate to action and its consequences.

In line with pragmatism, I used a 'contingency approach' to evaluate which method(s) would be best to address the study objectives (54). Using this approach meant that quantitative, qualitative, and mixed methods research were all considered potentially superior and appropriate depending on different circumstances. I embraced pluralism and analytic eclecticism and decided to use a mixed methods approach. The methods

chosen allowed for a flexible approach to capturing insight into the context of QRT and the different views and experiences of people and how these are shared.

In the final step, I took action by collecting data, analysing it and interpreting the results while considering the original research objectives. Pragmatism required a reflexive stance at all stages of the study as well as flexibility and adaptivity to ensure the outputs were useful and to improve their value. I used an iterative approach that moved between abductive, inductive, and deductive reasoning which supported emerging data and ideas.

When considering the findings of the study and making recommendations I acknowledged that all warranted beliefs including those arising from this study may not be generalisable (52, 53). Knowledge is rarely, if ever viewed as perfect or absolute (53, 54) and recommendations from this study should be considered within the context and conditions in which it was conducted (46). Rather than being concerned with generalisability, I consider the importance of the transferability of findings and recommendations and how they could contribute to wider knowledge in the field (54).

When considering the dissemination of findings and recommendations from the study I reflected on who would benefit most and how could I most effectively reach the people who would use them. People who may benefit from the outputs of this study include those who would have a role in planning, conducting, reviewing, and reporting QRT. To reach these people I planned to disseminate findings through journal articles, conferences, and research networks in which I am a member.

An introduction to the researcher

When I first started this study, I was a full time Trial Qualitative Researcher within Swansea Trials Unit at Swansea University. At this point, I had an interest in and experience of qualitative research in healthcare practice. I had gained a BSc in Psychology and MSc in Health Psychology and was fascinated with how research could improve patient care and how using mixed methods research could enhance understanding and increase the value of health research. This subsequently led to my

interest in and desire to conduct qualitative research in trials. At the time (2012) there was little in the way of good practice guidelines nor any synthesised information about the benefits of QRT, how QRT could be organised and carried out well and the roles of the people involved. Therefore, I sought to find a way to improve knowledge and understanding about the conduct of QRT and if this could be better supported and improved.

More recently within the study period, I have been working as a full-time researcher conducting QRT within the Bristol Medical School, University of Bristol. I have been involved in planning and implementing QRT and using qualitative research to understand and improve trial methodology. I have worked on many trials in a variety of settings, evaluating a range of interventions in different disease/healthcare areas. Each of the trials I have been involved in has used qualitative research for different reasons and used different approaches. This has given me an insight into the nature of trials, the challenges they face and how these challenges are not always insurmountable. I have witnessed the value of QRT and seen the appreciation colleagues have for the benefits of QRT. I have also experienced, directly and indirectly, resistance to the use of QRT. This can result in conflict, not only with regard to the trial methodology but also within the trial team. I have also experienced difficulties implementing qualitative research in trials and observed poor quality research being conducted. I have been privy to the 'good, the bad and the ugly,' and feel, therefore, that I have a balanced and open-minded view of the role of QRT.

Organisation the thesis

In the following chapters, I present a background to the study. This includes highlighting literature that identifies the benefits of QRT, a description of how qualitative research can be used with trials and some illustration of the reported challenges of using qualitative methods with trials (chapter 2). I then report on each of the individual study components in the following chapters (chapters 3-7). Finally, I bring together the findings of these individual studies in chapter 7 and conclude by discussing the key findings and recommendations for practice in chapter 8.

Use of language within the thesis

Healthcare professional: In this thesis, this term encompasses, but is not limited to: clinicians, nurses, doctors, General Practitioners (GPs), pharmacists, psychologists and allied health professionals.

Qualitative research: Within this thesis, I use the term 'qualitative research' to refer to the use of the methodological approach; that is, I aim to encompass the epistemological underpinnings of the approach and embrace the concepts inherent in its interpretative perspective to understand the world. When I use the term 'qualitative methods', this is specifically referring to the data collection and analysis methods that the qualitative methodology adopts to meet the aims of the research.

Trial oversight/Trial Management Group (TMG): In this thesis, I refer to the *'TMG'* and *'trial oversight'* as separate entities. I refer to the TMG as the group responsible for the day-to-day conduct of the trial. I use the term *'trial oversight'* to encompass independent Data Monitoring Committees (DMCs) and Trial Steering Committees (TSCs).

Trial: For brevity, following the definition of an RCT, I use the term 'trial' to refer to any RCT throughout the remaining thesis.

Qualitative research/methods in trials/trials using qualitative research/methods (QRT)*:* In this study, I use these terms to refer to studies that adopt a mixed methods experimental design which embeds/nests qualitative research as a secondary component within the wider framework of the primary trial design. Qualitative research could be conducted before a trial, during or after a trial but must be related to the trial endeavour and/or intervention being evaluated.

Publications and conference presentations

Publications

Clement C, Edwards SL, Rapport F, Russell IT, Hutchings HA. Exploring qualitative methods reported in registered trials and their yields (EQUITY): systematic review. Trials. 2018;19(1):589. The publication can be found in Appendix I.

Clement C, Edwards SL, Hutchings HA, Rapport F. Enquiry into how qualitative methods influence trials and their yields (EQUITY): exploring registered trials that include a reported qualitative component. Trials. 2017;18(Supp 1):422

Conference presentations

Oral presentation: "I felt she had to fight her corner:" How qualitative researchers can become vulnerable when conducting qualitative research in trials. Qualitative Research Symposium, University of Bath, February 2022. (accepted and abstract shared but unable to present on the day)

Oral presentation: Evaluating Qualitative methods In Trials and their Yields (EQUITY): exploring registered trials. Postgraduate Research Conference, Swansea University Medical School, May 2018

Poster presentation: Enquiry into how qualitative methods influence trials and their yields (EQUITY): exploring registered trials that include a reported qualitative component. 4th International Clinical Trials Methodology Conference (ICTMC) and the 38th Annual Meeting of the Society for Clinical Trials, Liverpool, May 2017

Chapter 2 An introduction to Qualitative Research in Trials

Evidence-based Healthcare decision making

To ensure patients receive the highest standards of care which result in the best possible outcomes, decisions about selected treatments should be informed by the best available information (1, 2, 61). When making healthcare decisions, people usually consider the interaction of information available to them, their values and preferences, previous experience and the current circumstances and context. This applies to both those giving care/treatment and those receiving it (1, 62). Information can come from a range of sources (62, 63) and it has been argued that healthcare decision making should be evidence based (3, 61, 62, 64). Evidence based decision making involves consideration of the best available, current, valid, and relevant evidence (1, 2, 64). Evidence can come from a range of sources and multiple or different methods can be important and useful for addressing different questions and layers of complexity required to inform decision making (61, 65).

Trials

Trials are widely considered to be a robust and rigorous approach to investigating the effectiveness of healthcare interventions (3, 66, 67). Trials are prospective studies which use an experimental approach to determine whether a cause-and-effect relationship exists between an intervention and outcomes (62, 66). Key characteristics of trials include randomisation, blinding and intention to treat analysis (62, 66). Randomisation involves participants being randomly allocated to an intervention or control group. The groups are as equivalent as possible except for the intervention (active or control) being received. This helps to ensure that groups are comparable as far as relevant characteristics are concerned and will therefore be able to provide a

more robust answer about whether the intervention works. Blinding or concealment requires that where feasible and appropriate participants and investigators should remain unaware of which intervention was received by participants. This can help to reduce the influence of preconceived views of participants and investigators on the outcomes being measured. Participants are usually analysed within the group they were allocated to, regardless of whether they received/experienced the intended intervention. This is usually called an intention to treat analysis (66). It can help to maintain the advantages of random allocation which can be lost if patients are excluded from analysis by withdrawing from the trial, not completing outcomes measures, or not engaging with the intervention (62, 66). Outcomes are usually measured quantitatively, and data can come from a range of sources and include, clinical data, costs, quality of life and Patient Reported Outcomes Measures (PROMS) (68). These outcomes are normally collected from medical records, questionnaires and participant reported measures (62, 68, 69). Outcomes are measured at specific times and any differences in groups are examined statistically (62, 67). Through its experimental design and collection and analysis of quantitative data trials have several advantages in informing decision making. Using randomisation and blinding, bias is reduced, and investigators can be more confident that the effects being measured are the result of the intervention being evaluated and not from other factors (66). Investigators can test and validate theories about how and whether an intervention works (54). Conclusions can be drawn from large numbers of people which makes findings more generalisable to the population (54, 70). The use of a range of measures allows the collection of information about various dimensions which can then be analysed in detail (71). Data can be precise and results such as effect sizes and statistical significance are relatively independent of the investigators (54).

Impact of trials

When conducted well trials can provide reliable evidence to answer effectiveness questions. They can make important contributions to decision making about diagnosis, treatment and informing practice. The findings from well-conducted trials can be beneficial for promoting the use of new treatments and services that are more effective, safer, or less invasive (5, 72-74). As well as new treatments and services, trial findings

have shown existing treatments can be as or more effective than newer approaches (4, 75). Findings can also help to improve diagnosis and screening processes (76-78). By informing better treatments and services and improving diagnosis, unnecessary harm can be avoided, and patient benefits maintained or improved. Findings from trials have led to changes to treatment guidelines (4, 5), policy (6) and reconfigurations of services (73, 79). Findings from trials have also been instrumental in reducing the cost of healthcare delivery by, for example reducing medication prescribing (4, 75) and removing unnecessary screening processes (78, 80, 81). One study has estimated the financial return on trials to be $37 billion over 10 years in the US (82).

Limitations and challenges of conducting trials

Trials can be challenging to conduct and several factors which can impede the successful delivery of well-designed trials have been highlighted. These can include poor recruitment and retention (8, 10, 11, 83), lack of equipoise (12, 84), poor knowledge and understanding of trials research (13, 85), problems with blinding and selection bias (86, 87), and problems with the implementation of trials in different settings (83, 88).

Recruitment and retention

A key challenge in successfully completing trials is the recruitment of a sufficient number of participants to make any meaningful conclusions about the effectiveness of an intervention (83). Trials often struggle to recruit (8, 9) and retain (10, 11) participants. Many trials do not meet initial recruitment targets (8, 83, 89) or require reduced target revisions (8, 90). In 2007, less than a third of trials funded and conducted in the UK were reported to have met their original recruitment targets (8, 89). More recently, in 2017, less than 50% were reported to have achieved their target (91). This suggests that recruitment rates may be either increasing over time (in the UK), or that investigators are being more realistic about recruitment targets. However, recruitment remains a key issue in trials. Poor recruitment can lead to trials being prematurely terminated (17, 90, 92, 93) or to costly time extensions being granted (8, 89). Trials can also have a high number of participants either drop out of the trial or fail

to provide sufficient levels of follow up data (11, 91, 94). Poor retention can lead to a lack of the production of insufficient data to answer the research questions and reduce how generalisable trial findings are to the wider population (11, 91). Several factors can influence recruitment and retention to trials including patient treatment preferences (95, 96), perceptions of benefit to the participant (83, 97), lack of equipoise (31), acceptability of the intervention (98) and trial processes (95, 99). These factors can also influence other aspects of trial delivery and reporting.

Treatment preferences

Patient treatment preferences can lead to people not being willing to be randomised (96). Allocation to a treatment that participants did not want can also lead to them later withdrawing from the trial or failing to complete outcome measures (31, 100). This can be problematic when recruiting to the trial because it can introduce bias and reduce the usefulness of data to inform the research question (12, 101).

Challenges to blinding

Blinding can also be an issue in trials which can lead to bias (86, 87). Blinding in surgical trials is particularly difficult as concealing techniques or outcomes (scars for example) from surgeons and patients is inherently problematic (86, 102). Selection bias, where recruiters enrol patients into a trial based on what they think the next treatment allocation will be, is also likely to be problematic in trials where blinding is not possible (13, 103).

Knowledge and understanding

A lack of professional and public knowledge and understanding of trials research can also be problematic in conducting and reporting trials (83, 85, 88). This can also affect recruitment. If people are not aware of or do not understand a trial and the processes involved such as randomisation, they are less likely to take part (83, 104, 105). If they do not understand what is expected of them, participants are also less likely to comply throughout the trial (83). Clinicians have also been reported to struggle with

understanding the concept of trials and the processes involved (13). This can lead to problems with clinician engagement and reporting (83, 85).

Trial context

The trial setting and context can influence how well the trial is implemented and affect successful delivery. Context has been defined as:

'Why and when of change, and concerns itself both with influence from the context external to the provider (such as the prevailing economic, social, political environment) and influences internal to the organisation under study (for example its resources, capabilities, structure, culture and politics)' (106). *(p.35)*

Context can be complex and multi-faceted and as this definition highlights can occur at the external and internal levels, although these can overlap and interact (106). Contexts which can influence how trials are understood, conducted and whether they are successful include regulatory frameworks and health policies, (107-109) the culture and socio-economic conditions of the trial setting (83, 88), the level of resources available, existing processes and practice, expertise, and organisational support between trial sites (95, 110). Context can influence how trials and their processes are perceived and conducted and whether they are successful. If trial protocols are perceived to be complex and difficult to implement because, for example, activities do not fit with existing practice such as patient pathways, they may not be conducted as planned (83, 88). This can adversely affect recruitment (95, 99) and threaten the internal validity of the trial (111). Local customs and beliefs can also have implications for the ethicality and feasibility of trials. Mistrust of medical practices and practitioners and cultural beliefs concerning health, sickness and death can mean measures are not culturally sensitive or ethically appropriate (83, 112). It can also be difficult to collect data (112).

Intervention

To be able to reliably compare the intervention with a control and make recommendations regarding its effectiveness, what is being delivered and evaluated needs to be defined (113, 114). To be able to explain how the intervention works and how it can be implemented across different settings, the process of implementation

needs to be understood (110, 115). Health interventions often involve multiple components and involve multi-disciplinary teams or strategies for organising and delivering these components (113, 114). It can be challenging to deliver these interventions as planned and to identify the 'active ingredients' of the interventions and which components, if any, are responsible for change (18, 114, 116). The cultural and setting context also needs to be considered when implementing an intervention and interpreting findings (115, 116). Context can influence whether the interventions being evaluated are acceptable, are implemented as intended and what effects an intervention has (14, 110, 116). Even if an intervention is delivered consistently across sites, it is possible it may have different effects due to the context (116, 117). A lack of understanding of the intervention being evaluated can lead to problems in selecting appropriate outcome measures (19) and interpreting trial findings (15, 19). If an intervention is not acceptable to participants or clinicians it can negatively affect willingness to engage with a trial and recruitment (95, 98). It can be difficult to fully understand how context influences trial conduct and interventions using quantitative approaches, thus insight and usefulness of findings from the trial can be limited (70, 118).

Implementation of trial findings

Challenges with implementing trials findings into practice have also been reported (15, 20, 21). Change in practice which reflects evidence from trials has been slow and variable across conditions (119-121). Few guidelines developed from trial findings have led to consistent changes in Healthcare Professional's behaviour and adherence to practice is reported to be around 50% in the UK (122) and as low as 36% in Australia (121). It is possible that reliance on quantitative measures and outcomes does not fully account for the complexity of healthcare settings and patient circumstances (63). Clinicians have reported being aware of guidelines and agreeing in principle with their content. However, it can be difficult to translate guidelines into practice as they do not always account for the complexity of patient cases (123). There is also concern that trial outcomes can have little relevance to clinicians and their patients and therefore do not translate into meaningful clinical practice (20). Statistical significance may not always translate into clinical significance (124) or practical importance for patients and

outcomes which are important to patients are not always identified or measured (20). Outcomes measured in the trial may also not be appropriate or relevant to those delivering care (54). Implementing trial findings outside of the trial setting can also be challenging as the trial environment and processes involved in delivering interventions may differ outside of the trial (15, 20, 21). Organisational factors such as unsupportive infrastructures, healthcare practice settings and culture and individual factors such as clinician behaviour and motivation can influence the implementation of recommendations from trial findings (119, 120).

When trials are not conducted well, have poor recruitment and retention, or fail to be completed this can lead to research waste (125, 126). Trials are costly and use a lot of resources including time and healthcare costs (125, 127, 128) and valuable patients and resources are taken away from other studies (125). The processes used in a trial may not suit the context and can lead to it be unethical (35) and limit the usefulness of findings resulting in the benefits of trials not being realised (125).

Qualitative research

Qualitative research is a strategy for the systematic collection, organisation, and interpretation of information that allows exploration of events as experienced by individuals (129, 130). It involves an iterative research process in which new insights into phenomena are created or understanding of existing knowledge is enhanced (131). It seeks to provide a comprehensive, detailed description of phenomena or events which can lead to improved and nuanced understanding (63, 131, 132). Qualitative research focusses not only on the objective nature of behaviour but also on subjective meanings that people use to make sense of their lives, experiences, and the world around them (131, 133, 134). It mainly emphasises individual views and experiences and people's accounts of their attitudes, motivations, and behaviours (63, 118, 135). Participants can also provide insight into a wider collective understanding of phenomena and their effect on behaviour (54, 112, 136). Qualitative research acknowledges the importance of context when trying to understand how information is gathered and knowledge is formed and the influence this has on associated behaviour

(131, 133, 137). It, therefore, focusses on social processes and environmental and organisational structures, and what meaning they have to people in specific circumstances (132, 133). To help understand this most qualitative research is conducted within a natural setting. Qualitative research is not experimental and does not seek to control factors that may influence the phenomena being investigated (130, 138). The questions qualitative research usually seeks to answer are the what, how, or why of a phenomenon rather than the how much or how often questions (133).

Qualitative research is a broad discipline, and a wide range of methodologies and methods can be used in a flexible and iterative manner (132, 137). Data usually takes the form of words or imagery (130, 138-140). Data are usually generated from the researcher's interaction with participants, such as interviews or focus groups, or from observation of participants and situations (130, 132, 141). However, it can also take the form of data generated from participants such as diaries (142) or recordings of interactions (143), online spaces (e.g., social media, forums) (144) or existing data such as images or historical documents (130). Qualitative research uses a range of sampling approaches which are primarily forms of non-probability sampling such as purposive sampling, convenience sampling or theoretical sampling (134, 137). The key feature of these approaches is that participants or forms of data (e.g., documents) are deliberately selected because they represent key characteristics of interest to the topic under investigation (134, 137). They can enable detailed exploration and in-depth understanding of the topic being investigated (130, 134). These methods are able to capture and scrutinise aspects of life such as individual explanations and interactions (132, 133). There is a range of qualitative analysis approaches, for example, thematic analysis (145), framework analysis (146), narrative analysis (147) and grounded theory (148) among many others. The approaches vary in terms of their focus and aims of the analysis, the way they treat and organise data and underlying assumptions of the nature of the inquiry (134). The common aim of these approaches is the identification of patterns and processes, commonalities and differences which can address the research question (149). Approaches generally try to retain the nuance and complexity of participant accounts and the context in which they are generated (134).

The nature of qualitative research and its approaches to data collection, analysis and consideration of context and experience offers several benefits. Qualitative research

through in-depth analysis allows for a more detailed examination of experience, thoughts, meaning, processes and related interactions, interpretation, and activity (63, 129, 150, 151). It can provide insight into complex phenomena and highlight nuances that can be difficult to access using quantitative approaches (63, 129). In health research, qualitative approaches can help to understand the provision of care within the organisational environment (152, 153) and provide insight into the influence of policy and social contexts of care (133, 154). It can capture and facilitate understanding of patients' and practitioners' experiences of health and illness and how these can shape perceptions and action (133, 155). It can help to identify what is important to patients and those delivering care (156, 157). Qualitative research is useful for understanding how complex and diverse perceptions and associated health behaviours can be framed within wider concepts and contexts (158). For example, how religious or cultural beliefs can influence how people understand health and illness (159) and how this can affect medication adherence (160). It can highlight the effects the context can have on behaviour within a given setting and help to tease out and explain complexity in healthcare delivery (129, 161). Because qualitative research gives priority to the participants' perspective and context it can help investigators to understand the full meaning of participant responses which can enhance the validity of findings (132). Methods such as interviews and focus groups can be useful when investigating sensitive issues and engaging disadvantaged or marginalised groups (132, 162). The flexible approach to questioning participants can allow for questions to be adapted to individual participants and for the interviewer to be responsive to changes in a participant's disposition. These approaches can also provide a forum for people to be heard. Focus groups, for example, if conducted well can provide a form of peer support to people expressing themselves. Observation approaches can also be particularly useful for uncovering actions or relationships that participants are unaware of, have trouble remembering or are not being honest about (130, 132). Qualitative research has value in providing descriptions of taken for granted practices or familiar settings. It can highlight aspects of these that can influence people that may otherwise go unnoticed or hidden (133, 151, 158).

However, there are several limitations of qualitative research. Qualitative research is not always appropriate to answer all research questions (70, 150). It can be difficult to make quantitative predictions and test hypotheses and theories to discover whether

they are statistically significant (54, 138). Qualitative research is dependent on the skills and expertise of the researcher which can affect the quality of research conducted (54, 132). The central role of the researcher in qualitative data collection and analysis can be problematic and their views and experiences can influence interpretation. Their presence can also influence participants' responses. Due to these factors, qualitative research can be open to criticism of bias (54, 132, 150). Rigour can be difficult to maintain, assess and demonstrate (54, 150). The knowledge produced from qualitative research may be unique to relatively few people as small samples are usually used. This can mean findings are not generalisable to other people and settings with the same degree of certainty as findings from quantitative analysis (54, 138). However, the in-depth investigation and knowledge gleaned may still be transferrable to different settings (130). Therefore, although qualitative research has benefits and can add to the understanding gleaned from using quantitative approaches, it does have its own limitations.

A mixed methods approach to intervention evaluation

Mixed methods research has been defined as:

'Research in which the investigator collects and analyses data, integrates the findings, and draws inferences using both qualitative and quantitative approaches or methods in a single study or a program of inquiry' (163). (p.4)

The benefits and value of qualitative research within a mixed methods approach to intervention evaluation have been advocated (22, 27, 29, 42). These include contributions to trials in general (23, 29, 40), but also trials in specific health/disease areas (15, 164, 165).

There are multiple reasons for using mixed methods. Mixed methods research recognises that both quantitative and qualitative approaches are important and useful. I have discussed how trials when using quantitative, experimental approaches can address important questions about effectiveness and provide a valuable contribution to decision making in healthcare. However, trials do have limitations and can be

challenging to conduct. Qualitative research can provide an alternative approach but answers different questions than those of effectiveness, whilst nonetheless making a valuable contribution to healthcare decision making. But qualitative research also has limitations. Although qualitative and quantitative research differ in the methodologies they adopt and where their focus lies, they do have similarities. Both approaches seek to understand the world better and use empirical observation to address research questions (131). Both approaches follow processes that include collecting and describing data and producing explanations about outcomes observed using that data (60, 166). Both approaches consider quality and incorporate safeguards into their enquiries to reduce sources of invalidity (66, 167, 168). Thus, using a mixed methods approach can be a way to harness the strengths and compensate for the limitations of each approach (28, 54). This can provide a more complete understanding of the research subject and increase the validity and usefulness of findings (28, 169).

Using a range of different methods can also add value to an inquiry by increasing its breadth and range (28, 169, 170). Different methods can address different research questions within the same study. It can address a range of questions for which using only quantitative or qualitative approaches may be insufficient and limit insight (28). The recent Medical Research Council (MRC) guidance for the development and evaluation of complex interventions (171) highlights this point.

'A purely quantitative approach, using an experimental design with no additional elements…is rarely adequate for complex intervention research, where qualitative and mixed methods designs might be necessary to answer questions beyond effectiveness.' (p.7)

Gathering and triangulating data from the different perspectives of mixed methods can provide a more accurate or adequate account. Data from different sources can be used to corroborate findings. It can also unearth contradictions which would not be discovered by using one approach alone (172). Having different methods produces consistent results or a detailed understanding of discrepancies can increase the credibility of reported findings (54, 173). Findings from one approach can be reformulated or reinterpreted using data from another approach (169). This can provide more nuanced insight and enhance an overall understanding of the problem. Mixed methods can also help to investigate what is unknown such as what questions

need to be asked, or to identify variables that need to be measured and how they can be measured appropriately (54).

To summarise, mixed methods can provide more robust, valid, and useful evidence for studying a research problem and making recommendations to healthcare practitioners. By being able to use all types of data collection and not those associated with one approach, mixed methods research can increase the breadth and depth of inquiry. It can address a broader and more complete range of research questions (54) and provide different perspectives and insight into different levels of meaning (169). Mixed methods research also aligns with the natural way people approach and understand the real world (52, 60). People often use a mix of numbers and words and use different approaches to establishing logic when coming to a decision (52). Therefore findings may be more applicable in the world outside of the research context (28).

There are many ways to approach the design of a mixed methods study and up to 40 different typologies have been identified (174). One such approach is the mixed method experimental (or interventional) design which is characteristic of the approach adopted when using QRT. Within these designs, qualitative research is embedded or nested as a secondary component within the framework of the primary quantitative experimental design (the trial) (28, 29).

The contribution of qualitative research alongside quantitative research within a mixed method evaluation design has been considered in different ways and several frameworks have been proposed. These include temporal frameworks where qualitative research is described in terms of being conducted before (an exploratory sequential core design), during (a convergent core design) or after intervention delivery, or 'the trial', (an explanatory sequential core design) (28). Or, within the stages of intervention development and evaluation (19, 113). Others have focussed on how qualitative research can be used in trials for a range of purposes (22, 23). O'Cathain et al. (23) identified 22 different ways in which QRT can be used to enhance trials. Use covered five broad categories; intervention (which accounted for most of the qualitative research reported being used in trials), trial design and conduct, conditions, measures, and outcomes. Others have suggested it to be more useful to consider both the timing and purpose of using QRT (28, 165). Therefore, the following section discusses how qualitative research can be used across the temporal stages of a trial. These include 1)

the development stage where interventions are developed or identified, research questions are identified and research proposals are developed, 2) the pilot or feasibility stages where feasibility and acceptability of the intervention and trial design are assessed and decisions about whether to progress to the main trial stage are made, 3) the main stage where interventions are definitively tested and, 4) an implementation stage which takes place after a trial (which is considered here to be when findings are known) and where efforts are made to implement trial findings into practice.

Use of Qualitative Research within Trials

The use of qualitative research at any stage of a trial can be beneficial and potentially enhance the final product and make research more meaningful. Although presented within specific (linear) stages here, the use of QRT can be used within any stage, at multiple stages and occur in a cyclical manner with activities moving between stages. Table 2 presents a summary of how QRT can be used across trial stages.

Table 2 How QRT can be used across trial stages

Stage	**Use of QRT**
Development stage (pre-trial)	- Identifying gaps in knowledge - Defining and refining research questions - Identification of appropriate interventions - Refinement of existing interventions which may include adapting interventions to new settings or situations - Development of new interventions - Identification of important/relevant outcomes - Identification or development of new outcome measures
Pilot/feasibility stage	*Intervention development and feasibility* - Examine intervention acceptability in principle or practice - Explore effects of the intervention (intended, unintended or harms)

	- Explore the feasibility of delivery of the intervention in practice (this may include content, context, setting, target population and delivery)
	- Identify intervention components that are responsible for change i.e., likely to be having an effect
	- Help to adapt/refine and optimise the intervention (this may include content, context, setting, target population and delivery)
	Trial design and conduct
	- Examine acceptability of the trial design and processes in principle and practice
	- Explore feasibility of trial practices and processes and identify issues
	- Help to refine and optimise the trial including
	  - Information given to participants
	  - Informed consent and ethical conduct
	  - Recruitment and retention
	  - Data collection and monitoring processes
	Outcomes and measures
	- Assess appropriateness of breadth and selection of outcomes
	- Development of outcome measures
	- Explore feasibility of collecting outcome measure data
	- Improve completion rates for outcome measures
	- Informing progression criteria and decisions for continuing to the main trial

Main trial stage	*Intervention evaluation* - Examine intervention acceptability in practice - Explore effects of the intervention (intended, unintended or harms) - Explore how interventions are delivered in practice (this may include content, context, setting, target population and delivery) - Understanding why an intervention works or does not work

	- Identify intervention components that are responsible for change i.e., likely to be having an effect
	Trial design and conduct
	- Examine acceptability of the trial design and processes in practice
	- Identify issues with implementation of the intervention or control arms
	- Help to identify issues with and to refine and optimise the trial including
	  - Information given to participants
	  - Informed consent and ethical conduct
	  - Recruitment and retention
	  - Data collection and monitoring processes
	Outcomes and measures
	- Improve completion rates for outcome measures

After a trial	- To help interpret trial findings (positive or negative) to inform future intervention implementation - Evaluate how an intervention is implemented outside the trial context - Inform how interventions can be adapted/optimised for implementation outside of the trial context - Help to inform dissemination strategies - Help to understand and inform intervention sustainability outside of the trial

Development stage (pre-trial)

Defining and refining research questions

Within the development stages, qualitative research can be used to identify gaps in knowledge and help to define research questions that are important to stakeholders and relevant to practice (15, 171). It can also inform what type of information would be useful to inform decision making (15, 165). This can then inform where researchers focus their efforts, what questions need to be addressed within trials and the types of

data that need to be collected to be useful to those making decisions, such as policy makers, practitioners, and patients.

Identification, development, or adaptation of the intervention to be evaluated.

Qualitative research can be used to identify existing interventions, to refine these interventions if needed, or to develop new interventions to ensure they are appropriate, acceptable, and feasible (15, 19, 23, 25, 165). Engaging with stakeholders (those who have a personal or professional interest or stake in the intervention) to explore and understand what their needs are in a robust and rigorous manner is important (171). Qualitative research is well placed to do this as it can help to explain what is important in terms of what the intervention needs to do to result in the intended outcome and, why it is important (22, 164, 171). This can help shape the intervention and inform what the components need to be or what steps or processes are needed to implement it (23, 25). Figure 1 provides an example of this (175).

General practitioners' views on the acceptability and applicability of a web-based intervention to reduce antibiotic prescribing for acute cough in multiple European countries: a qualitative study prior to a randomised trial

Trial description

Trial comparing appropriate antibiotic prescribing rates between General Practitioner (GP) practices who received training in Internet Training for antibiotic use (INTRO intervention) to those not trained (usual care). The trial was conducted across 15 European countries and aimed to increase GP communication skills with patients and promote prudent antibiotic prescribing.

Purpose of qualitative research

To help develop an intervention which would be appropriate to deliver in multiple countries before the trial had started. To explore views and acceptability of the intervention across countries to help increase applicability of the final intervention in the trial.

Qualitative methods

'Think aloud' and semi-structured interviews were conducted with GPs from five different countries. Analysis was conducted using a thematic approach.

Findings and contribution of the qualitative research

Findings reported that the intervention was feasible and acceptable but, that there were aspects of the intervention which were at odds with GPs' national culture or healthcare system. As a result, the intervention was modified to include information which accounted for local contexts. This helped to ensure it was more sensitive to local beliefs and increase acceptability of the trial. This could aid successful implementation of the intervention in practice.

Figure 1 Trial example: The Genomics to combat Resistance against Antibiotics in Community-acquired LRTI in Europe (GRACE), INternet Training for antibiOtic use (INTRO) trial which used qualitative research before the trial to explore stakeholder views on the intervention and how it suited different contexts

Existing interventions and the way they are delivered may need to be adapted to new settings, different modes of delivery or populations (165). Or the way new interventions will be integrated into existing practice may need to be explored and potential barriers

identified (176). Qualitative research can explore the context an intervention will be delivered in and provide key insights into how the intervention may or may not work in practice. It can also inform changes that may be required to optimise it (110, 165, 176). These changes may relate to the intervention itself or how it is implemented. Qualitative research can also be used to determine whether an intervention is acceptable in principle to stakeholders (98, 175). Ensuring an intervention is likely to have its intended effect, is acceptable and is likely to fit within practice can lead to more successful implementation in the trial. It can also avoid the evaluation of a flawed intervention that is likely to be ineffective (43). It is also important to ensure that comparator arms in trials are acceptable to participants. A key facilitator to trial participation is the perceived benefit of receiving something that will improve people's situation (177). If participants do not receive active interventions, they may feel they are missing out and withdraw from the trial (100). It is therefore important to ensure control arms are as acceptable to people as interventions are. Qualitative research can be used to explore the acceptability of interventions as well as comparator/usual care arms to identify potential issues and make changes if appropriate. See Figure 2 for an example of how qualitative research helped to develop a comparator arm in a trial to facilitate the acceptability of the trial to participants (178).

The development and description of the comparison group in the Look AHEAD trial

Trial description

A future trial comparing the effect of an Intensive Lifestyle Intervention (active group) and a Support and Education Intervention (comparison group) on the physical activity levels and clinical health outcomes in people with Type 2 diabetes.

Purpose of qualitative research

To help develop a comparison intervention which would help maintain high retention rates over the 13.5-year trial period.

Qualitative methods

Stakeholder committees and focus groups were used during the trial planning stages. They explored views of being randomised to a less intensive comparator group and what may help maintain participant investment in the trial.

Findings and contribution of the qualitative research

Findings highlighted the disappointment felt by potential participants who would be randomised to the comparison group. They wanted access to weight loss information and support which is why they were interested in taking part in the trial. This resulted in this information being included in the comparison group in the main trial. Using qualitative methods during the planning stages of the trial helped to ensure the comparison arm in the trial was acceptable and increase the likelihood participants would remain in the trial.

Figure 2 Trial example: The Action for HEAlth in Diabetes (Look AHEAD) trial which used qualitative methods during trial planning stages to develop an appropriate comparator arm

Identifying or developing relevant and appropriate outcome measures.

To ensure trial findings are relevant and can inform practice it is important that outcomes measured in the trial reflect issues important to participants and those responsible for providing/delivering the intervention (15, 171). It is crucial that outcome measures are asking the right questions and capture useful data. Implementation of trial findings can also be affected if the outcome measures do not reflect issues relevant to practice (15, 25). Qualitative research can be used to

understand priorities for stakeholders and what is important to capture within the trial (23, 25, 36). It can help to determine the range and relevance of outcomes and to question whether outcomes are missing or do not fit with their experiences and behaviour (179). This insight can help to identify or develop appropriate quantitative outcome measures (28, 34, 179). Qualitative research can also be used to ensure measures such as patient reported outcome measures are appropriate and valid. See Figure 3 for an example of the use of qualitative research to develop an outcome measure (34).

Outcomes important to burn patients during scar management and how they compare to the concepts captured in burn-specific patient reported outcome measures

Trial description

A future trial that would test effectiveness and cost-effectiveness of Pressure Garment Therapy (PGT) for prevention of abdominal scaring after burn injury in adults and children.

Purpose of qualitative research

To explore patient priorities and perspectives on scar management with the aim of understanding what was important to them in terms of outcomes to be measured in the trial.

Qualitative methods

Semi-structured interviews were conducted with adults and parents of paediatric and adolescent burns patients who had experienced the intervention. Outcomes identified from interviews were then mapped against concepts captured within existing burn specific patient reported outcomes. Data were analysed using thematic analysis.

Findings and contribution of the qualitative research

Qualitative research revealed patient experiences of scar management and the intervention to be complex and multi-faceted. Eight core outcome domains that were important to patients were identified. These were then included in the development of an outcome measure to be used in future trials in burn scar management.

Figure 3 Trial example: The Pressure Garment Therapy with no Pressure Garment Therapy for the prevention of abnormal scarring after burn injury (PEGASUS) trial which used qualitative research to develop trial outcome measures

Pilot/feasibility stages

The use of qualitative research within pilot and feasibility studies can be crucial to ensure interventions, trial design and processes are likely to be acceptable and viable for the main trial stage where the intervention is definitively evaluated (22, 42, 176).

Intervention acceptability and delivery

A key strength of using qualitative research within feasibility studies is its ability to examine whether an intervention is acceptable and the factors influencing its implementation from the perspectives of those receiving and delivering it (25, 42, 165).

For interventions to work and be implemented as intended they need to be acceptable (180). If an intervention is not acceptable people are unlikely to engage with it (15, 181) or decline to take part in the trial (98). Qualitative research can explore whether the intervention is acceptable in principle and practice from the perspectives of those receiving and delivering it (25, 42, 165). It can help to identify whether specific components of an intervention are unacceptable or require changing (25, 42, 165). Qualitative research can also help to understand what the value of the intervention may be to people (42, 180, 182, 183). It can identify what the perceived benefits, harms or unintended consequences are from the perspective of those delivering and receiving the intervention. This can not only inform researchers about the acceptability of the intervention but also what outcomes may need to be measured in the main trial stage (15, 42, 179).

Qualitative research can be used to determine whether an intervention can be delivered as intended and explore issues with implementation or variation within/across different contexts. These may include different settings, the target population and processes involved in the delivery (42, 165, 181). Qualitative research can also be used to develop or refine a theory of how the intervention works to inform delivery and measurement in the main trial (42, 110, 165). Qualitative research can explore whether interventions can be delivered within the resources available. Financial scarcity for example has been identified as a key barrier to using an intervention in low-middle income countries using qualitative research (181).

By identifying what is and is not acceptable and what factors may hinder or help the implementation of interventions, qualitative research can help researchers to refine and

optimise their content and delivery in the main trial. It can help rectify problems with the intervention and help researchers recognise components that are likely to make the intervention more effective (18, 165). Qualitative research can help to identify for example whether different aspects of the intervention can be flexible and adapted to specific settings or are required to be fixed (42). Figure 4 provides an example of where qualitative research was used to develop, test, and refine an intervention during the pilot stages of a trial (18).

Novel ways to explore surgical interventions in randomised controlled trials: applying case study methodology in the operating theatre

Trial description

A two-arm trial comparing the effectiveness and cost-effectiveness of gastric band and gastric bypass for the treatment of obesity.

Purpose of qualitative methods

To help develop and test the intervention.

Qualitative methods

Within an internal pilot phase 8 qualitative case studies explored the surgical interventions to inform their description and standardisations for the main trial. A range of qualitative methods were used including video recordings of the operations using the laparoscopic equipment, non-participant observations of operations in the theatre and interviews at two timepoints with surgeons whose operations were recorded and observed.

Findings and contribution of the qualitative research

Using the combination of methods, they identified variations in intervention delivery across surgeons and centres. Surgeons conceded that there was a lack of evidence and no consensus for the best way to perform the surgery. Strict standardisation of the procedures would be difficult but minimum standards would be important to compare procedures within the trial and critical components were identified.

The use of qualitative research helped researchers to identify that their expectations for the way the surgery would be performed were unrealistic. Rather than have surgeons adhere to strict specification of surgical steps, it would be more realistic to provide key functions that needed to be performed. This led to the establishment of minimum standards for procedures in the main trial. This helped ensure the intervention was acceptable and feasible and more likely to be implemented within the main trial stage.

Figure 4 Trial example: Gastric Bypass, adjustable gastric Banding or Sleeve gastrectomy surgery to treat severe and complex obesity: a multi-centre randomised controlled trial which used qualitative research to develop, test and refine the intervention

Trial design

Qualitative research can be used within the feasibility stages of trials to help explore and inform appropriate and efficient trial design, conduct and processes (23, 42, 165, 176). It can be used to explore the views and experiences of people involved in the trial such as participants, Healthcare Professionals' and the researchers. This can help to understand the impact of the trial on these groups and identify challenges they face and highlight things that have gone well to inform the main trial. Findings can then be used to refine and optimise the design and processes for the main trial stage.

QRT can be used to ensure trials are conducted ethically by helping to develop information provided to participants (143, 165, 184). It can also explore and help to refine informed consent procedures (42, 165, 185) and ensure trial processes are sensitive to the trial population, setting and cultural contexts (15, 32, 181). It can also explore and highlight whether there are any misconceptions about trial processes and interventions (31, 85, 165, 184). By helping to address misconceptions qualitative research can help to ensure participants are appropriately informed about what is involved (12, 184).

Qualitative research can be used to assess acceptability of the trial in principle and practice (42). This may include whether the questions the trial is trying to answer are useful and relevant to those involved or whether the design is understood and deemed appropriate (13, 85) and acceptable in practice (42, 165). Qualitative research can investigate whether people believe the trial is feasible and that they would be able to run it within their practice (42). It can investigate what the perceived and actual impact of the study is on those involved and identify challenges they face and highlight aspects that have gone well (15, 42, 165). By understanding stakeholder views, qualitative research can highlight misconceptions and help to address these and increase buy in for the trial which can increase viability (39).

Qualitative research can be used to explore and identify barriers and facilitators to recruitment and retention and provide solutions for overcoming challenges (42, 143, 165). This can be particularly useful in trials which are challenging to conduct such as surgical trials (185), or those with vulnerable or hard to reach groups such as those who are near the end of life (15), those who lack capacity (164) or live in rural areas (186).

Within feasibility studies, qualitative research can help to assess whether outcome measures are appropriate and valid for the participant group and identify and rectify issues with outcome measure completion (42, 165). Figure 5 provides an example of where qualitative research was used to optimise recruitment during a feasibility study (185).

Optimising recruitment to the HAND-1 RCT feasibility study

Trial description

A two-arm randomised study to assess the feasibility of a large multi-centre trial comparing the effectiveness and cost effectiveness of two surgical treatments for Dupuytren's contracture.

Purpose of qualitative methods

To identify recruitment difficulties and possible solutions to optimise recruitment and informed consent.

Qualitative methods

The QuinteT Recruitment Intervention (QRI) was embedded within the feasibility study. This involved interviews with trial staff, analysis of audio-recordings of patient consultations and assessment of screening logs.

Findings and contribution of the qualitative research

Qualitative research identified issues with the recruitment pathway including difficulties with methods to identify potentially eligible participants. A lack of patient and recruiter treatment equipoise also hindered recruitment. Potential solutions were identified and implemented within the feasibility and main trial phases. Recruitment targets for the trial were met.

Figure 5 Trial example: A feasibility study of treatments for Dupuytren's contracture (HAND-1) which used qualitative research to optimise recruitment

The result of a pilot or feasibility stage is a recommendation on whether a definitive evaluation is feasible, whether it can be carried out at a reasonable cost and using which methods (171, 187). To assess this and inform the decision to proceed or not

progression criteria relating to the main trial are often adopted and assessed at key time points (188, 189). This usually includes assessing recruitment levels and the feasibility of data collection and retention. Qualitative research can be used to understand factors affecting these criteria and help to overcome any issues arising to continue the trial (190). It can also be used to inform the decision not to proceed to the main trial stage (14). Figure 6 provides an example of where qualitative research was used to assess intervention feasibility of implementation (14). Therefore, the use of qualitative research within pilot or feasibility studies offers the opportunity to gather a detailed and nuanced understanding of key challenges and facilitators to implementing trial interventions and processes. This can help to fine tune the design and conduct on the main evaluative stage of the trial (185, 191).

Feasibility and impact of a computerised clinical decision support system on investigation and initial management of new onset chest pain: a mixed methods study

Trial description

The feasibility trial assessed the use of The Optimising Management of Angina (OMA), a Clinical Decision Support System (CDSS) which supports diagnostic and treatment decisions for patients with suspected unstable angina. The trial was set in chest pain clinics.

Purpose of qualitative methods

To assess how the intervention was used in practice, to explore its perceived usefulness and relevance, and to identify the benefits and difficulties to potential implementation of the intervention in practice.

Qualitative methods

Observations of clinic processes were conducted as well as interviews and focus groups with healthcare professionals after incorporation of the CDSS. Data were analysed using thematic analysis.

Findings and contribution of the qualitative research

The qualitative research proved essential in deepening understanding of factors affecting intervention use in practice. It identified intrinsic issues with the intervention and demonstrated that it was not being used as intended and, was unlikely to be used in the future. As a result, the planned main trial did not go ahead.

Figure 6 Trial example: The Optimising Management of Angina (OMA) trial which used qualitative methods to assess intervention acceptability and implementation

During main stages

Many of the ways in which qualitative research can be used within feasibility studies are also applicable to the main stages (see Table 2) (23, 165). Conducting qualitative research in the main trial as well as feasibility studies may be particularly relevant if changes have been made to interventions and trial design and processes between the feasibility and main stage; or if a pilot or feasibility study has not been carried out or resources did not allow qualitative research to be carried out within earlier stages (23).

Also, interventions and trial processes may now be implemented across more or different sites to those in the pilot or feasibility study. These sites may have different settings, care pathways, processes, people who are involved or have more heterogeneous or different patient populations. These factors can influence how an intervention and the trial is perceived and implemented (99, 110, 192, 193). Therefore, further qualitative research may be warranted to explore these factors. For example, recruitment and retention can be further addressed using qualitative research in the main trial (96, 143, 165, 194). See Figure 7 for an example of where qualitative research identified issues with the consent processes within an ongoing trial and helped to make the trial more viable (32).

Taking social relationships seriously: Lessons learned from the informed consent practices of a vaccine trial on the Kenyan Coast

Trial description

The trial tested the safety and efficacy of new malaria vaccines in children in Kenya.

Purpose of qualitative research

To explore community and participant understanding and perceptions of the trial in a low-income rural setting.

Qualitative methods

Interviews and focus groups were conducted with trial staff, community leaders and community workers mid-way through the trial. Data were analysed using a thematic framework.

Findings and contribution of the qualitative research

The qualitative research identified the critical role of researchers and community members in forming participants perceptions of a study. It also highlighted locally appropriate ethical practice for informed consent which challenged the adequacy for existing ethical practice guidelines. This led to changes to the informed consent processes and supported the viability of the remainder of the trial.

Figure 7 Trial example: The Malaria Vaccine Trial which used qualitative methods to explore community and participant trial understanding

As interventions are being definitively evaluated within the main trial stage, it is particularly important to understand how they were implemented and how this may have influenced its effects on those receiving it (110, 171). Using qualitative research within a process evaluation can be useful (110, 195). Qualitative research can be useful for capturing and improving knowledge about how an intervention has resulted in a change (22, 25, 110, 165). By engaging with the views and experiences of participants, researchers can understand which of the core components of the complex intervention were useful (196). Qualitative research can be particularly valuable for contextualising the impact of treatments for participants (15). Qualitative research can broaden understanding of how interventions affect participants (36). See Figure 8 for an example of how using both qualitative and quantitative approaches within a trial broadened understanding of intervention outcomes (36).

Qualitative methods in early-phase drug trials: Broadening the scope of data and methods from an RCT of N-Acetylcysteine in schizophrenia

Trial description

Phase 1 trial comparing the effectiveness of N-Acetylcysteine (NAC) with placebo for schizophrenia.

Purpose of qualitative research

As with all drug trials therapeutic effects were measured using quantitative tools. This trial used qualitative research to explore whether additional insights into the therapeutic profile of the drugs in patients could be gleaned.

Qualitative methods

Summaries of observations of clinical interviews. Data were analysed using an interpretive approach including aspects of grounded theory.

Findings and contribution of the qualitative research

The qualitative findings confirmed the principal findings from the quantitative measures in the trial. Additional significant differences between the active and placebo arms were found which were not captured by the quantitative rating scales. The use of qualitative data provided 'broader' data and supported the reporting of a positive trial outcome.

Figure 8 Trial example: The N-Acetylcysteine (NAC) in schizophrenia trial which used qualitative methods to explore the therapeutic profiles of the drugs

By exploring participant experiences of receiving interventions from their perspective, a more detailed and nuanced understanding of its effects can be achieved (36, 164). Variation in outcomes across participant groups and settings can be explored and reasons for variation identified (197). This can add to quantitative data and provide a more comprehensive interpretation of intervention outcomes (36). Using qualitative methods can provide insight into and assess outcomes that may be difficult to measure using quantitative measures such as questionnaires (27). For example, people with cognitive impairment may be able to take part in an intervention but not be able to complete questionnaires. Qualitative observations could negate this issue and capture how they interact with the intervention and what the effects on them are (164, 198).

Qualitative research can provide a more detailed understanding of how interventions are implemented within trials (110, 165, 179). This can include insight into the processes through which delivery is achieved and how external factors can influence this delivery (25). It can highlight whether interventions are delivered the same, similarly or differently in the different settings and by different people across trial sites (110). This can help researchers understand variation in outcomes and inform whether and how trial interventions are transferrable to different contexts (110). This can contribute to a better understanding of the implementation and evaluation of intervention components. This can strengthen the interpretation of results and the ability to make recommendations for future roll out of the intervention (196). Qualitative research can also be used to identify critical issues with interventions or comparison arms within the main trial stage (33, 100). Figure 9 provides an example of how qualitative research was used to identify issues with a trial arm which resulted in this arm being discontinued (33).

Qualitative methods in a randomised controlled trial: the role of an integrated qualitative process evaluation in providing evidence to discontinue the intervention in one arm of a trial of a decision support tool

Trial description

Comparison of three versions of a computerised decision support tool; explicit (enhanced) version, implicit (basic) version and a paper-based guidelines version (control group). Trial participants were patients with atrial fibrillation being considered for anti-coagulant treatment.

Purpose of qualitative research

To explore interactional processes of the trial consultations and participants experiences and understandings of the trial and the advice given to them.

Qualitative methods

A qualitative process evaluation was carried out alongside the trial. Non-participant observations and semi-structured interviews with trial participants were conducted. Data were analysed using a constant comparison approach.

Findings and contribution of the qualitative research

Findings indicated that participants found the enhanced arm confusing, and they didn't understand it's purpose. The intervention was therefore flawed, and it was unlikely that any valid data would be produced by participants using this arm. As a result of this the trial arm was discontinued at an early stage in the trial. This helped to ensure the trial would be ethical and increased its validity.

Figure 9 Trial example: The Decision Analysis in Routine Treatment Study II (DARTSII) efficacy trial which conducted a qualitative process evaluation

Qualitative research can also be used to help inform the health economic aspects of intervention evaluation (171, 199, 200). It can explore whether the cost is considered an important outcome to stakeholders (199) and whether this influences the uptake of an intervention (201, 202). It can inform how decisions about financing and resources for interventions are made in practice through understanding local prioritisation (199). It can help to understand how economic data may be useful to decision makers and in

what format they would like it (171, 199). Qualitative research can also help to inform on the financial sustainability of interventions which may influence whether and how they are implemented beyond the trial (199, 203).

Researchers conducting trials are required to meet ethical and scientific standards for conducting and reporting trials that include the collection of high quality data (204, 205). To help ensure compliance with these guidelines, high quality data monitoring and adherence to trial procedures is recommended (204). Qualitative research can help to understand how trial processes such as data monitoring are enacted. It can help to assess fidelity to trial processes and procedures and to identify and overcome obstacles to good practice (28, 165, 203, 204).

After a trial (implementation)

Qualitative research can be used after a trial to help interpret trial findings to inform the implementation of interventions in practice (15, 28, 165). It can help to inform those implementing it about which settings it may be effective in, and the processes required to ensure it is implemented appropriately to maximise benefits. Or it can inform on which aspects of an intervention can be adapted, and which cannot (117). It can also explore whether and how the intervention evaluated in the trial is implemented outside of the trial context (21, 206). If trial findings indicate negative outcomes, qualitative research can help to examine retrospectively why this was the case (15, 22). It can explore why the intervention did not elicit the intended outcomes (165). It can help to answer questions such as was the intervention delivered as intended? if not why? It can inform what aspects of the study context, participant characteristics or choice of the comparator may have affected findings (165). Also, whether aspects of an intervention or the way it is delivered can be modified to result in a positive outcome (207, 208). Figure 10 provides an example of how qualitative research was used after a trial to understand negative outcomes (207).

'Did the trial kill the intervention?' Experiences from the development, implementation and evaluation of a complex intervention

Trial description

Two arm trial comparing structured rehabilitation delivered by healthcare professionals in a hospital setting with a home-based self-management rehabilitation programme. Participants had received stem cell transplantation for haematological malignancies in a haematology unit.

Purpose of qualitative research

The qualitative research was conducted after completion of the trial. The trial found no beneficial differences between the two rehabilitation programmes. This conflicted earlier indication and staff beliefs of intervention benefit. To help understand this, the qualitative research was used to understand possible complexities of testing the complex intervention within the trial framework. It aimed to explore experiences of the development, implementation and evaluation of the rehabilitation programme and trial experiences.

Qualitative methods

Semi-structured interviews were conducted with trial patients and staff responsible for developing and implementing the complex intervention. Patients were asked about their experiences of rehabilitation and their involvement in the trial. Staff were asked about their views of the rehabilitation programme and the appropriateness of using a trial to evaluate its effectiveness. Analysis was conducted using a thematic content approach.

Findings and contribution of the qualitative research

Qualitative research revealed several challenges when evaluating the complex intervention within the trial framework which could help explain the unexpected findings.

Figure 10 Trial example: Rehabilitation programme after stem cell transplantation trial which used qualitative research after the trial to help understand intervention implementation and interpret trial findings

Qualitative research can help gather stakeholder views of the trial results, such as healthcare professionals, commissioners, and policy makers. This can help to inform dissemination strategies and how interventions may be sustained outside of the trial context. It can also explore whether interventions that were found to be effective in the

trial context can be implemented in real world practice (206). This can provide useful information to decision makers and those delivering the intervention in practice. Figure 11 provides an example of when qualitative research was used to explore whether and how an intervention found to be effective within the trial was implemented outside of the trial context (206).

Implementation of the Identification and Referral to Improve Safety programme for patients with experience of domestic violence and abuse: A theory-based mixed-method process evaluation.

Trial description

A trial of an intervention to improve the health care response to domestic violence and abuse in women attending primary care. The Identification and Referral to Improve Safety (IRIS) intervention involved providing training and support to practice staff to help identify and record potential domestic abuse and to refer women to a domestic abuse advocate. The intervention was compared to a no training and support control group.

The trial demonstrated improved healthcare response by increasing referrals to the domestic abuse advocate within the intervention arm. The positive trial result led to the programme being commissioned and implemented nationally across the UK. However, it was not known whether the programme was sustainable and effective when implemented outside of the trial context.

Purpose of qualitative research

To evaluate the impact of a wider implementation of the IRIS intervention outside of the trial context.

Qualitative methods

As part of a mixed-method process evaluation case studies were conducted which involved interviews with general practice staff, local stakeholders and IRIS service users, participant observations and documents analysis. A theoretically informed inductive and deductive analysis was conducted.

Findings and contribution of the qualitative research

The qualitative findings indicated the intervention was being used in practice but levels of referrals to services differed across sites. This variability was the result of the way people made sense of the intervention and the extent to which they saw it as part of their routine care. Solutions to successful adoption of the intervention across different context were identified. Qualitative research helped inform whether it was possible to implement an intervention, which has previously been found to improve health outcomes in women experiencing domestic abuse, outside of the trial context. They helped inform what works or doesn't work and help inform commissioners of the appropriateness of funding the wider intervention implementation.

Figure 11 Trial example: Identification and Referral to Improve Safety (IRIS) trial which used qualitative research after the trial to evaluate implementation of the intervention outside of a trial setting.

Summary

In summary, QRT can be used to reduce research waste, to save money and time. By conducting QRT to inform effective trial designs and conduct, trial viability can be facilitated (39). This can also improve the efficiency of trials and their internal and external validity can be improved. QRT can prevent attempts to undertake poor or unacceptable trial designs and can prevent full trials from taking place inappropriately. It can help to avoid conducting trials with flawed interventions by providing insight into potential issues or what works well to help optimise the interventions being evaluated. QRT can help to ensure that trials and interventions are relevant by facilitating understanding of the value of trials and interventions to stakeholders, and ensuring they are relevant and appropriate. Using qualitative research to develop and optimise interventions based on participant and HCP perspectives can also strengthen the relevance of a trial. Qualitative research can ensure trials are ethically conducted by making the trial sensitive to the participant's needs, their dignity and ensuring they are respected (15). Qualitative research can contribute to the interpretation of trial findings. It can enhance or elaborate on findings from other data sources within the trial. This is particularly useful if findings are unusual, unexpected, or null. Qualitative research can facilitate the effective and successful implementation of trial findings outside of the trial context. As well as optimising the trial endeavour and subsequent implementation of findings, qualitative research can generate knowledge that goes beyond the trial and contribute to the wider literature and healthcare practice (183). So, conducting QRT can help to develop a more complete picture, enrich our understanding, and give greater credibility to the research. This can lead to more useful evidence for decision makers. QRT is being conducted, however, the overall prevalence of its use is low. To understand why this is the case and to identify where there is potential to increase its use, it is important to consider the characteristics of trials using

qualitative research. If we can understand this, it may be possible to identify areas where use could be increased so that the full potential of QRT can be realised.

The next chapter presents a systematic review of trial registries that considers the characteristics of trials that report on the use of qualitative research.

Chapter 3 Exploring qualitative methods reported in registered trials: A systematic review of trial registries

As discussed in chapter two the value of using QRT is widely recognised. While qualitative research is being used with trials, their full potential is not always realised (22). To identify how to improve QRT, it is important to analyse how trials report the use of qualitative methods, and whether this has changed over time. This chapter will report on a systematic review of trial registries I conducted to assess the number and characteristics of trials reporting the use of qualitative methods. I will consider some of the characteristics already reported about trials which use qualitative methods but warrant further investigation. I then present the methods used, findings and implications of the review.

Previous reviews have reported the prevalence of trials which use qualitative research (15, 22, 26). Though the reported number of trials using qualitative research differed across reviews, its use was consistently low compared to the number of trials conducted and published. The proportion of trials that have reported using qualitative research varies from 1% in palliative care trials (15) to 30% in trials of complex interventions (26).

Flemming et al. (15) reviewed palliative care trials within systematic reviews in the Cochrane Library. They reported only 1 trial from the 146 trials reviewed to have used qualitative research which is less than 1%. O'Cathain et al. (22) reviewed a trials metaRegister between 2001 and 2010. They reported that 122 of the 3812 trials reviewed used qualitative research which is only 3%. O'Cathain et al. (22) also conducted a survey with trial investigators. From the 8 respondents, they reported that eight of the 89 trials reported in the survey used qualitative methods (9%). When O'Cathain et al. (22) considered the number of non-respondents and combined calculations they estimated that this number would increase to 18%. Lewin et al. (26) reviewed published trials within the Cochrane Effective Practice and Organisation of Care Review Group. They reviewed trials using complex interventions for reported use of qualitative research. They reported that 30 of the 100 trials reviewed used qualitative methods (30%). However, none of the reviews mapped the number of trials using

qualitative research over time and were essentially cross-sectional, encompassing a few years. This makes it difficult to determine patterns over time. Most reviews were limited to a single source of information, for example, only one trial registry.

The O'Cathain et al. (23) review also revealed that, though trials including qualitative research are conducted worldwide with multi-national authorships, they are mainly within rich countries. Trials using qualitative research have been reported across the world in a range of countries (22, 26, 40). Most reviews have reported that trials using qualitative research have lead authors or investigators based in high income countries including the US, and the UK. All trials reported by Lewin et al. (26) were conducted in high income countries. O'Cathain et al. (22) reported that 36% of papers had first authors based in the US and 32% were based in the UK. However, other than O'Cathain et al. (23) whose review encompassed publications from across the world, other reviews have been UK centric.

As previously discussed these reviews are essentially cross-sectional, encompassing short timeframes, for example, 2008-2010 (23). Moreover, searches cover only single registries or published trials. Furthermore, these reviews have focused mainly on trials of 'complex interventions' which evaluated 'behavioural interventions' aimed at changing participants' behaviour at the individual or community level (15, 209). More recently what constitutes a 'complex intervention' has evolved to include a wider range of interventions, including surgical procedures, medical devices, and drugs. This reflects the increasing complexity of implementing clinical interventions (18, 86, 113) and the need to consider the context in which interventions are delivered (171). It is therefore important to subdivide these 'complex interventions' from previous reviews to characterise the trials that report qualitative research.

Depending on the country of the sponsor, clinical trials are either required or encouraged to register prospectively with a trial registry. These registries have been established across the world to address concerns about access to trials, publication bias, and more recently, trial results. In the US, the Food and Drug Administration Modernization (FDAM) Act of 1997 (210) and subsequent amendments mandated the development of a registry and registration of both federally funded and privately funded trials, with penalties for non-compliance (210). In 2004 the members of the International Committee of Medical Journal Editors (ICMJE) published an editorial

promoting the prospective registration of all clinical trials leading to the establishment of the trial registry within the UK (211). This was later supported by the World Health Organisation (WHO) which promoted registration further afield (212). Registries aim to provide increased access to information and transparency about trials for researchers, clinicians, patients, and members of the public. These registries give access to information about each trial provided by the trial team, including the lead researcher's name and organisation; study design including the type of trial and methods; and the organisation responsible for overseeing governance. In principle, they also report the extent of qualitative research in the trial.

Objectives

This review addressed the following objectives:

- To assess the prevalence of use of QRT over time.
- To describe the characteristics of trials that report using qualitative methods.

This review builds on previous reviews by estimating the frequency of reported use of QRT over 16 years, longer than previous reviews. Examining the use of QRT over a longer period can inform with greater accuracy whether use has increased or not. This can help identify patterns in use over time which can inform a greater understanding of their use. Analysing trials that report using qualitative methods, specifically the types of intervention evaluated and their locations, can help identify areas which can be improved. Not all QRT may be published (22). Reviewing trial registries as well as published literature (reported in chapter 4) may identify additional trials and enhance insight into the use of QRT.

Methods

To assess the use of QRT, I reviewed existing clinical trial registries and identified trials which reported using qualitative methods, in four main steps:

Step 1: I used internet search engines to identify existing clinical trial registries. I included registries if: they could be searched for keywords; they held records of individual trials, not merely reports or publications; and they held records in English. I searched all included registries from the first available record, which varied across registries, until 31 December 2016.

Step 2: I searched these registries for the keyword 'qualitative'. I then reviewed all identified trials and extracted the following data into an Excel spreadsheet:

- registry name - to allow comparison across registries
- registry record number - as a unique identifier
- trial title
- year of first registration with registry country responsible for overseeing governance of the trial (as many trials recorded multiple recruiting countries, I chose the most likely source of decisions about trial design), and
- type of trial intervention - categorised as surgical, medical device, drug, behavioural (aiming to modify the behaviour of individuals or communities), or other. I derived these types from descriptions used by the registries, existing literature and previous reports (22, 213, 214).

Step 3: I checked the registry records for documented use of qualitative methods. I defined these as qualitative data collection tools such as observation, interviews, focus groups, documents or visual data; qualitative data analysis such as textual or visual; or both (30, 137).

Step 4: I analysed these data using the filter and count features within Excel. To avoid double counting of trials across the registries I identified duplicated registry IDs and trial names using the duplication function in excel. Duplicated records were removed. I counted frequencies for:

- number of registered trials reporting the use of qualitative methods
- year of first registration with the registry
- country responsible for overseeing the governance of the trial

- and type of trial intervention as defined in Step 2.

I used frequencies and percentages to present findings.

Findings

Trial Registries

My search identified five main clinical trial registries: ClinicalTrials.gov; World Health Organisation International Clinical Trial Registry Platform (WHO ICTRP); International Standard Randomised Controlled Trial Number (ISRCTN) Registry; Cochrane Central Register of Controlled Trials (Cochrane CENTRAL); European Union Clinical Trials Register. However, I excluded the last, as it forms part of the WHO ICTRP; and Cochrane, as it is a database of trial reports rather than a registry of trials.

Included registries

ClinicalTrials.gov

This registry was created in response to patient pressure for access to information on clinical trials. It is run by the US National Library of Medicine (NLM) at the National Institutes of Health (NIH) and claims to be the largest clinical trials database in the world, registering trials from 200 countries (214). The registry records information on federally, commercially, and privately funded clinical trials, including information on participant eligibility, locations of trial activity, point of contact and, more recently, basic results. US law enforces penalties for non-compliance with this registry. Approximately 38% of the trials registered within ClinicalTrials.gov are based only inside the US, 56% are based only outside the US, and 5% are based in both (214).

International Standard Randomised Controlled Trial Number (ISRCTN) Registry

The ISRCTN registry contains basic data on all clinical trials which have been assigned an ISRCTN number. The registry is a not-for-profit organisation sponsored by the

Canadian Institute of Health Research, the Italian Instituto di Ricerche Farnacologiche 'Mario Negri', the Netherlands Organisation for Health Research and Development, the UK Department of Health, and the UK Medical Research Council. Most of the registered trials are based in the UK (215). The ISRCTN is a simple numeric system that facilitates the identification and tracking of trials throughout their life cycle. The registry uses the WHO 20-item Trial Registration Data Set covering: study hypothesis, study design, countries of recruitment, selection criteria, disease or condition, intervention, sponsor and contact information (215).

World Health Organisation International Clinical Trials Registry Platform (WHO ICTRP).
This registry also uses the WHO Trial Registration Data Set. The portal provides access to 16 separate registries from across the world, (216) including ClinicalTrials.gov and ISRCTN. So, I took care not to duplicate trials from those registries.

Trials with confirmed use of qualitative methods

The three included registries recorded a total of 615,311 trials from their first record (occurring in 1999 for ClinicalTrials.gov, 2004 for ISRCTN and 2006 for WHO ICTRP) until 31 December 2016. The WHO ICTRP registry was the largest with 366,753 trials registered, ClinicalTrials.gov the second largest with 233,277 trials, and ISRCTN the smallest with 15,301 trials. Of these, 2,477 records included the keyword 'qualitative': 144 (0.03%) from WHO ICTRP; 1668 (0.7%) from ClinicalTrials.gov; and 665 (4.6%) from ISRCTN. Of these 2,477 records, I confirmed that 1,492 (60.2%) trials had used qualitative methods. The main reasons for excluding 985 records were: use of the term 'qualitative' to describe quality of life measures; to refer to medical tests like 'qualitative urine test' or 'MRI imaging' or to cite statistical tests such as 'qualitative Fishers Exact Test'. None of these fit my criteria for qualitative methods.

Table 3 shows that ISRCTN contributed by far the highest percentage of registered trials subsequently confirmed as using qualitative methods (3.4%). In contrast, ClinicalTrials.gov had only 0.3%, and WHO ICTRP had the smallest proportion at 0.03%.

Table 3 Registered trials using qualitative methods by registry

	WHO ICTRP	ClincalTrials.gov	ISRCTN	Overall
Total trials in registry from 1999-2016	366,753	233,277	15,301	615,311
Total identified with qualitative keyword	144	1668	665	2,477
Total records excluded	46	790	149	985
Total confirmed with qualitative methods	98	878	516	1,492
% confirmed with qualitative methods	**0.03%**	**0.4%**	**3.4%**	**0.2%**

Trials confirmed as using qualitative methods by year registered

The number of registered trials increased over time from 1999, when first reported in ClinicalTrials.gov, to the end of 2016. The number and percentage of these trials reported as having used qualitative methods also increased steadily over time across all registries (Figure 12 and Figure 13). The year in which the first trial reported to use qualitative methods was identified differed across the registries: 2000 in ISRCTN, 2001 in ClinicalTrials.gov, and 2004 in WHO-ICTRP. As all registries held records of trials reported as using qualitative methods from 2004, I compared the number across time within each registry between 2004 and 2016. This revealed increases across time in all three registries: from 1.2% to 8.4% in ISRCTN; from 0.03% to 0.59% in ClinicalTrials.gov; and from 0% to 0.06% in WHO ICTRP.

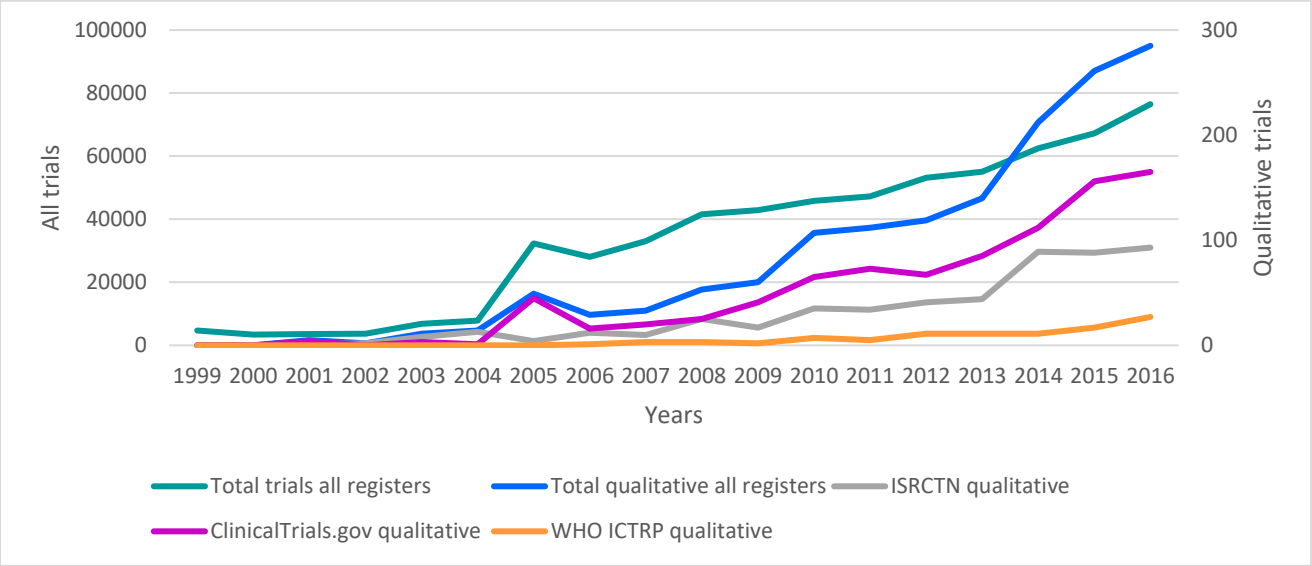

Figure 12 Number of registered trials confirmed as using qualitative methods by register by year

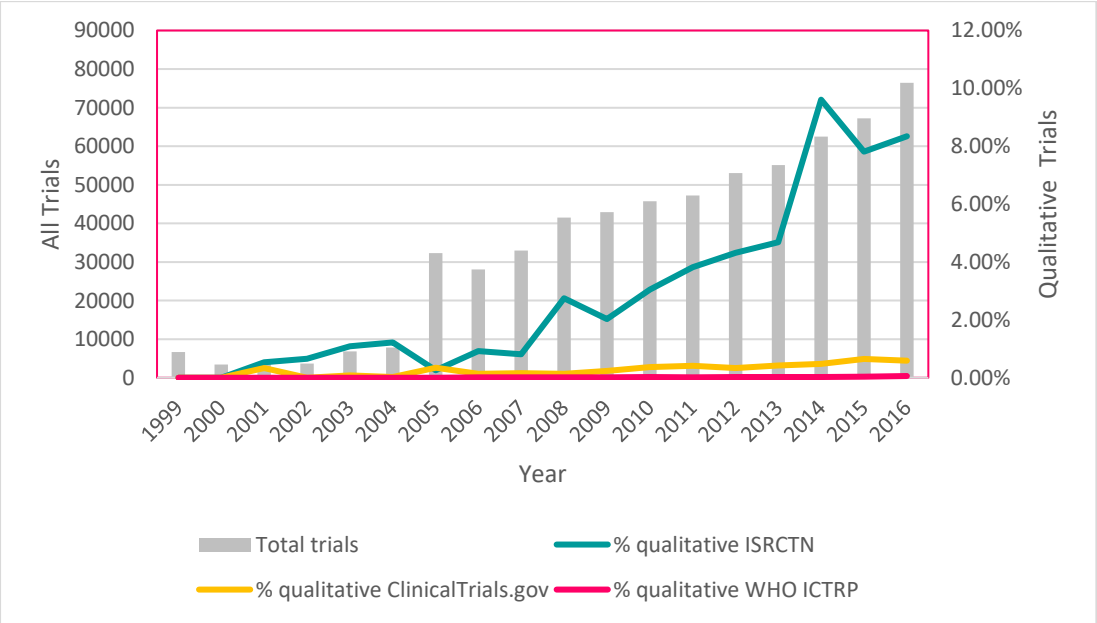

Figure 13 Percentage of registered trials confirmed as using qualitative methods by register by year

Types of registered trials confirmed as using qualitative methods

Of the 1,492 registered trials confirmed as reporting the use of qualitative methods, most were evaluating a behavioural intervention (39%) or an 'other' intervention which did not fit the defined categories. These were mainly trials evaluating vaccines, nutritional supplements, and diagnostic testing (47%). In contrast trials evaluating drugs (5%), medical devices (5%) or surgical interventions (4%) were much less likely to report the use of qualitative methods. This was broadly consistent across the three trial registries (Table 4).

Table 4 Registered trials confirmed as using qualitative methods by type of intervention by registry

Type of trial intervention	WHO ICTRP	ClinicalTrial.gov	ISRCTN	Total
Other	75 (76.5%)	335(38.2%)	289 (56.0%)	699 (46.9%)
Behavioural	20 (20.4%)	419 (47.7%)	147 (28.5%)	586 (39.3%)
Drug	2 (2%)	43 (4.9%)	37 (7.2%)	82 (5.5%)
Medical device	1 (1%)	54 (6.2%)	14 (2.7%)	69 (4.6%)
Surgical	0 (0%)	27 (3.1%)	29 (5.6%)	56 (3.8%)

Registered trials confirmed as using qualitative methods by country

Trials with confirmed use of qualitative methods registered from 52 countries across the world; the highest number were registered in the UK (570 trials, 38.2%), followed by the US (425 trials, 28.5%), Canada (71 trials, 4.6%), France (67 trials, 4.5%), Australia (43 trials, 2.9%), Germany (37 trials, 2.5%) and Denmark (34 trials, 2.3%). None of the remaining 45 countries accounted for more than 2% of all trials confirmed to use qualitative methods.

I examined each registry for the country overseeing the registered trials reported to use qualitative methods. Most of the trials registered within ISRCTN were conducted in the UK (444, 77.9%); 124 UK trials (21.8%) were registered in ClinicalTrials.gov and 2 UK

trials in WHO ICTRP. Most of the trials within ClinicalTrials.gov were conducted in the US (419, 98.6%), with 6 US trials (1.4%) in ISRCTN but no US trials (0%) in WHO ICTRP. Most of the trials within WHO ICTRP were conducted in Australia (36, 15.5%), with 4 Australian trials (9.3%) in ClinicalTrials.gov, and 3 Australian trials (6.8%) in ISRCTN.

I classified countries by Gross National Income (GNI), formerly known as Gross Domestic Product (GDP) estimated by the World Bank Group using the World Bank Atlas Method (217). Most registered trials reported to use qualitative methods were conducted in high-income countries like the UK (570 trials, 38.2%) and the US (425 trials, 28.5%). Low- and low-middle income countries had very few trials reported as using qualitative methods, for example, Uganda (4 trials, 0.26%) and Ethiopia (2 trials, 0.13%) (Table 5). All the registries had most of the trials which reported using qualitative methods in the high-income category. However, the distributions for each category differed across registries: most of the trials which reported using qualitative methods within low income or low-to-middle income countries were registered with ClinicalTrials.gov.

Table 5 Registered trials confirmed as using qualitative methods by country income by registry

Country income category	Gross National Income	WHO ICTRP	ClinicalTrials.gov	ISRCTN	Total
Low	$1,005 or less	0 (0%)	14 (73.6%)	5 (26.3%)	19 (1.3%)
Low-middle	$1,006 - $3,955	2 (7%)	21 (72.4%)	6 (20.7%)	29 (1.9%)
Upper-middle	$3,956 - $12,235	5 (11%)	41 (89.1%)	1 (2.17%)	46 (3.1%)
High	$12,236 or more	91 (7%)	802 (57.4%)	504 (36.1%)	1398 (93.7%)

Discussion

Summary of findings

This review has characterised trials registered in trial registries and confirmed as using qualitative methods, both across time between 1999 and 2016 and across countries. Only 1492 (0.24%) of the 615,311 registered trials identified across the three included trial registries, either completed or in progress, reported the use of qualitative methods. Most of these were based in US or UK, rich Western counties where the number of trials reported to use qualitative methods has increased steadily over time. Most trials reporting the use of qualitative methods investigated behavioural or 'other' interventions, while trials evaluating drugs, medical devices, or surgical procedures each contributed fewer than 5% of registered trials reported to use qualitative methods.

Interpretation

My finding that reported use of qualitative methods is more common in behavioural trials is consistent with O'Cathain et al. (22) who found that few published drug or medical device trials employed qualitative methods. This review therefore suggests a continuing trend in low usage of qualitative research with trials investigating drugs, medical devices, or surgical interventions. My findings indicate that the number of surgical trials using qualitative methods remains low. It is important to consider the benefits of using qualitative methods in surgical trials. Surgical trials are reputedly difficult to design and conduct, so until recently, surgeons resisted the use of RCTs (86). Although the number of surgical trials is increasing, (86, 218) they face challenges; in particular the beliefs and preferences of participating surgeons threaten their equipoise, that is whether they are genuinely uncertain about the effectiveness of an intervention (219). Many surgeons prefer not to standardise interventions, which contributes to good trial design (13). However, qualitative research can describe experiences and beliefs and help understand complex phenomena. They can explore factors affecting equipoise and how to overcome these and help to establish core outcomes and minimum standards for interventions (18). Hence, qualitative methods can describe surgical behaviour and explore recruitment issues in surgical trials. For example, Donovan et al. (143) developed the QuinteT Recruitment Intervention (QRI),

(143) which has been implemented in surgical trials (99). However, qualitative methods remain rare in such trials and research is needed to explore why.

As drug trials are better established, it is unclear why they too rarely report using qualitative methods. There is evidence of the benefits of qualitative research with drug trials, for example in understanding, identifying, and addressing barriers to recruitment, (143) and exploring equipoise (201). As medical devices are increasing in variety and complexity, (220) there is a strong case for evaluating their benefits and harms through trials (221). Such trials face similar issues to surgical trials including when to initiate trials; when to assess outcomes; the acceptability of the intervention; the choice of outcome measures, and how to implement devices into routine practice (221). Qualitative methods can help to tease out these issues, especially by conceptualising core outcomes, (222) showing how medical devices are perceived and integrated into existing practice, (220) and exploring the most appropriate trial design (23). For example, qualitative research with key stakeholders, notably patients and professionals, can illuminate decisions about: trial arms; study outcomes, such as clinical versus patient reported outcomes; and frequency of reporting.

It is important to consider why registered trials of behavioural interventions are more likely to report using qualitative methods, as this could help to increase their use in other types of trials (134). One possible explanation may be the influence of the MRC framework (19, 25). This framework advocates the use of qualitative research when evaluating complex interventions. When discussing what a complex intervention is, the authors identify behaviours as key components to be evaluated. Also, examples of complex interventions given, refer to what could be considered mainly behavioural interventions (19). For example, *'interventions directed at health professionals,' behaviour and group psychotherapies or behaviour change strategies' (19). (p.694)* The framework does not explicitly address surgical, drug or medical device trials. The MRC framework has likely been a key influence in the use of QRT. It is possible that those designing and conducting behavioural trials are more likely to consider using qualitative research. A further explanation may be the early adoption of qualitative and mixed methods research methods in the behaviourally orientated social sciences (28, 133). It is possible researchers in these fields may be more open to using qualitative

research with trials and lead to a greater uptake in behavioural trials. However, these hypotheses need investigation.

The continuing increase in reported use of qualitative methods in registered trials may indicate increased awareness of qualitative research or of the potential benefits of including it in trials. Publications that may have contributed to this increase include the MRC framework as discussed (19, 25), the empirical work of O'Cathain et al. (22) Lewin et al. (26) and Flemming et al. (15) and guidance on using QRT (22, 23, 39, 42, 223). Indeed, the timing of these publications appears to coincide with an uptick in use after 2000 and 2008 which is when the MRC frameworks were published. Also, around 2013, when O'Cathain et al's. (22, 179, 224) work started being disseminated. As these publications primarily addressed UK trials, this may also account for the greater use of qualitative methods in the UK and the UK-based ISRCTN registry.

This review has found that, though relatively few registered trials reported using qualitative methods worldwide, most of these were conducted within rich Western countries, consistent with previous reports (22, 26). There have been calls for more trials within poorer countries – with greater potential to improve public health (225-227). However, obstacles to such trials include less capacity to deliver trials; weaker links between trial conduct and current practice; regulatory obstacles and the need to adapt trials to local context and culture (226-228). These issues make QRT even more challenging (225, 229). Nevertheless, researchers have shown how qualitative research can help to address these issues in low-income countries. Vischer et al. (225) interviewed key informants in Burkino Faso, Ghana, Kenya and Senegal to investigate factors slowing the progress of clinical trials. Trial staff described factors apparently hindering trials, including lack of planning and poor understanding of trial processes. This generated recommendations for explicit trial planning and site organisation (225). Camlin et al. (230) used qualitative methods to investigate why men were not engaging with HIV testing within a trial being conducted in Kenya and Uganda. They found that work requirements in a low resource area and cultural gender norms meant men were unable or unwilling to engage with the trial intervention. As a result, additional steps were taken in the trial to adapt the intervention delivery to encourage men to engage more. Thus, qualitative research can improve the conduct of trials in poorer countries by consulting stakeholders, not least about cultural acceptability, for example of trial

outcome measures. It is important, therefore, to test whether applying this approach more widely can help identify and address challenges with conducting trials and increase their efficiency and relevance. It is also important to disseminate such work through publication in international journals and rigorous training.

Strengths and limitations

This review is limited to trials reported by researchers in trial registries as using 'qualitative' methods and confirmed by inspecting their registry summaries. However, there may be registered trials that use qualitative methods without reporting this to the registry. Indeed, searching the three registers for trials using the terms "interviews", "focus groups" or "mixed methods" identified 8,267 registered trials. I checked a random sample of 177 of these and found that 50 of their register summaries reported the use of qualitative methods (0.61%). Hence the true number of clinical trials in these registers using qualitative methods is closer to 3800 (0.61%) (0.61% of 615311 = 3738). This assumes the sample of trials is generalisable. However, as the information collected is reliant on researchers entering it into the trial summaries, ascertainment bias may be present.

A strength of this review is the inclusion of all trials registered between the start of 1999 and the end of 2016. This has shown a clearly increasing trajectory of trials using qualitative methods. Previous reviews covered short periods of time and could not analyse changes over time (23, 26). Including the three main international registries has improved understanding of when and where trials are using qualitative methods as they cover a wide range of trials across different countries.

This review reports on important characteristics of registered trials which reported using qualitative methods, namely: when they registered, where they were conducted, and the type of intervention they evaluated. Unfortunately, information was limited and inconsistent about other trial features, notably: the health area and conditions in which trials using qualitative research were conducted, their use of qualitative data collection and analysis methods, the use of theory, or the quality of QRT and how it is reported. Much of this information was available in peer-reviewed publications and were explored through a critical review of published literature (reported in chapter four).

Conclusion

This review has highlighted the reported use of QRT has increased over time and across countries. However, these methods are more prevalent in rich Western countries and less so in drug, medical device, or surgical trials. Trialists and other people involved in QRT need to recognise the potential benefits of using qualitative research with surgical, device and drug trials such as understanding clinician equipoise, establishing core outcome sets, increasing recruitment, and exploring intervention implementation. Trials conducted in poorer countries should also consider the use of qualitative research to help ensure trial processes are appropriate and acceptable to participants and inform the adaptation of interventions to local contexts.

The next chapter reports on the critical review of published literature which further considers the characteristics of trials and the characteristics of the qualitative research being carried out in trials.

Chapter 4 Exploring the use of qualitative research in trials: A critical review of the literature

In chapter three I presented a systematic review of trial registries for trials reporting the use of qualitative methods. Due to the limitations of the systematic review, I was unable to explore additional trial features which are associated with the use of QRT. It is also possible that QRT was not reported in the trial registries but may have been published. This chapter will report on a critical review of the literature I conducted to further explore the characteristics of trials and the qualitative research they use. I will also consider additional characteristics which warranted further investigation. I then present the methods used, findings and consider their implications.

Healthcare areas/conditions

There is an indication that trials in certain areas of healthcare use qualitative research more than others. Flemming et al. (15) reported only trials in palliative care, whereas Lewin et al. (26) reported trials in mental health and sexual health to be the most prevalent in using qualitative research. This may suggest these areas are more amenable to qualitative methods in trials than others. Or it may be that researchers in these areas see the potential of qualitative and mixed methods research and are therefore more interested in their use (231). However, these reports are based on a small number of trials reviewed and it remains unclear whether trials in different healthcare areas use qualitative research. This, therefore, requires further exploration.

Qualitative methods

Some authors have suggested that researchers conducting QRT only use a limited range of available qualitative methods which can limit the usefulness of QRT (26, 232). Trials examined by Lewin et al. (26) within their review mostly used interviews, focus groups and observations or a combination of these methods. The most common analysis methods used were thematic and a grounded theory or constant comparative approach. Anecdotal reports also suggest the use of qualitative methods in trials is limited to

interviews and focus groups (232). Limiting the use of qualitative methods to focus groups and interviews could exclude individuals who do not wish to discuss sensitive topics in these settings or those with communication difficulties (144). Insights from these individuals could be particularly valuable in research seeking to understand barriers to participation in trials for example. Considering the wide range of qualitative data collection and analysis methods available it is unclear why only a limited number of methods have been reported. The Lewin et al. (26) review considered a small number of publications and there are no other rigorous reviews which have examined the types of qualitative methods used in trials. It may be that other methods are being used but were not identified in previous reviews and reports. This needs further exploration on a larger scale to help further our understanding of how qualitative research is used in trials.

Stages of a trial qualitative research conducted

As discussed in chapter 2 qualitative research can be used at different stages of a trial. Reports differ on the percentage of qualitative research undertaken before, during or after trials. O'Cathain et al.'s (23) review of QRT found that most qualitative research was undertaken during or after the trials (72% of publications reviewed) with less qualitative research undertaken in preparation for the main trial, for example, in pilot studies or feasibility work (28%). In contrast Lewin et al. (26) reported most qualitative research reviewed being undertaken before the trial. As discussed previously these reviews are limited by the number of trials included and short timeframes they cover. The aim of this critical review is to provide a more comprehensive review over a longer and more recent time period, which may provide more insight into when qualitative research is conducted in relation to the trial phase (pre-trial, pilot/feasibility, during or after).

Use of theoretical frameworks with QRT

The use of theoretical frameworks with QRT can be beneficial and used to help inform the design, conduct and interpretation of QRT (192, 233-235). Theories as defined by Davis et al. (236) are

'A set of concepts and/or statements with specification of how phenomena relate to each other. A theory provides an organising description of a system that accounts for what is known and explains and predicts phenomena.' (p.327)

They offer evidence-based frameworks for understanding more about intervention development and implementation and for evaluating their effectiveness (237-239). Theoretical frameworks can help researchers define factors involved, for example, behaviours to be targeted for change or which require support and can permit development or tailoring of interventions (240, 241). They can help researchers understand how interventions work, are implemented in practice and why they succeed or fail (239, 242-244). Theoretical frameworks can also help to enhance patient engagement with trials (245, 246) and highlight potential issues with recruitment or data collection (245, 247). Qualitative research can be used to develop or refine theories of interventions and their implementation within trials (248, 249). Theoretical frameworks can also help guide the research questions, data collection, analysis, interpreting and reporting of QRT (43, 249). Although the benefits of using theoretical frameworks with QRT have been advocated there has been no systematic investigation into the use of them with QRT. Little is known about whether theoretical frameworks are used and the extent of their use. Understanding more about their use can help inform those wanting to use them with QRT and can identify potential areas for improvement or further investigation.

Objectives

- To assess the prevalence of use of QRT over time.
- To describe the characteristics of trials that report the use of qualitative methods.
- To describe the characteristics of the qualitative research carried out in trials. These included
    - Year of publication
    - Type of trial intervention

- Timing of qualitative research in relation to the trial stage
- Health areas/conditions
- Qualitative methods used
- Use of theoretical frameworks

To address these objectives, I conducted a modified critical review of the literature (250-252). Critical reviews aim to identify, synthesise, analyse, and evaluate information on a topic to identify problems, weaknesses, controversies, or inconsistencies (250-252). They are useful for advancing knowledge and identifying areas for further investigation (250). I therefore adopted this approach to explore, synthesise, and critically evaluate the use of QRT, and to identify any areas for improvement for further investigation. The conduct and reporting of this review was informed by guidance from de Klerk & Pretorius (253).

Methods

Search Strategy

I used a search strategy which sought to identify both published literature and unpublished (grey) material which reported on QRT. The search strategy included three main approaches: 1) search of electronic databases (including grey literature databases), 2) a search of references from included publications, and 3) web-based searching through Google scholar. As O'Cathain et al. (22) had previously conducted a review in the same topic area, I used an adaptation of their reported search strategy. See Appendix II for the full search strategy.

The search term strategy was applied to nine databases: MEDLINE, CINAHL Plus with full text, The Cochrane Library, PsychINFO, British Nursing Index, Social Sciences Citation Index, Applied Social Sciences Index and Abstracts (ASSIA), Open Grey, and ProQuest. Searches were conducted between 1st January 2011 and 31st December 2017.

Inclusion and exclusion criteria

To maximise the range and content of evidence all types of publications were assessed for inclusion; these included published study findings from QRT, published trial protocols and main reports such as Health Technology Assessment (HTA) monographs and theses. Publications were included if they included information on QRT and how it was conducted, were in English and had full texts available. Publications not meeting these conditions and duplicates were excluded. Methodological publications which discussed QRT, for example, guidance for conducting QRT or studies investigating QRT and which didn't discuss a specific study (actual or hypothetical) were excluded from the critical review. These publications were however retained to be considered for inclusion in the narrative synthesis reported in Chapter 5.

Data extraction and analysis

I analysed these data using the filter and count features within Excel. For each publication included I extracted and counted frequencies for the following data:

- year of publication
- publication type (findings, protocols, main report and thesis)
- trial intervention type:
    - (behavioural (aiming to modify behaviour or individuals or communities)
    - drug
    - medical device
    - surgical (involving assessment of a surgical procedure)
    - other (those which did not fit the defined categories)
- when the qualitative research was conducted in relation to the trial
    - pre-trial
    - pilot/feasibility trial phase
    - during the main trial
    - after the completion of the trial

    - other (these included where it was unclear when conducted or conducted at multiple time points and those that were not specific to one trial),
- method(s) of qualitative data collection
- method(s) of qualitative analysis
- health/disease topic area
- use of theoretical framework yes/no
- name of theoretical framework used

I used frequencies and percentages to present findings.

Updated search (2018-2020)

When preparing this thesis for submission I was aware the time gap from the original search (2017) to submission (2022) could lead to the search being considered outdated. To address this to an extent and provide some insight into whether an updated search would yield considerably different outcomes I repeated the search as described above for years 2018-2020. For all the publications included in the updated review, I extracted and counted frequencies for the year of publication and publication type (findings, protocols, main report, and thesis).

Findings

Search outcomes (2011-2017)

The search strategy generated 39,457 publications. Of these 12,937 were duplicates and therefore excluded. Following review of abstracts and full texts, 2,343 publications were included in the review. (See Figure 14)

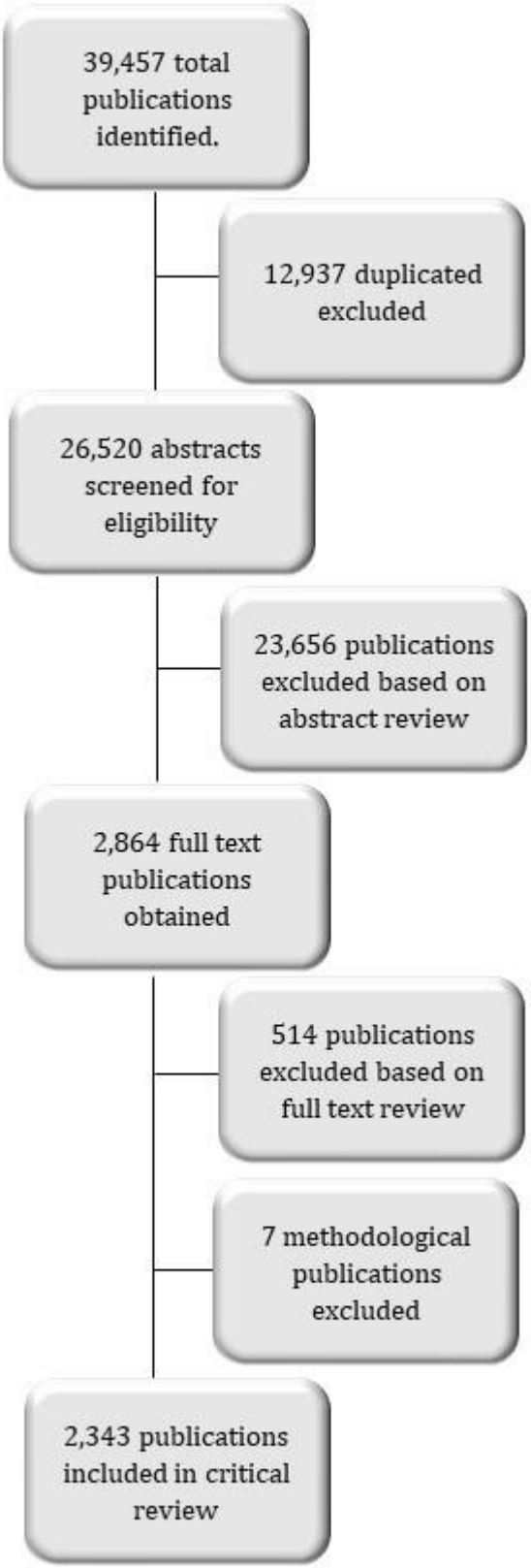

Figure 14 Flow diagram of critical review search outcomes

Of the 2,343 publications reporting on the use of qualitative methods in trials, most presented study findings, which included study reports (e.g., HTA monographs) (1709 publications, 72.9%) or were trial protocols (586 publications, 25.0%). (See Table 6)

Table 6 Types of publications included in the critical review

	Number	Percentage
Findings	1709	72.9%
Protocol	586	25.0%
Theses	48	2.1%
Total	**2343**	

Characteristics of the trials and the qualitative methods used (2011-2017)

Year of publication

The number of publications reporting on the use of QRT increased over time from 2011 to 2015 (from 243 to 446). The number fell in 2016 with a further increase in 2017. (Figure 15)

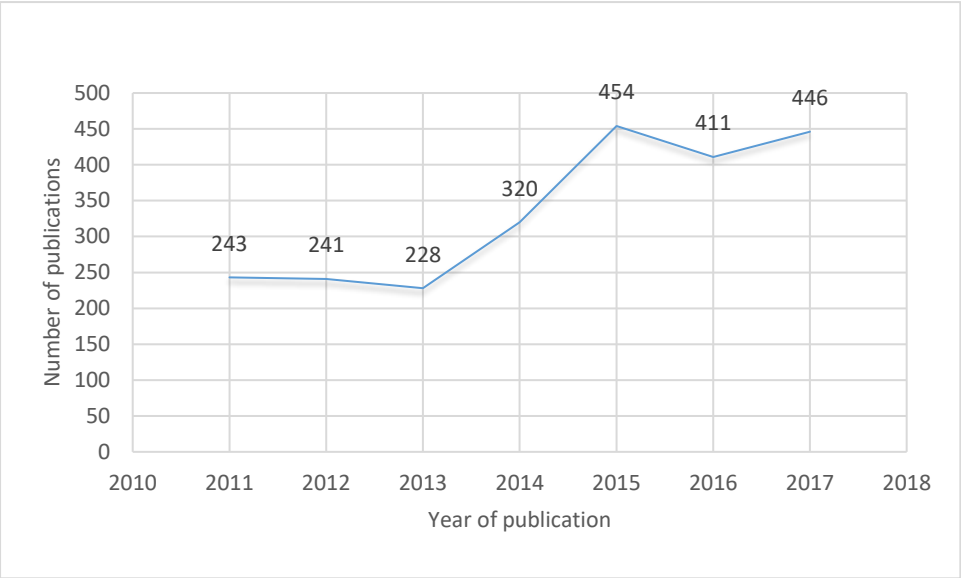

Figure 15 Number of publications over time reporting on trials using qualitative research

Type of trial intervention

Of the 2,343 publications reviewed, most reported on trials evaluating a behavioural intervention (1362 publications, 57.7%) or an 'other' intervention which included nutritional supplements, acupuncture or diagnostic testing (705 publications, 30.1%). In contrast, trials evaluating drugs (194 publications, 8.3%), surgical interventions (64, publications, 2.7%) and medical devices (18 publications, 0.8%) were much less likely to be reported (Table 7).

Table 7 Publications reporting on trials using qualitative research by type of intervention

	Number	Percentage
Behavioural	1362	57.7%
Other	705	30.1%
Drug	194	8.3%
Surgical	64	2.7%
Medical Device	18	0.8%
Total	**2343**	

Timing of qualitative research in relation to the trial

Most of the publications reported on the use of qualitative research during the main trial (1620 publications, 69.1%) or within pilot or feasibility trials (407, 17.4%) (Table 8).

Table 8 When qualitative research was used in relation to the trial stage

	Number	Percentage
Pre-trial	195	8.3%
Pilot/Feasibility	407	17.4%
Main trial	1620	69.1%
After the trial	92	3.9%
Other	29	1.2%
Total	**2343**	

Health area/conditions

Trials using qualitative research within the publications were investigating interventions across a range of 51 different health areas/conditions. Most trials were investigating interventions across more than one health area or in people with co-morbidities (347 publications, 14.8%). This was followed by mental health (322 publications, 13.7%), oncology (231 publications, 9.9%) and infectious diseases such as HIV or AIDS or malaria (194 publications, 8.3%). Table 9 displays the health areas/conditions that were greater than 0.1% of the total. For the full list and individual numbers and percentages see Appendix III.

Table 9 The health areas and conditions in which trials using qualitative research were conducted

	Number	Percentage
Mixed (2 or more health conditions)	347	14.8%
Mental health	322	13.7%
Oncology	231	9.9%
Infectious diseases	194	8.3%
Diabetes	114	4.9%
Maternity and natal	107	4.6%
Obesity	104	4.4%
Cardiovascular	99	4.2%
Gerontology	85	3.6%
Orthopaedic	83	3.5%
Respiratory	68	2.9%
Neurology	64	2.7%
Healthy participants	59	2.5%
Dementia	51	2.2%
Alcohol and substance use	32	1.4%
Musculoskeletal	30	1.3%
Smoking	29	1.2%
Palliative care	26	1.1%
Other (each accounting for less than 0.1%)	13	<0.1%
Total	**2343**	

Qualitative data collection and analysis methods

Most of the publications reported on the qualitative method(s) used in the trial (2,334 publications, 99.6%). A wide range of different qualitative methods were used in trials and some used a combination of methods. The most used qualitative methods in trials were interviews (1402 publications, 59.8%), focus groups (273 publications, 15.9%) or a combination of both (269 publications, 11.5%). Table 10 displays the full range of methods used.

Table 10 Qualitative methods used in trials reported

	Number	Percentage
Interviews	1402	59.8%
Focus groups	273	15.9%
Interviews and focus groups	269	11.5%
Multiple (3 or more methods)	150	6.4%
Interviews and observations	63	2.7%
Questionnaire	60	2.6%
Intervention data	33	1.4%
Interviews and questionnaire	20	0.9%
Case study	13	0.6%
Documents	9	0.4%
Not specified	9	0.4%
Observations	12	0.5%
Interviews and intervention data	7	0.3%
Diaries	5	0.2%
Interviews and documents	5	0.2%
Focus groups and questionnaire	4	0.2%
Narratives	4	0.2%
Online discussion forums	3	0.1%
Focus groups and observations	2	0.1%
Total	**2343**	

A range of 48 different qualitative analysis approaches was reported in the publications. Of the 2,343, the most common analysis approaches reported were thematic analysis (32.6%) and content analysis (10.5%). All other analysis approaches accounted for less than 10% of use. Many of the publications (794 publications, 33.8%) did not describe the analysis approach. Table 11 displays the analysis approaches accounting for more than 0.1% of the publications. For the full list and individualised numbers and percentages see Appendix III.

Table 11 Qualitative analysis approaches used in trials

	Number	Percentage
Not described	791	33.8%
Thematic analysis	764	32.6%
Content analysis	247	10.5%
Framework analysis	181	7.7%
Grounded theory	153	7.7%
Constant comparative	90	3.8%
Interpretive Phenomenological Analysis (IPA)	21	0.9%
Mixed analysis (2 or more analysis approaches)	13	0.6%
Systematic text condensation	11	0.5%
Discourse analysis	9	0.4%
Narrative analysis	7	0.3%
Conversation analysis	5	0.2%
Immersion Crystallization Approach	5	0.2%
Template analysis	5	0.2%
Interpretive analysis	4	0.2%
Matrix analysis	3	0.1%
Socio-ecological framework	3	0.1%
Critical analysis	2	0.1%
Descriptive analysis	2	0.1%
Dimensional analysis	2	0.1%
Editing analysis	2	0.1%
Interaction analysis	2	0.1%
Schema analysis	2	0.1%
Other (each accounting for less than 0.1%)	2	<0.1%
Total	**2343**	

Theoretical frameworks

Of the 2,343 publications reviewed only 4.4% (104 publications) discussed using a theoretical framework with the qualitative research in the trial. A range of 43 different frameworks were described across the publications. The most used approach was Normalization Process Theory (NPT) (26 publications, 25.0%). Table 12 displays a range of approaches reported. For all the approaches used see Appendix III.

Table 12 Theoretical frameworks used with QRT

Theory Name	Number	Percentage
Normalisation Process Theory (NPT)	26	25.0%
Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM)	9	8.7%
Theoretical domains framework	7	7.7%
Consolidation Framework for Implementation Theory (CFIT)	6	5.8%
Social Ecological Model	6	5.8%
Theory of Planned Behaviour	4	3.8%
Health Belief Model	3	2.9%
Self Determination Theory	3	2.9%
Social Cognitive Theory	3	2.9%
Study specific conceptual framework	3	2.9%
Programme theory	2	1.9%
Other (each accounting for 1.0%)	32	1.0%
Total	**104**	

Updated search outcomes and findings (2018-2020)

The updated search strategy generated 23,294 publications. Of these 6,925 were duplicates and therefore excluded. Following review of abstracts and full texts 3,176 publications were eligible to be included in the review. Appendix IV provides a detailed breakdown up the updated search and presents total publications from the 2011-2017 and updated 2018-2020 searches.

Of the 3,176 publications reporting on the use of qualitative methods in trials, most presented study findings (2,484 publications, 78.1%) others were trial protocols (636 publications, 20.0%) and theses (57 publications, 1.8%). This is consistent with the 2011-2017 search.

Consistent with the 2011-2017 search, the number of publications reporting on the use of qualitative research in trials increased over time from 2018 to 2020 (from 931 to 1096). 931 publications were published in 2018, 1,149 in 2019 and 1,096 in 2020.

Assessment of the inclusion of evidence through both the systematic and critical reviews

Methods and Findings

The aim of conducting both the systematic review of trial registries and the critical review was to maximise the identification of QRT. To assess whether additional QRT was identified by conducting the review of trial registries and the critical review I cross checked records included in the systematic review with publications included in the critical review.

I randomly sampled 20% (300) of the 1,492 systematic review records using the randomise function in Excel. For each of the records I used two approaches to locate publications for the registered trial. 1. The trial record in the relevant registry was checked for reported publications. 2. I searched Pub Med and Web of Science databases using the trial registration number. If publications were located, I then searched the spreadsheet of publications included in the critical review using the title and author. Of the 300 records checked 193 (64.2%) could be linked to publications from the trial. 112 of these (37.3%) reported on the qualitative research in the trial. Of these 28 (9.3%) were matched with publications included in the critical review I conducted. Therefore, 9.3% of the trial registry records checked had publications included in the critical review.

I also randomly sampled 467 (20%) of the 2,343 publications included in the critical review using the randomise function in Excel. I then searched the publications for a trial registration number. A trial registration number could be located for 247 (52.9%) of the publications. 45 (18.2%) of these could be matched with records in the registry review.

Therefore, additional qualitative research being conducted in trials was located and included in this study by conducting both the systematic review of trial registries and the critical review of publications.

Discussion

Summary of findings

Findings from the critical review of 2,343 publications over seven years (2011-2017), indicated that the number of trials using qualitative research over time has increased.

Findings from the updated search (3,176 over 2018-2020) also demonstrated a continued increase in reported use of QRT. Most of the trials using qualitative research in the publications were investigating behavioural (57.7%) or other interventions (30.1%). Relatively few trials were investigating drugs, surgical procedures, or medical devices. Most of the qualitative research was conducted during the main trial period (69.1%). Few publications reported the use of qualitative research before the trial (before pilot/feasibility) or after the trial was complete. Most of the publications reported on qualitative research being conducted in trials investigating interventions for people with co-morbidities, mental health, oncology, and infectious diseases. Most of the trials used interviews, focus groups or both. A large range of other methods was reported but most accounted for less than 0.1%. Most trials used thematic analysis to analyse the qualitative data. However, a high number of trials did not report the data analysis approach used for the qualitative data. Few of the trials using qualitative research reported using a theoretical framework with the qualitative research. The most used approach was Normalisation Process Theory (NPT).

Interpretation

Findings from the critical review of published literature support findings from the systematic review reported in chapter 3. The reported use of QRT has continued to increase over time but remains limited to trials evaluating behavioural interventions. The continued increase may be likely due to those conducting QRT seeing the benefits of QRT and continuing to use it. The increased number of publications of QRT may also have increased awareness and knowledge of QRT and led to its use. The publication of guidance for process evaluations in 2015 (110) may also have contributed to the increase. This guidance outlined the benefits of and how to use qualitative research for process evaluations in trials. The trends in the types of intervention being evaluated in trials which use qualitative research were also consistent across trials reported in trial registries (reported in chapter 3) and publications included in the critical review. The use of QRT was found to be limited to trials evaluating behavioural interventions.

Findings indicate that most (69.1%) of qualitative research reported took place during the main trial. My findings are consistent with O'Cathain et al. (179) who reported 72% of qualitative research being used in the main trial phase. Few publications reported

using qualitative research before the trial or in pilot or feasibility phases or after the trial which is also consistent with O'Cathain et al. (23). Findings are inconsistent with Lewin et al. (26) however, who reported higher use before the main trial phase. It may be my review encompasses a larger number of publications over a longer period and has provided a more comprehensive and robust insight.

Conducting qualitative research during the earlier stages of trials such as pilot/feasibility stages can be beneficial (22, 42). As discussed in chapter 2 qualitative research can help when developing interventions, (42, 165, 175), help develop and refine research questions for the trial, (15, 22) develop and test outcome measures to be used in the trial (34, 42), and explore whether trial processes are acceptable and feasible in principle and in practice (42, 165). Findings from this critical review support the need for more qualitative research in earlier stages of trials. It may be that more qualitative research is being carried out during the earlier trial stages, but it is either not being published or is not linked to the upcoming trial. Therefore, the amount of such qualitative research may be higher.

Findings indicate a range of qualitative methods are being used in trials, but most were limited to interviews and focus groups. This is consistent with the literature (144, 232, 254). It has been argued that a wide range of qualitative methods are available and that by not considering and using this range the impact qualitative research can have in trials is limited. For example, Davis et al. (232) have argued that QRT is often haphazardly or poorly used and that researchers overly rely on interviews and focus groups. Their assertion that there is limited usage of a range of available qualitative methods is consistent with my findings from this critical review. However, Davis et al.'s. (232) claim was not based on a review of methods used in QRT. Therefore, my findings support this claim. Davis et al. (232) suggest that limited use is the result of a lack of guidance and frameworks to help inform qualitative researchers working in trials about the appropriate use of the methods available. As a result, they have produced a guidance framework that encourages qualitative researchers in trials to consider a range of methods depending on the challenge being addressed within the trial. Bouchard and Tulloch (144) also argued for the consideration of different qualitative methods to increase their value and impact on trials. They advocate the use of more online qualitative methods and provide guidance on how this could be done. However, none of

the publications addressed why interviews or focus groups are not appropriate methods to be used in trials. It could be the case that the advantages of these methods for capturing views and experiences from those participating in or conducting trials are being recognised. These methods may be the most appropriate methods to use and there may not be the need to use alternative methods. Indeed Hennessey et al. (255) recommended the use of interviews and focus groups in trials for facilitating in-depth understanding of recruitment issues in a range of stakeholders. As I did not explore the reasons for why the methods were used in the publications within this critical review it is difficult to discern whether they were appropriate or whether other methods may have yielded better data. I think what is important to take away from this is not that interviews, and focus groups should not be used but that the full range of qualitative methods should be considered, and discussions had about how they best suit the aims of the QRT. Researchers considering QRT should consider the wide range of qualitative methods available and use the guidance and frameworks available to help inform their decisions.

Findings from the critical review indicate that QRT is being used in a wide range of healthcare areas and conditions. However, there is a higher prevalence in trials within mental health and oncology. This supports findings from Lewin et al. (26) who also found a higher prevalence of QRT being conducted in mental health. O'Cathain (43) also suggested that researchers in some healthcare areas may be more engaged with qualitative research approaches than others. Borreani et al. (256) reviewed the use of qualitative research in oncology research and reported an increased awareness of qualitative research in healthcare professionals. Oncology and mental health trials often have methodological issues including difficulties recruiting due to a highly selective patient population, issues of mental capacity for consent and clinician bias in patient selection (257, 258). Further issues include data collection and interpretation of findings (259) and mental health trials have been reported to have difficulties translating findings into clinical practice (257). Qualitative research is well placed to address these issues (23). For example, qualitative research can identify barriers to the implementation of mental health interventions in practice within a trial setting (260). Qualitative research has also been used to explore why patients decline to participate in oncology trials, and whether clinician preference influences recruitment in oncology (12) and mental health trials (31). The use of qualitative research in mental health

research has also been advocated in several papers (231, 261). Therefore, researchers in these areas may utilise qualitative research more than others and it may explain the higher prevalence of use found in this review. However, the increased use may be reflective of the higher number of trials being conducted in these areas than others. Goswami et al. (262) and Viergever et al. (263) conducted reviews of registered trials and assessed the number of trials conducted across different healthcare areas. Both reviews reported higher numbers of trials in oncology, mental health, and infectious diseases than other health areas. The publications reviewed did not discuss why qualitative research was used in relation to the healthcare area. Therefore, it was not possible to determine why certain healthcare areas utilise QRT.

Few of the publications reviewed explicitly discussed the use of theoretical frameworks indicating low use. Low reported use of theoretical frameworks has also been reported in implementation and evaluation research which range from 14% to 22.5% (237, 264-266). This suggests the low reported uptake of theoretical frameworks in this critical review may not only be an issue in QRT but may reflect low reported use in other research areas and approaches.

Several reasons for the low uptake of theory in research have been proposed which may be relevant to the use of theoretical frameworks in QRT. There appears to be a general lack of understanding of what theories are and how they can be used in evaluation research (249, 267). A lack of guidance and published examples of the use of theory in research have previously been highlighted (249, 267). However, more recently, general guidance for the use of theory in research (237, 249) has been published, as well as more specific guidance for qualitative research (243) and mixed methods (243, 265). Guidance for the use of specific theoretical frameworks has also been produced (234, 268). Both the NPT and Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) frameworks have extensive online toolkits which include guidance and examples of their use in trials, qualitative and mixed methods research approaches (244, 269-272). This may be why the NPT and RE-AIM are the most used frameworks in QRT within this critical review. Guidance for the use of other theoretical frameworks in trials and mixed methods research is lacking and may explain the less frequent use.

As shown by the 43 different theoretical frameworks reported within this review, a diverse and wide range of theoretical frameworks exist. These stem from different disciplines including psychology, anthropology, organisational and sociology. Research suggests that the diversity of theories and a lack of understanding can make theories difficult to engage with and alienate non-academics (133, 237, 249). Theoretical frameworks can also be seen as abstract and it can be difficult for clinicians and service providers to see their practical application and usefulness (237). This could be contributing to the low uptake of theoretical frameworks in QRT as trials usually involve multidisciplinary teams.

Drawing on the wide range and diversity of theoretical frameworks can however be beneficial in QRT. There is overlap in the aims and benefits of using theoretical frameworks and qualitative research. Therefore, using them together can maximise their respective value. Theoretical frameworks and qualitative research can be used, for example, to inform intervention development and inform researchers how they may be used and why they may work (141, 241, 273). Implementation frameworks can also guide factors to be examined within the qualitative research and aid interpretation of findings of how interventions and trial processes are used in practice (192, 274, 275).

Further key benefits of using theoretical frameworks are the facilitation of knowledge accumulation, keeping current understanding updated and the generalisability of study findings across studies and settings (133, 237, 243, 249). By not using theoretical frameworks these benefits may not be realised. The diversity and multidisciplinary nature of theoretical frameworks can mean they can be used by different groups for different reasons. This can mean that people have different expectations about how results must relate to existing ideas. It can be difficult to know which audience to address for QRT. This can result in researchers conducting QRT avoiding the use of theoretical frameworks to make findings more accessible (133). To maximise the benefits of theoretical frameworks with QRT, multidisciplinary trial teams need to engage in a dialogue about what theoretical frameworks can be used and how, and how findings can be reported to ensure they add to the wider knowledge base. Those using theoretical frameworks with QRT should make clear the value of this endeavour and why and how it was done to help facilitate future use.

Strengths and limitations

Strengths of this critical review include the systematic and comprehensive identification of all possible literature reporting on QRT. Generally, critical reviews only require a representative sample of the literature to be examined (250). Previous critical reviews have been criticised for a lack of systematicity and identification and consideration of all the available literature (250). A further strength of this critical review is the large number of publications reviewed and the inclusion of a range of different types of publications. Previous reviews have focussed primarily on published findings from trials which may limit insight (15, 23, 26). Including different types of publications may have increased the number reviewed and the type of information available and again increased the insight gleaned. Previous reviews exploring the use of QRT have been relatively small and therefore insight and understanding may have been limited (23, 26). This review of 2,343 publications is likely to have provided greater insight and more comprehensive understanding of the use of QRT than previous reviews. This review also covered a wider time frame than previous reviews (6 years in this review compared to 2-3 years in previous reviews) which has allowed for the identification of changes over time.

Although this critical review provides a comprehensive insight into the frequency of use and characteristics of QRT, there are limitations to the identification and inclusion of literature reporting QRT. Only publications where qualitative research and the trial were explicitly linked have been included. It is possible that QRT may have been undertaken and published but, within the publications, the two are not linked by trial name, registration number or any other discernible means. As it is difficult to identify these publications, I may have underestimated the extent of QRT reporting. It is also possible that non-dissemination or publication bias has led to QRT being conducted but not reported. Several publications have reported that qualitative research is conducted but not subsequently published (276, 277). To assess the potential extent of dissemination bias within QRT reporting, I sampled 300 records (20%) from trials which reported the use of qualitative research included in the registry review (chapter 3). I could only locate papers for 37.3% of trials included in the registry review. It is therefore likely that dissemination bias is present in QRT and will have affected the extent of QRT represented in this critical review. It is therefore likely that a higher

number of trials have used qualitative research but not reported this in publications. This research would not have been identified in this critical review. It is possible that multiple publications from the same trial may have been included, for example a protocol, main trial findings and qualitative paper. It is difficult to assess this as the publications do not always cross reference each other and may have different authors. Therefore, the number of trials using qualitative research and the characteristics reported may have been over reported. The inclusion of publications up to 2018 may be considered a limitation as findings may be outdated. The updated search and analysis for publications between 2018-2020 addresses this limitation to a degree. However, due to limited time and resources, I was not able to fully explore the trial and qualitative characteristics in the more recent publications. This limits insight into the more recent use of QRT. The cross checking of systematic and critical review supports the additional insight gleaned from conducting both pieces of work. Triangulation of findings from these two pieces of work (see chapter 7), therefore, strengthens conclusions drawn from them.

There are also limitations to the cross checking of trials included through the systematic review and publications in the critical review. One, I could only cross check critical review publications which included a trial registry number with the registry review records. It is possible that trials included in the registry review did relate to critical review publications, but they could not be linked. Two, the cross-checking relied on publications being located for registry review trials through the two methods outlined. It is also possible that the QRT was published but not able to be located through these methods.

Critical reviews typically result in a model or hypothesis that represents the synthesis and interpretation of data (251). This model then acts as a launch pad for a new phase of conceptual development and subsequent testing. The modified approach taken in this study meant a model or hypothesis was not developed as the aim was to critically identify areas where the use of QRT could be improved. The purpose of the thesis was to deliver a model of the use of QRT and its implementation in a later stage (this is discussed in the chapter presenting the narrative synthesis and case study). However, not developing a model at this (critical review) stage may have limited understanding

and conceptualisation of the use of QRT including the characteristics of trials using qualitative research and the qualitative research.

Conclusion

The reported use of QRT continues to increase over time. But its use remains limited to trials that are evaluating behavioural interventions and are being conducted within mental health and oncology fields. QRT offers benefits to other fields and the evaluation of other types of interventions and trialists, qualitative researchers and practitioners should consider using QRT. QRT also appears to be mainly conducted within the main stages of a trial which can limit its usefulness. Those planning and conducting QRT should also consider the wide range of qualitative methods which could provide different or additional insight to answer research questions. They could also consider the wider use of theoretical frameworks to aid the design, conduct and interpretation of QRT.

The next chapter reports on a narrative synthesis and case study which explored factors that can influence the implementation of QRT.

Chapter 5 Exploring what influences the implementation of QRT: a narrative synthesis and case study

Findings from the systematic review of trial registries and critical review of publications (chapters 3 and 4) have indicated that although QRT is being used, its use is low in comparison to the number of trials being conducted. The use of QRT is also limited to trials evaluating certain types of interventions, is conducted in a few healthcare areas and most QRT is conducted during the main stages of a trial. However, due to the limitations of the quantitative approaches of the two reviews conducted so far, I had not been able to explore why use may be low and what can be done to improve use.

In addition to examining the prevalence and characteristics of QRT it is also important to understand how QRT is planned, conducted, and reported and what can influence its implementation. As discussed in chapter 1, the implementation of research activities can be influenced by a range of factors (47). These can include how a researcher's beliefs, prior experience and current situation interact to inform their actions (46, 54, 58). Researchers can also draw on other researchers' knowledge and experiences (46, 58) and the beliefs and actions of the wider research community (58, 59). Understanding how these factors can influence QRT can help researchers conducting this research to understand what the challenges may be and to develop and use strategies to facilitate successful planning, conduct and reporting of QRT.

Several publications have highlighted challenges to conducting QRT that can lead to poor conduct and reporting of QRT as well as its potential value not being realised (15, 22, 37, 39, 278, 279). These challenges can include a lack of integration of qualitative research within trial designs (22, 37). Qualitative research is often viewed as and conducted as an 'add on' to the trial or 'integral in principle' which limits its value (39). This can also lead to qualitative research not being planned well and qualitative methods being used inappropriately (37, 39). Additionally, concerns that qualitative research is often under resourced have been expressed (15, 39, 278, 279). Reported concerns included insufficient funding, not enough time to conduct the qualitative

research and a lack of appropriate qualitative expertise. A lack of meaningful integration of qualitative and other trial data sets and findings has also been highlighted (22, 26). This can limit the benefits and value of using a mixed methods approach to intervention evaluation and reduce study rigour (41, 278). Concerns have also been raised about the visibility of qualitative findings within reports and publications and poor reporting of qualitative methods and findings (22, 26, 37). This can lead to issues with transparency and reduce the usefulness of reports for practitioners (41, 279, 280). Guidance and recommendations for overcoming some of these challenges and maximising the value and impact of QRT (22, 42, 278) and the conduct of QRT in CTUs (37, 38) have been published. Since the publication of these guidelines and recommendations (2013-2016), it is possible that others have reported on the use of QRT and discussed factors that can influence its use including barriers and facilitators. It is possible that over time and, as the use of QRT has increased, the factors and how they influence the implementation of QRT has changed. Knowing what factors need to be considered when planning, conducting, and reporting QRT can help inform recommendations for researchers using QRT.

Objective

- To explore how factors influence the planning, conduct, and reporting of QRT.

To address this objective, I conducted a modified narrative synthesis of publications that addressed the implementation of QRT and a case study of three trials that used qualitative research. As the case study builds on findings from the narrative synthesis I will present the methods, findings and strengths and limitations of each approach separately and consider the implications of both sets of findings at the end of the chapter.

Narrative Synthesis

Narrative synthesis is a storytelling approach that seeks to organise, explore, describe and interpret findings from multiple studies (281). Narrative synthesis is useful for generating new insights or knowledge by systematically synthesising data and findings from different sources (281, 282). Therefore, I used the narrative synthesis approach to explore how the implementation of QRT has been discussed in publications and synthesise data sets to bring together reported views and experiences of the planning, conduct and reporting of QRT. The conduct of this narrative synthesis was informed by guidance from Popay et al. (281).

Methods

Publication identification

Publications identified in the critical review (1st January 2011 to 31st December 2020) were considered for inclusion in this narrative synthesis. This included the publications included in the final critical review (n=5519) (2011-2020) in addition to methodological publications excluded from the critical review (n=11). Therefore, the number of total publications screened for this narrative synthesis = 5,530 (see chapter 4 for the full search strategy and search outcomes).

Inclusion criteria

The inclusion criteria for publications for the narrative synthesis were publications that explicitly discussed factors influencing the conduct and reporting of QRT (including barriers and facilitators) or, which made recommendations for good practice for conducting QRT.

Narrative synthesis elements

Popay et al. (281) described and suggests 4 key elements when conducting a narrative synthesis: 1) Developing a theoretical model of how interventions work, why and for whom, 2) developing a preliminary synthesis, 3) exploration of relationships within and between data and 4) assessing the robustness of the synthesis. The focus of this study was on the implementation of a methodology (QRT) and why QRT may be used or not used, not the effectiveness or implementation of an intervention. Therefore, I did not develop a model of how interventions work, why and for whom. Rather, I focussed on elements 2, 3 and 4 which were deemed more useful in this context and developed a conceptual map at the end of the narrative synthesis outlining influences on the use of, conduct and reporting of QRT and relationships between these. Further to this the purpose of the thesis was to deliver a model of QRT use in the case study component where an interlinked set of causal propositions are presented (see later in this chapter).

Elements 2 and 3 (Developing a preliminary synthesis and exploring relationships within and between the data)

Throughout the synthesis, I moved between elements 2 & 3 iteratively and therefore I present the methods and findings for both elements together.

Tabulation of publication characteristics

I used tabulation to provide an initial description of the publications included in the narrative synthesis and the types of information they provided (281). This helped me familiarise myself with the data. It also provided insight into the context of the QRT being reported on within the papers. This was useful when trying to understand the perspectives of the authors and helped explore relationships across the publications. I used tabulation to provide an initial description of the publications included in the narrative synthesis and the types of information they provided. Information collected included

- author(s) and year of publication

- type of publication (e.g., report on findings from QRT or methodological publications)
- the aim/focus of the paper
- research setting (National (UK) or international (outside of the UK), setting (e.g., primary, secondary care) and type of intervention being evaluated).

Reflexive thematic analysis

I used a reflexive thematic approach (283) to explore, identify and report on important patterns and relationships within and across the publications. I chose to use this approach as it is not aligned with any theoretical perspective and could be used within the pragmatic approach I took to the study. Thematic analysis is also one of the approaches recommended within the Popay et al. (281) guidance. Using a reflexive thematic analysis approach allowed me to follow the focus on the barriers and facilitators during element 2 as recommended by the narrative synthesis guidance (281), through deductive coding. But it also allowed the use of inductive coding to allow what contributed to those barriers and facilitators and relationships across concepts to be grounded in the data without any preconceptions. Reflexive thematic analysis also enabled me to move beyond a focus on barriers and facilitators towards establishing overarching patterns, relationships and linking concepts for factors that influenced QRT use. Reflexive thematic analysis also allowed me to bring in my professional experience and perspectives, as an active researcher in QRT which helped sensitise me to the issues discussed within the publications. It allowed me to engage in a meaningful way with the data using a lens, not unlike that which may be used by others conducting QRT and thus make the findings more useful to them.

When conducting the reflexive thematic analysis, I followed the six stages recommended by Braun and Clarke (283). Initially, I read through each of the publications once before extracting any data or making any analysis notes. Upon a second reading, I extracted the data for tabulation from each of the publications. I then began the coding process upon a third reading of the publications. Working through each paper I made notes for sections within the publications which were relevant for

exploring factors that influence the use of QRT. I did this on paper (hardcopy) versions of the publications. I then created a list of codes from the notes on the paper copies within NVivo (Pro version 11 and 12) (284) and coded the data within the electronic versions of the publications to the codes. I created the codes by assigning key ideas or concepts within the data to labels that reflected them. I then grouped these codes under barriers and facilitators to QRT (see Appendix V for these lists). During this stage, I continued to make notes about ideas and patterns I identified across the data and codes to help develop themes during the later stages. At this point, two further independent researchers read three of the publications and made notes about potential codes. We then discussed their notes and I incorporated them into the codes and notes for themes. This was to help gain richer insight and enhanced understanding of the data using multiple perspectives.

The next stage was to begin examining relationships across the two categories and codes and identify patterns at a broader level to develop themes. I used thematic mapping to help me visualise patterns of meaning and possible connections and relationships within and across the codes and data. At this point, I named the themes and wrote a descriptive summary for each of the themes and reviewed these narratives against the coded extracts within NVivo. I assessed whether each theme contained coherent patterns and that each theme was self-contained, allowing for necessary overlap across the themes. This required some reworking of some themes and consideration for the coherence of the new themes. I then considered the themes in relation to the data set as a whole and assessed whether the themes fitted with the publications. At this point, I reread each publication starting with the earliest published to the most recent and compared them against the coded sections within the themes. This was to explore whether themes identified in the earlier publications were consistent across the later ones and vice versa. To ensure the themes could be supported by the data when being reported, I selected illustrative quotes from the publications.

Finally, I reviewed the final themes and supporting evidence to ensure each had a coherent and internally consistent account which was reflected in the accompanying narrative and quotes. At this point, my supervisors also reviewed the themes and

provided feedback which was incorporated into the final reported version of the themes.

Conceptual mapping

Once the themes were finalised and the narrative accounts were written, I used these accounts and the thematic maps developed earlier to develop conceptual maps (281). These maps helped to simplify and visualise the influences on the use, conduct and reporting of QRT and the relationships between the themes.

Findings

Publications included

Twenty-six publications were identified using the inclusion criteria. However, three of the publications were reporting on findings from the same study as the main report identified. I assessed the content of these publications to identify whether they reported any additional information to the main report. This was not the case, and the three publications were excluded. Therefore, 23 publications were included in the narrative synthesis. Publications were published between 2011 and 2019 with most published in 2019 (n=7, 30.4%), 2013 (n=5, 21.8%) and 2014 (n=4, 17.4%). Most of the publications were methodological publications (n=17, 74.0%) with others reporting on findings from QRT with some discussion about QRT implementation (n=11, 21.7%) and one study protocol (4.3%). The publications reported on QRT across a range of settings and intervention types with most conducted nationally (n=14, 60.9%). See Table 13 for the publication characteristics.

Table 13 Description of publication characteristics

Publication ID	Author and year	Type of publication	Aim/focus of the paper	Setting/type of intervention
Pub 1	Glenton et al. 2011 (40)	Study findings	To explore heterogeneity in trial findings using QRT. Included reflections on the use of QRT.	International, mixed settings, mixed interventions.
Pub 2	Catallo et al. 2013 (285)	Methodological	To describe the process of implementing a mixed methods trial using an example study.	International, emergency care, behavioural intervention.
Pub 3	Milne et al. 2013 (286)	Study findings	To report on a feasibility study that used qualitative research to help inform the conduct of the definitive trial. Also reflected on implementing QRT.	National, social care, other type intervention.
Pub 4	Nelson et al. 2013 (97)	Study findings	To report on a qualitative sub-study of a trial. Also reflected on implementing QRT.	National, secondary care, drug intervention
Pub 5	Plano Clark et al. 2013 (29)	Methodological	Discussion of lessons learnt from conducting QRT using a trial as an example.	International, secondary care,

				behavioural intervention.
Pub 6	Rapport et al. 2013 (37)	Methodological	To describe the development and context of a Standard Operating Procedure (SOP) for QRT within a Clinical Trials Unit (CTU). Provided guidelines and recommendations for QRT.	National, CTUs, nonspecific interventions.
Pub 7	Cooper et al. 2014 (38)	Methodological	Guidelines and recommendations for improving the management of QRT within CTUs.	National, CTUs, nonspecific interventions.
Pub 8	Midgley et al. 2014 (287)	Methodological	To argue for the benefits of using QRT using a study example and describe the way QRT was used.	National, mental health services, behavioural intervention.
Pub 9	O'Cathain et al. 2014 (22)	Methodological	To report on a study exploring how QRT is used and how to maximise its value. Included recommendations.	Different aspects were national and international, mixed settings and mixed interventions.
Pub 10	Presseau et al. 2014 (288)	Protocol	To outline a protocol for a trial that included qualitative research.	National, primary care, behavioural intervention.

Pub 11	Marzan-Rodriguez et al. 2015 (196)	Study findings	To report on the qualitative contributions to a trial. Included reflection on using QRT.	International, medical education, behavioural intervention.
Pub 12	O'Cathain et al. 2015 (42)	Methodological	To provide guidance for the design and conduct of qualitative research in feasibility studies using study examples.	National, mixed settings and interventions.
Pub 13	Bartlam et al. 2016 (279)	Methodological	Using a feasibility study example, outline why and how QRT was carried out and present study findings to aid description of use.	National, mixed settings, other types of intervention.
Pub 14	Russell et al. 2016 (278)	Methodological	To describe the use of QRT using a pilot study example and discuss lessons learnt.	National, mental health in the workplace, behavioural intervention.
Pub 15	Toye et al. 2016 (289)	Study findings	To explore the benefits of using QRT using a study example and to reflect on epistemological challenges.	National, secondary care, behavioural intervention.
Pub 16	Wright 2017 (290)	Methodological	An editorial that discusses the role of qualitative research to inform trial recruitment challenges.	National, no information was provided about setting and interventions.

Pub 17	Bouchard et al. 2019 (144)	Methodological	To discuss the role and benefits of using online qualitative methods with trials.	International, non-specific setting, behavioural interventions.
Pub 18	Davis et al. 2019 (232)	Methodological	Provides a framework for integrating innovative qualitative methods into trials.	International, mixed settings and mixed interventions
Pub 19	Maher et al. 2019 (165)	Methodological	Provides a framework for integrating qualitative research into trials in addiction prevention and management.	International, does not specify the setting or types of intervention.
Pub 20	Mannell et al. 2019 (254)	Methodological	Commentary that reflects on and discusses the need for further development of QRT and how this can be achieved.	National, does not specify setting or types of intervention.
Pub 21	Richards et al. 2019 (41)	Methodological	To present findings from an expert meeting to discuss the integration of qualitative and quantitative data and findings in trials. This included examples of integration.	National, does not specify setting or types of intervention.
Pub 22	Rooshenas et al. 2019 (291)	Methodological	Describe the methods involved when using QRT for recruitment issues.	National, mixed settings and intervention types.

Pub 23	Simoni et al. 2019 (292)	Methodological	To report on an evaluation of debrief reports to facilitate the use of QRT.	International, setting not specified, drug intervention.

Themes

Four themes were developed through the analysis; 'multi-disciplinary working', 'methodological tensions and maintaining rigour and validity', 'integration, integration, integration' and 'helpers or a hindrance: Key stakeholders in QRT'. A conceptual map of the themes for influences on the use of, conduct and reporting of QRT and the relationships between these are presented in Figure 16. When presenting quotes from the publications omissions are indicated by … and paraphrasing by [].

Multidisciplinary teamworking

Who was in the trial team, how they worked together and awareness and understanding of the qualitative research within the wider trial was a key influence on the use of and conduct of the QRT. Taking a multidisciplinary team-based approach where qualitative researchers are responsible for the qualitative components of the trial but who also work with the wider trial team was important. This can help to ensure the needs of the overall trial and the qualitative research were considered and helped to ensure the qualitative research was integrated well within the trial. This in turn can lead to the development and delivery of a more meaningful and useful piece of research.

> *"To fit with a trial most effectively, these [qualitative] methods and methodological underpinning would need to be fully supported by a knowledgeable TQR (Trial Qualitative Researcher) … The TQR took a lead role in shaping these [qualitative] objectives, and worked with colleagues to ensure that, together with the quantitative objectives, they formed a coherent and integrated whole. The TQR then took on the task of designing and managing the qualitative aspects of the study: planning the data-collection methods and timetable, designing interview schedules and focus-group topic guides, and planning analysis of the qualitative data." (P6)*

Qualitative expertise and shared understanding

Having qualitative researchers with sufficient skills and experience which include an awareness of trials methodology and QRT involved for the duration of the trial from planning and obtaining funding to reporting is crucial for ensuring rigorous planning, conduct and reporting of QRT. To enable qualitative researchers to sufficiently contribute to the trial their roles needed to be appropriately funded. It was recommended that at least one qualitative researcher should be included in the team, however, multiple qualitative researchers using a *"team-based approach" (P5)* could increase the quality and value of the qualitative research being conducted.

> *"Planning the feasibility study needs qualitative expertise to determine what can be done, how long it might take, how it is best done, and the resources needed. It is therefore important that an expert in qualitative methods be included in both the planning and delivery teams." (P12)*

> *"An RCT with a qualitative study running concurrently should have at least one qualitative researcher as part of the investigative team who is committed from the start to the finish. This should be factored into the resources at the proposal submission stage." (P7)*

Having all trial team members develop a shared understanding and appreciation for all the research approaches in the trial and how they are being used together is important. Team members from different backgrounds may not understand what qualitative research is or see its value within the trial.

> *"Differences [in methodology] can raise tensions between qualitative and quantitative researchers… Researchers embedded in either of these approaches can find it difficult to understand the alternative or see its value as a research strategy." (P2)*

Therefore, it can be important to facilitate *"methodological bilingualism" (P13)* to help ensure the bigger picture of the trial and its aims and objectives, including both qualitative and quantitative approaches are considered. This can help encourage shared decision making within the team and maintain the rigour of all approaches. Key people the qualitative researchers should work with included the Chief Investigator, trial manager, other methodologists, clinicians and laypeople.

"When using a grounded theory [qualitative approach] within an RCT, it is necessary to have a research team with experts in both trial and qualitative methodologies. A team with expertise in both methods will help to identify challenges to study implementation and effective strategies to address while maintaining the overall rigour of both methods." (P2)

"First we would agree that building a strong team is critical, with shared goals and understanding that supports consensus building across all aspects of the work." (P13)

Without appropriate qualitative expertise embedded within the trial team for its duration, problems can arise. Issues with qualitative research being planned and conducted by non-qualitative researchers and a lack of continuity of researchers in the post and disjointed working practices can lead to the qualitative research being poorly conducted and limit its value.

"Another logistical challenge is the attempt to include new researchers in the qualitative analysis process. Due to the high level of interpretation developing over several years, it is challenging to bring in new individuals who do not have the long-term continuity of working with the analysis and emergent findings." (P5)

"The effect of not having [qualitative] expertise… on the quality of the qualitative research was not evident until too late… transcripts of in-depth interviewees read like clinic interviews in which the participant only got the choice of saying yes or no." (P9)

Issues can also arise when qualitative expertise is not available for interpretation and reporting of the qualitative research. Opportunities to add to the interpretation of the 'main' trial findings and to report on the qualitative research can be missed.

"Where reporting of the qualitative research was undertaken mid-RCT and qualitative research staff were on short-term contracts (e.g., Study K), they were not funded towards the end of the trial to help interpret the trial results." (P7)

"They would not publish [the qualitative research] because they ran out of time and money and the [qualitative] research assistant had moved on to another study… there is an issue of will here… we've moved onto new projects… and the question here is who in our team is going to develop the qualitative publications?" (P9)

Relationships and tensions within the team

The relationship and positioning of the qualitative researcher(s) within the trial team were important considerations when planning teams and the conduct and reporting of the QRT. Difficulties could arise if qualitative researchers had different priorities to other trial team members or were reporting findings that challenged other team members perceptions or understandings.

> *"Qualitative researchers may identify issues [with the intervention] that are uncomfortable for the rest of the research team… This may be particularly difficult if the intervention developer is part of the team… the wider team may need to challenge the findings of the qualitative research… There may also be tensions between what the trial design team need and what the qualitative researcher sees as important. For instance, the trial team may want to understand the feasibility of the intervention whilst the qualitative researcher is more interested in understanding mechanisms of action of the intervention." (P12)*

Such tensions can lead to qualitative research and its findings being perceived as problematic or being contended which can result in them being devalued or downplayed.

> *"Ultimately the qualitative findings raised critical questions about the appropriateness of the experimental design of the RCT… pointed to the need to consider an alternative to the trial design for the main study… However during the study and final report writing period, the continuing assumption was that the full study would follow a similar trial design." (P14)*

> *"Qualitative research directed at assessing the feasibility of a trial which resulted in the main trial not proceeding may be viewed by some as a success but viewed by others as failure because the trialist could not proceed along their planned route of undertaking the main trial… this was viewed as problematic." (P9)*

Communication, meetings and activities

Communication was key to maintaining good relationships and facilitating good working practices which included overcoming any tension which may arise. Meetings were important for building good working relationships and could help foster communication between qualitative researchers and other trial team members. They could also ensure qualitative researchers were included as valued members of the team.

> *"The meetings encouraged communication and often involved everyone attending all the team meetings, especially at the beginning of the project, so that good relationships could be forged from the start… the main thing was openness of communication, fostering an environment where everybody's views counts and everybody's methodology is on the same level… keeping those channels of communication open was seen to be very good… Importantly, this contributed to qualitative researchers feeling that their work was valued, particularly if they were part of the highest meeting in the hierarchy of meetings: 'I think we felt valued because the trial steering group valued that work stream'." (P9)*

Meetings could also be useful for reporting on progress and highlighting any issues arising with the qualitative research which can then be discussed with the wider team. This can enhance the usefulness of the qualitative research and ensure findings are fully considered within the context of the wider trial and by others with different perspectives within the multidisciplinary team. Meetings were reported to work best when they were regular, had a clear purpose and provided an open and shared, safe place where all views were sought and considered. The timing of meetings could be important, particularly if issues had arisen with the trial or intervention or if held to discuss reporting. The inclusion of qualitative research on Trial Management Group (TMG) agendas and the use of progress or update reports could help guide the discussion, update the team and ensure the qualitative research is visible and considered appropriately.

> *"There were regular monthly team meetings over 2 years to which all members of the team were expected to attend and contribute… All members of the team were included in the development and refinement of all aspects of the research, and comments and input encouraged by the different method leads... Meetings were chaired in such a way that the views of each individual were actively sought and received constructively. While*

some items featured more prominently at particular moments in the research process, there was a standing agenda that included all aspects of the research. Emerging findings from the qualitative research were regularly presented to the full team, and divergent explanations were considered. It was during the team meetings that the discussions around how these did or did not reflect the findings from the survey took place. This triangulation increased confidence about integrating the findings into the pilot RCT." (P13)

"An effective form of monitoring lies in progress reports to trial management meetings. These bring all aspects of trial methods to the attention of the trial management group at regular intervals." (P6)

Involving non qualitative team members in qualitative research activities such as analysis can help to enhance mutual understanding. It can also help form a more complete picture of the data which can increase the rigour of the qualitative research.

"Members of the [trial] team learned about the strengths and weaknesses of distinct paradigms and their associated methodologies by entering into conversation about what each could offer the other. For example, health economists, trialists, and gastroenterologists in [trial] took part in elements of the qualitative group analysis, to understand the rich detail of the interviews with health professionals and patients… and as a result, understood the qualitative datasets more clearly, which had an effect on both health economic and statistical analysis… this coming together of methodological groups, through a greater respect of the different paradigms, enhanced mutual understanding." (P6)

Methodological 'tensions' and maintaining rigour and validity

When using QRT, the publications highlighted the importance of considering and maintaining the integrity, rigour, and validity of all methodological approaches within the trial. They discussed the challenges of using both qualitative and quantitative approaches without compromising one or both methodologies. Different paradigmatic or epistemological differences for qualitative and quantitative approaches can lead to

methodological tensions with the experimental components of the trial often taking priority. This can lead to researchers not using qualitative research in trials, conducting the qualitative research poorly and assigning it a lower status or priority within the trial.

> *"Combining two paradigmatically different methodological approaches is challenging." (P19)*

> *"When different assumptions are used for the two components of an embedded design such as those with post-positivism and constructionism, then points of contentions and discord in the design decisions may be expected to arise." (P5)*

Maintaining integrity and validity of the experimental aspects of the trial

Fears about the qualitative research negatively impacting the scientific integrity and validity of the experimental aspects of the trial were reported. Key areas of concern included contamination of the trial arms and the intervention, unblinding of investigators and additional participant burden.

> *"It is also possible that qualitative research… can threaten the scientific integrity or successful completion of the trial." (P17)*

Qualitative research may function as an additional intervention or influence the way people perceived the intervention's impact. Taking part in qualitative approaches that can involve in-depth discussion and reflection about the intervention may provide a therapeutic effect. This can potentially contaminate the trial arms, influence how people perceive the intervention and affect responses on quantitative outcome measures. This can threaten the validity of the trial and be concerning for trialists.

> *"Concern about the contamination of the experiment by the qualitative research, with concern, that some intensive techniques, such as diary keeping, and interviews… particularly where the intervention you're evaluating has got a psychosocial component, you do worry a little bit… can offer therapeutic effect… which can water down the impact of the actual intervention." (P9)*

To help address this, it was important to consider the timing of the qualitative research in relation to other trial activities. For example, collecting qualitative data after the key

quantitative outcome measures are administered can help mitigate contamination, or streamlining the area of questioning within the qualitative research can help to reduce participant burden.

"This requires thought at the planning stage so that intensive qualitative data collection… can be taken after the collection of the important outcome data." (P9)

"Given that interviews involve a time burden and may constitute a co-intervention involving prompting, we will conduct the interviews after the follow-up outcome data has been collected." (P10)

"Since our qualitative approach was implemented 12 months after completion of the initial study, participants had completed a great deal of quantitative measures in the process. Therefore, we concentrated our line of inquiry on issues of importance for intervention development in order to reduce potential burden." (P11)

Those conducting trials also needed to consider how qualitative findings could potentially influence those delivering or receiving the intervention. Negative feedback for example could lead to those delivering the intervention to change their behaviour and delivery of the intervention or trial processes which may not be in line with the protocol. This can make it difficult to evaluate what is being delivered and measured. It could also make the delivery and completion of the trial difficult.

"Knowledge of dissatisfaction with, or acceptability of, the intervention may result in attempts by the team (consciously or unconsciously) to adapt or improve the intervention. Such changes may be acceptable as part of a feasibility or pilot trial where development of the intervention is an aim of the study but is unlikely to be acceptable within a pragmatic phase III trial of effectiveness." (P1)

"Findings from the qualitative research indicated that the intervention was unpopular and poorly adhered to by participants. As trial recruitment was still open, there was a concern that reporting of these findings to trial staff may compromise recruitment due to de-motivation of the recruiting staff… putting findings about problems expressed the intervention into the public domain might lead to demoralisation of participants and affect outcome assessment and attrition." (P7)

However, feedback from qualitative findings could be useful at certain points in the trial process, such as in pilot or feasibility studies leading to qualitative research being perceived positively. It was, therefore, important to carefully consider when qualitative findings were reported.

> *"Where qualitative research was undertaken concurrently with the full RCT, the purpose of the regular interchanges between the qualitative researchers and the RCT team was planned in the qualitative research protocol. The purpose of the feedback of the qualitative findings whilst the trial was in progress was to allow the qualitative study to adapt to the needs of the trial and the trial processes to also be adapted if necessary." (P 7)*

Constraints placed on qualitative research by the trial

These tensions can lead to the qualitative research being constrained or compromised by the needs of the primary experimental trial design. Qualitative research was reported to be positioned at a lower status or priority within the trial compared to other quantitative components.

> *"[They] raised concerns specific to the use of qualitative methods within experiments, arguing that such mixed methods design typically limit qualitative research to auxiliary, non-interpretive roles." (P5)*

> *"There are concerns… that qualitative research has been assigned to second-class status when used with RCTs, with undermining of its epistemological roots." (P9)*

> *"In the case of an embedded RCT, the constraints required by the primary RCT design aim to achieve a high level of internal validity so that researchers can make a strong cause-and-effect claim…We might anticipate that the assumptions behind an RCT may be at odds with and place constraints on the design of an interpretive qualitative approach… constraining these [qualitative] approaches to adhere to the parameters of an RCT potentially limits the value of the methods for uncovering participant meanings and experiences." (P5)*

This can lead to the standards and expectations usually applied to quantitative research being inappropriately applied to qualitative research. Concerns were raised in the publications that this compromised the methodological approach of qualitative research and the benefits and value of using it can be lost.

"The qualitative research could have a very quantitative approach imposed on it to make it acceptable to the team, for example, the topic guide being highly structured and resembling an interviewer-administered questionnaire... some researchers described implicit pressure to undertake large samples." (P9)

"There are concerns in educational evaluation that qualitative research has been assigned to second-class status when used with RCTs, with undermining of its epistemological roots. We found some evidence of this in our interviews in which some researchers described implicit pressure to undertake large samples and structured interviews." (P9)

"Some researchers propose the need to attend more to the epistemological roots of qualitative research to maximise its potential." (P15)

Qualitative research can be constrained by the need to rely on timely progression and recruitment to the trial. Slow recruitment to the trial for example can impact qualitative researchers meeting targets for the qualitative sampling, recruitment, and data collection. This can compromise the rigour and usefulness of qualitative research findings.

"We had intended a purposive, maximum variation sampling approach, but due to slow recruitment [to the trial], we interviewed all available willing participants and caregivers in order to gain a full range of experience/perceptions and maximise the chances of data saturation." (P3)

"There were occasions when participants were sought for the [qualitative] phase but were no longer being followed up by the RCT… This created challenges for the [qualitative] phase, as participants who had completed the trial were no longer interested in participating in an additional study. As a result, it is uncertain what the overall impact was for having fewer participants." (P2)

Adaptation and flexibility

Publications discussed the importance of being flexible with how qualitative research was used within the trial and to be innovative and adapting traditional methods of sampling, data collection and data analysis. This could help address some of the issues with reconciling differences in approaches within the trial and addressing the constraints that may be placed on qualitative research.

> *"The process of maximum variation sampling required modification to conduct the grounded theory [qualitative] phase. Typically, when this type of sampling is used in grounded theory, new participants outside of the study are sought to test the full spectrum of a category's properties and dimensions… Our purpose was to understand violence disclosure from the perspective of the RCT participants, so we did not recruit participants from outside of the trial. We addressed maximum variation sampling by examining variants of intimate partner violence IPV disclosure events at opposing spectrums." (P2)*

Qualitative research which is completed in a shorter time frame (compared with traditional longer time frames), and which is more focussed within trials can also be more conducive to trials methodology and help to overcome or adapt to some of the perceived constraints of the experimental design.

> *"Drawing on ethnographic techniques in anthropology, observation as a method often involves sustained immersion in the research setting for a long period, which is not always possible as part of formative research leading up to a trial or within the constraints of a process evaluation. As an alternative, quicker approaches to ethnography were mentioned by interview participants, including social mapping, non-participant observation, and "Broad Brush Surveys", which systematically gather data on communities in a period of 5–12 days… These rapid techniques draw on the advantages of ethnographic techniques while adhering to the limitations of a trial and the need for rapid results." (P18)*

It was important to consider both qualitative and quantitative approaches together and how they can work together while maintaining the integrity of both within the trial. Although the qualitative research may be perceived to be constrained by the trial,

rigorous and useful qualitative research can still be conducted with some consideration and structural changes.

"As a result of implementing a mixed methods study during the course of an RCT, methodological considerations were made in order to maintain the integrity of the trial and the mixed methods component." (P2)

"To make the most out of qualitative research alongside quantitative research designs, it would be useful to (a) agree specific qualitative study aims that underpin specific research designs; (b) understand the impact of differences in epistemological truth claims." (P15)

"Due to the embedded nature of the study, the design of the qualitative data collection methods was directly shaped by the requirements of the RCT… Decisions were made in designing the embedded qualitative methods… of the study adhered to the parameters of the larger RCT design framework… We identified that it is possible to integrate a qualitative approach with an RCT if modifications are made… Despite adaptations to the grounded theory, we still maintained methodological rigour which made it possible to combine with an RCT." (P5)

To help address the challenges of reconciling mixed paradigmatic approaches and maintaining rigour and integrity of all approaches, a turn to using a pragmatic mixed methods approach was used and recommended. Within this approach, the qualitative and quantitative components are used together to answer different but complementary questions.

"Researchers found that those who take an "integrated methods approach" also see qualitative research as essential to the trial and as producing evidence related to the "real world" [3]. The [name] study therefore recommends that researchers design and implement "studies not trials", with the outcomes of the qualitative research being "central to the team's thinking"… In practice, the implementation of "studies" rather than "trials" requires researchers to adopt a neutral approach to methods. This essentially means selecting the best method for the research question posed rather than making presumptions about which methods are best based on a hierarchy of evidence." (P9)

"Instead, we argue that there needs to be a fundamental shift in thinking that moves away from implementing trials altogether (which implicate a focus on quantitative evaluation) and toward conducting studies (which include a mixed-methods approach to understanding the impact of interventions)." (P20)

"RCTs and qualitative studies fulfil different roles and are complementary." (P19)

Planning and documenting

It was important to consider how qualitative research can be designed to ensure the needs of the quantitative and qualitative components of the trial can be met the during planning stages. This could help improve the quality of the qualitative research, ensure the full potential of the qualitative research was being realised and facilitate its successful implementation. The preparation of funding applications and designing the trial were critical timepoints where the needs of both the qualitative and quantitative approaches within the trial could be considered.

"The importance of the qualitative component for the current… study was recognised and valued from the earliest planning stages, and this was critical in facilitating the quality of its implementation throughout the study." (P5)

"To make the most out of qualitative research alongside trial designs, it would be useful to agree specific qualitative study aims." (P15)

Thinking through how the qualitative research related to the overarching trial framework and conduct was believed to be key to upholding the importance, value and rigour of all approaches in the trial. It was essential to consider how the qualitative research may influence the experimental components of the trial and how this may be addressed.

"Consider whether it is intended that the qualitative research will be used to adapt, amend or refine either the intervention or aspects of trial conduct during the trial. If this is intended; this should be made explicit and the processes by which it will occur should be clear before the trial commences." (P1)

To help think through the processes involved, it can be useful to document the qualitative research and its relationship to the other aspects of the trial. This can be

done with trial protocols, separate qualitative protocols, standard operating procedures, or analysis plans. This can also help make other trial team members aware of the qualitative research and establish explicitly what is expected from the team.

> *"The potential influence of the qualitative research on the conduct of the full trial… was built into the protocol for the full RCT… particularly clarifying whether the qualitative research is intended to be used to adapt… the trial." (P13)*

> *"Trial protocols provide rationales for each method chosen. When there is more than one method used, the trial protocol should describe how these together will enhance the study… it is important to plan mapping in advance to avoid one method undercutting another which should therefore yield greater understanding in depth." (P6)*

Integration, integration, integration

Having *"meaningful integration" (P2)* of the qualitative and quantitative components of the trial was seen to be an important part of good practice in QRT. Integration was believed to enhance the benefits of using both approaches together which can provide greater insight for the investigators.

> *"The integration of both approaches offers something that neither a clinical trial nor qualitative data can offer when looked at separately." (P2)*

> *"Researchers… saw integration of the qualitative and quantitative findings as a mark of quality… when interviewees perceived a lack of impact of the qualitative research on the specific trial, they explained it in terms of a failure of the two methods to be integrated." (P9)*

Early consideration of opportunities for integration throughout all stages of the trial could maximise the points at which integration occurred and therefore the value of integration. Key points in the trial where integration could occur were highlighted including sampling, data collection, analysis, interpretation, and reporting. Connecting methods and data can help to develop the qualitative research and make it more appropriate and useful for addressing the overarching trial research questions, aims and objectives.

"Planning for a mixed methods design at the outset of a study will enable consideration of the design needs including the implementation of the quantitative and qualitative components and opportunities for mixing the two data sets… plan for multiple data mixing opportunities such as at the later stages… to aid in recruitment data collection and analysis." (P2)

"Determining an appropriate sampling scheme is pivotal to the preservation of rigour and the overall integration of results for a mixed methods study… Embedding quantitative data during qualitative analysis helped to support theoretical coding and this drove decisions about continued sampling of participants." (P2)

"After the initial analysis phase, the qualitative and quantitative strands of the study will be re-integrated, so that the final stages of analysis and writing, two complementary sets of learning will be reported together." (P6)

Having integrated teams where the members from different disciplines worked together for practical day to day working was also important to promote integration. Communication between the different team members could help facilitate understanding of how different approaches could be integrated and the interpretation of findings.

"It [qualitative research] is integrated with the RCT, and its leadership and personnel, providing nuanced understanding that can drive changes to the way the RCT is delivered." (P22)

"TMG to consider qualitative and quantitative results together with advice from TQR [trial qualitative researcher] and trial statistician and synthesise findings." (P13)

"Opportunities were missed for joint problematisation through more in-depth integrative team communication." (P14)

However, achieving meaningful integration can be difficult.

"Difficulties relating to appropriate integration... question was how to… address the question of data analysis and integration procedures. There was a challenge of how to

transform the data from one study [qualitative research] in such a way that could be integrated with findings from another study [quantitative research]." (P2)

"Integration problems occurred around the inclusion of appropriate data collection." (P6)

A lack of, or inconsistent integration was highlighted which was concerning to researchers who felt that integration was often overlooked or avoided. Qualitative and quantitative components of trials were often considered and presented separately.

"Little discussion of the integration of methods and few studies presented the contribution of both qualitative and quantitative methods to overall study interpretation." (P2)

"Integration rarely occurs in practice… Researchers tend to analyse these data sets separately then consider their findings separately within the discussion section of the final report to funders. Researchers rarely integrate quantitative data or findings." (P21)

A lack of integration can stem from a lack of awareness and skills and knowledge of why and *how* to integrate qualitative and quantitative trial components. Most researchers are trained or focus their expertise in one area and lack training in both approaches and how to successfully achieve integration. There is also a lack of good examples and guidance for researchers.

"This may be because researchers are not aware of existing integration techniques or do not see the value of these techniques to the context of RCTs." (P21)

"While many investigators have received formal graduate training, few have been exposed to the specifics of mixed methods designs and the process for mixing and integration of data." (P2)

"Attendees struggled to identify many published examples of integration undertaken in the context of RCTs". (P21)

Issues with time and resources to appropriately integrate qualitative data and findings were reported. Preoccupation with the day-to-day conduct of the trial including

qualitative components and the time required to collect and analyse data can mean there is not always time to undertake integration. Components can be conducted and completed at different times which can lead to data not being available for consideration together. Time needs to be factored in if researchers wish to achieve any meaningful integration of QRT.

> *"It has been argued that insufficient account is taken of the challenges around resources including the time needed for not only data collection, but analysis at a mixed methods level." (P13)*

> *"Future mixed methods studies build in time for ongoing integrative thinking to ensure that qualitative and quantitative components add up to more than the sum of their parts." (P14)*

How qualitative research is perceived and conducted with the trial can influence whether and how integration occurs. Whether the qualitative research is viewed as valuable and how it is positioned in relation to the trial can influence integration.

> *"Qualitative methods often are poorly or haphazardly integrated into existing trials, contributing to variation in the quality of qualitative research used alongside trials… This is evidenced by the lack of explicit reference to how qualitative findings have been used to interpret or help explain quantitative trial results in published articles… and is compounded by… the "add-on status of qualitative research"." (P18)*

> *"An important step is to communicate the potential value of integration to the research community through relevant examples." (P21)*

Even if integration has been considered and achieved at the data collection and analysis stages, it can be difficult to deliver integrated reporting. Often the qualitative and quantitative components of QRT are reported separately.

> *"Regardless of the degree of integration of the two during the trial, capitalising on the value of the qualitative research to trials at the publication state seemed to present a final challenge that proved insurmountable for many." (P9)*

"*Typically, two separate journal articles were published." (P9)*

A key factor in the lack of integration at reporting stage appeared to be journal reporting conventions, particularly article structures and word limits for publications which inhibited comprehensive and integrated reporting of QRT. This limited integration when reporting with separate articles for separate trial components being reported.

> *"Journal formats may prevent findings from qualitative studies and trials… being integrated or presented together." (P1)*

> *"In a digital age, while an emphasis on being concise is clearly appropriate, we would suggest that word counts per se are increasingly irrelevant not least because of the limits they impose in reporting integrated findings from mixed methods research, as our experience indicates." (P13)*

Helpers or a hindrance: Key stakeholders in QRT

Whether QRT was used, how it was conducted and how it was reported was influenced by the attitudes, beliefs, and practices of key stakeholders. These stakeholders could influence the use and delivery of QRT at different levels including at an institutional or organisational level, through the shared belief systems of the trials research community and at an individual level.

Within the research community, higher importance and value has historically been placed on quantitative research which is perceived to be more credible than qualitative research. This view appears to be reinforced through a reluctance to fund and publish qualitative research and can lead to people not using QRT.

> *"RCTs have historically been afforded more credibility and legitimacy in the scientific community than qualitative studies, and an important consequence of this is the RCTs have attracted funding without the need to even consider qualitative research." (P18)*

Funding organisations

Members of funding organisations including panel members and reviewers are key stakeholders who can influence whether and the extent to which QRT is funded.

Sufficient funding is essential for QRT to be conducted well, however, a bias against funding qualitative research, prioritising the funding of other aspects of the trial and issues with funding applications can lead to funding either not being requested or being denied by funding bodies.

"Due to budget constraints, only the first quantitative aim… was initially funded." (P5)

"There was a bias against funding qualitative research with trials… the qualitative research was underfunded." (P9)

To combat these issues, researchers tended to minimise qualitative costs within trial grant applications. Although this approach could secure funding it was often not sufficient for the needs of the qualitative research. This led to a sense of pressure on qualitative researchers to deliver high quality results with limited resources.

"To keep the costs of a bid down, either by second guessing their chances of securing a large enough grant to fund the qualitative research properly or by trading in the goodwill of qualitative researchers to squeeze it in without proper funding… This minimalist cost approach was felt to compromise the depth and quality and therefore the value of the qualitative research." (P9)

Those reviewing funding applications for QRT could find it difficult to make informed decisions about approving the requested funding. Funding applications were reported to lack adequate information about what the qualitative research would achieve and how it would be conducted. This was attributed to a lack of space within the application forms, but responsibility also lay with applicants who did not appear to utilise space when it was available.

"It's a difficult one for funders… I sit on funding panels, and I sometimes think you can look at proposals and see they just squeeze something in and it's not really clear what the linkages are and the value, so I think researchers have a real job to sell the value of these different methods in their proposals… and then funders make the decision of whether to fund it or not." (P9)

"As a grant reviewer, you tend to get very tired of people saying, 'Oh yes we'll do a mixed methods evaluation… because it's very important blah blah blah, and then they say

absolutely nothing about what exactly they're going to do… there are very few applications you get where they can't say a lot because of the fact that the forms aren't helpful to support that." (P9)

Journals and reporting conventions

Journal editors and reviewers were believed to have a role in hindering or encouraging the reporting of QRT. These people are responsible for establishing, maintaining, or changing reporting conventions including how articles are structured and the types of research deemed valuable or important. Journals can reinforce perceptions that qualitative research is inferior to quantitative research through a persistent focus on publishing quantitative articles. This was believed to be more prevalent in medical rather than methodological journals. Journal structures such as small word counts can also be problematic for people wanting to publish in-depth and rich findings from qualitative research as more space and words are required.

"Qualitative findings are often perceived as less robust and therefore less valid than quantitative research findings. This contributes to a bias against qualitative research findings by health journals and a reluctance by researchers to publish anything qualitative alongside their "clean" trial. This publishing bias is reinforced by small word counts by quantitative journals that do not allow for the inclusion of robust qualitative findings as part of trial results." (P20)

"Part of the problem is the continued reluctance of high impact medical journals to publish qualitative research." (P17)

"Even if qualitative studies are completed, journal editors can impede publications by refusing to review qualitative research or by imposing word limits that make it impossible to adequately report qualitative methods and findings." (P19)

Qualitative research has also been considered a lower priority when publishing trials research as quantitative articles are believed to be more valuable and more readily accepted. Due to this, it was unlikely that the qualitative research would be published if time was limited and people had moved onto new projects as people would focus on the other aspects of trial reporting.

"Teams breaking up before non-priority papers were written, which in this case were the qualitative papers were unlikely to be published in three-star journals." (P9)

By allowing more flexibility in the way research is reported and publishing more qualitative research, it is likely that the amount and quality of QRT being reported would increase. Having journal editors and reviewers who understand qualitative research could also ensure articles are appropriately reviewed and help recognise where qualitative research could be included.

"A consideration of a more flexible approach on the part on the health science journals would appear warranted… only when there is sufficient critical mass of cross-disciplinary understanding within the wider research community – including at the level of editorial and review teams – can we genuinely reconceptualise disciplinary boundaries." (P13)

"In the case of the [name] study the draft manuscript of the main paper included very little about the qualitative study; encouragingly however, journal reviewers requested that more detail be included, arguably indicating a growing awareness of the need for mixed methods studies to be reported and published." (P14)

Institutions

Institutions such as universities, research hubs and CTUs can be key organisations to support and actively encourage the use of QRT. They can help to ensure it is conducted well by providing infrastructure which promotes collaboration of multidisciplinary working and use of QRT. The inclusion of qualitative researchers within CTUs can be mutually beneficial as it can help to develop expertise and bring in funding to the CTU as well as promote and provide a supportive environment for qualitative researchers to conduct the qualitative research.

"The culture for collaboration necessary for effective inter-disciplinary mixed methods will struggle to exist without broader, strategic support structure… Within the institute there is a strong emphasis on interdisciplinary collaboration… Staff are expected to develop research proposals in collaboration with a range of colleagues –[including] clinical trials and a wide range of qualitative methods." (P13)

"To promote the sustainability of qualitative research within trials, the SOP advocated recruiting staff with qualitative expertise, and retaining them to enhance resources and profile of the CTU." (P6)

"One interviewee suggested that locating someone committed to qualitative research permanently within a clinical trials unit could facilitate this early understanding of the need for qualitative research and expertise in designing it." (P9)

Individual beliefs and motivations

The aspirations of stakeholders such as researchers and their attitudes towards developing qualitative research skills and expertise could influence the use of QRT. To further their career, researchers believed they needed to secure funding, conduct prestigious trials and publish their research in high impact journals. However, as it can be difficult to achieve this with QRT, there is less incentive and therefore motivation for people to engage with and conduct QRT. Qualitative researchers may also become disadvantaged by these limitations.

"Pursuit of an academic career within the current structures also include the need to bring in more funding and move on to the next project… They [researchers] are essentially driven by the task of undertaking a highbrow RCT, getting publications on it and moving on to the next best thing." (P9)

"A hierarchy that positions quantitative results as more valuable, policy-oriented, and actionable than qualitative findings. From the amount of funding to the number of papers published in top journals this hierarchy is explicit and tangible in the disadvantages it creates for career recognition and advancement among qualitative researchers working in the health sciences." (P20)

Working with people who did not value or understand qualitative research could be challenging, particularly for the qualitative researchers who were designing or conducting QRT. Qualitative researchers found themselves having to challenge existing negative assumptions about qualitative research and defend their discipline.

"Could be challenging when working with people who are from a more quantitative background… helping then understand… qualitative research… researchers described

an experience of distance being created by colleagues perceiving their research as unimportant compared with the trial." (P9)

"The challenges are more to do with convincing traditional trialists and traditional medics who think in terms of experimental designs only, and really don't think that qualitative research is any more than something that is a bit woolly. So… the latest challenge is presenting and selling the importance of doing qualitative research and what it actually achieves." (P9)

However, those who had seen the benefits of using QRT previously were seen to be more open to it and include it in the trial. This was welcomed by qualitative researchers trying to design and implement QRT.

"From the outset, the principal investigator, research teams and project steering committee welcomed the contribution they considered qualitative research could make to the trial." (P14)

"The research team had experienced the value of qualitative research in the prior pain management RCT study… This led to a commitment by the research team to include a more substantial qualitative component on the current study from the beginning." (P5)

The health area the stakeholder was working in, and the type of trial intervention being evaluated by the trial could influence whether QRT was valued and used with some areas appearing more open to QRT.

"Examples were cited in which qualitative research was not seen to have any potential value to add to the trial, for example, drug trials or trials with clinical rather than behavioural outcomes… some clinical specialities were seen to be more sympathetic to qualitative research than others – palliative care, public health and primary care – for which one might argue the complexity of intervention is more obvious than other specialities." (P9)

Increasing knowledge and skills

Increasing knowledge, understanding and the perceived value of QRT was believed to be important for challenging the negative assumptions around QRT and promoting its use. Communication to the research community about the benefits of using QRT, its

value and how it can best be used and conducted could achieve this. Potential avenues for this communication included publications and training.

> *"Important step is to communicate the potential value of integration to the research community through relevant examples. Once researchers see evidence of value, in terms of this practice generating credible new and useful insights, formal guidance could be developed to ensure the quality of this endeavour." (P21)*

Being clear and transparent in reporting could increase knowledge and understanding and appreciation of what QRT can contribute to the evidence base, and raise the profile of QRT.

> *"Such transparency in reporting is increasingly recognised as critical in learning and improving evidence-based research and practice." (P13)*

> *"Qualitative research findings can go beyond the clinical trial in which they are embedded and make an independent contribution to knowledge." (P15)*

> *"Some researchers have developed considerable expertise and skills in undertaking qualitative research within trials and could share this expertise by running training course and writing about how to undertake this work well." (P3)*

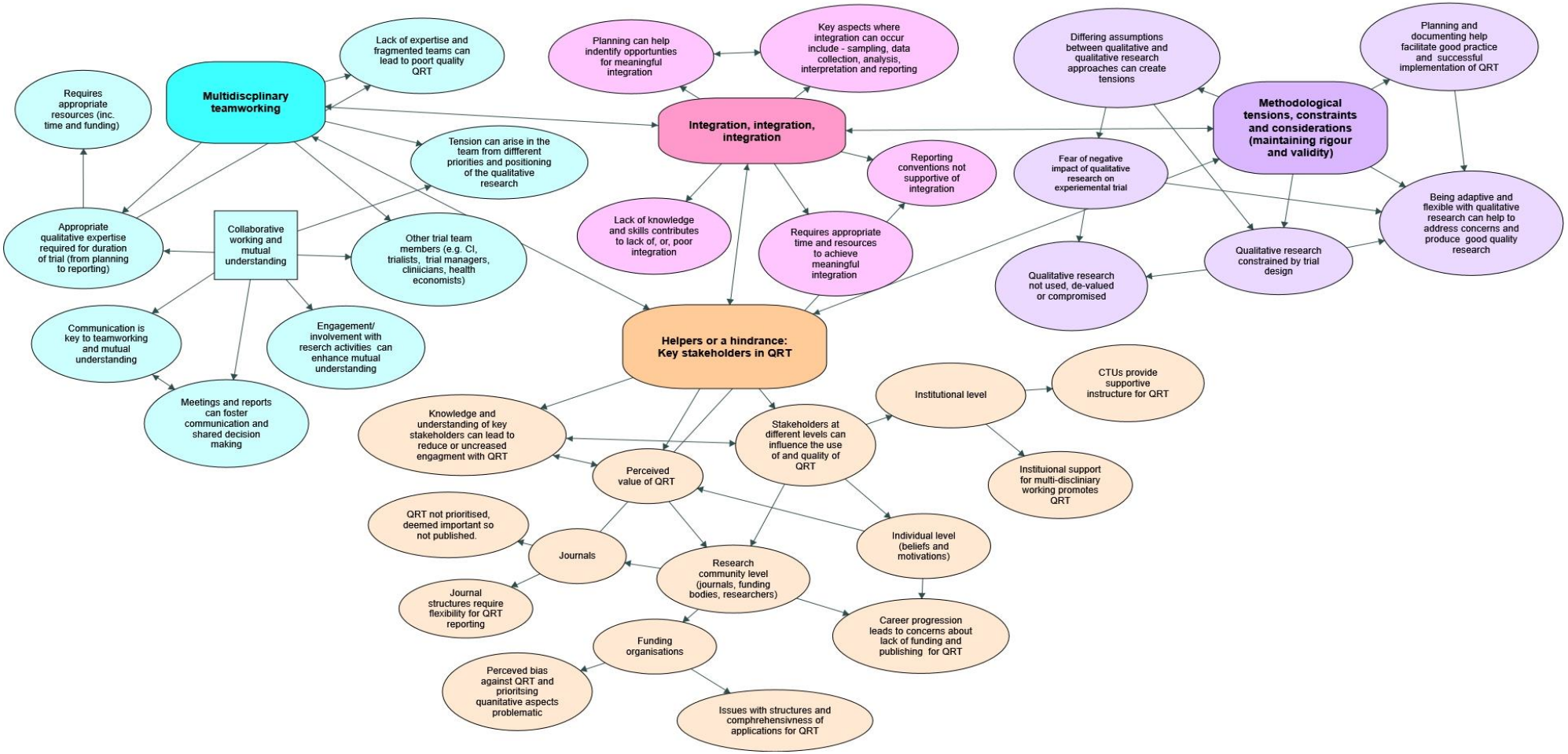

Figure 16 Conceptual map of themes and factors influencing QRT

Summary of findings

This narrative synthesis has explored and identified several key influences on the planning, conduct and reporting of QRT described within 23 publications published between 2011 and 2019. Multidisciplinary teamwork which involved qualitative researchers being embedded within trials teams and working with team members from other disciplines for the duration of the trial was important. Awareness, understanding and discussion of all approaches by all team members within the trial could help to ensure that qualitative research and its appropriate conduct in relation to other trial approaches was recognised and encouraged. Frequent and open communication as well as involving non qualitative team members in qualitative research decision making and activities could help to build and maintain good working relationships and promote awareness and understanding of the purpose and value of the QRT. Without this, tensions could arise and result in qualitative research and its findings being perceived negatively, being downplayed, or dismissed and not being appropriately utilised.

Resistance to qualitative research and greater credibility being given to quantitative research appears to stem from the perceived dichotomy between them. This led to methodological tensions when using both approaches and greater importance being given to quantitative approaches and led to constraints being placed on the qualitative research trial components. It was important to be mindful of how each approach could affect each other and take steps to help reconcile differences and ensure the integrity and usefulness of both the qualitative and quantitative research. This could be achieved through being flexible and adapting the qualitative methods throughout the trial in a way that maximised the value using both approaches within a mixed methods evaluation. Early planning and documenting the qualitative research and its relationship with other trial components could help with bringing team members together to discuss and understand potential issues and the best ways of designing and conducting the QRT.

As well as a consideration of methods, the integration of qualitative data and findings with other trial sets during interpretation and reporting was believed to be important

for maximising the benefits of using multiple approaches. However, meaningful integration was difficult to achieve and often the components were conducted and reported separately. This appeared to stem from a lack of knowledge and skill in mixing the approaches, time constraints, how valuable the QRT was believed to be and restrictive reporting conventions.

The beliefs and actions of key stakeholders influenced whether QRT was used and how it was conducted and reported. Obtaining sufficient funding for QRT was challenging as it was often not requested by applicants or denied by funding panel members. This was believed to be the result of preferences for funding quantitative research, applicants prioritising quantitative components of trials and reviewers having difficulties making decisions based on limited information about the QRT. Levels of knowledge and understanding of the value of QRT, negative attitudes towards qualitative research and reduced incentives to engage with it were key barriers to the uptake of QRT and its conduct and reporting. These beliefs and actions were reinforced by journal editors and reviewers and reporting conventions which can inhibit QRT reporting. They could also reinforce ongoing perceptions that qualitative research is less credible and valuable. Due to the noted difficulties, the environment in which QRT is conducted can be challenging for researchers who are planning, conducting, and reporting qualitative research while attempting to progress their careers. Institutions such as CTUs can play an important role in encouraging QRT by providing supportive infrastructure and promoting its use and good conduct. Continuing to challenge negative assumptions and promoting the use of QRT through increasing knowledge and skills was seen to be important for encouraging use of QRT and conducting it well.

The influences reported appeared to be consistent over time. Although authors have continued to contribute to ongoing discussions about how QRT can be used, the focus of discussion appears to have shifted more towards how different qualitative methods can be used to address the challenges trials face.

Robustness of the synthesis (strengths and limitations)

This is the first narrative synthesis of the literature on QRT implementation and has brought together different types of publications discussing different areas of QRT. This has enabled the synthesis of wider perspectives on QRT and has covered the range of stages through planning and conduct to reporting. Previous reviews have focussed on published findings from trials which may limit insight (15, 23, 26). Including different types of publications using a range of data types and authors has enabled the inclusion of different perspectives from people in different roles involved in conducting QRT. By not relying on a single source or publications from one author, I have ensured a wider range of views and experiences in different areas have been accounted for. This increases the usefulness and transferability of findings. Views and experiences presented across the publications were largely consistent and no major discrepancies or disagreements were highlighted. This strengthens reported findings. The synthesis has included publications across several years which has allowed updated insight into the factors that influence the use of QRT. The use of reflexive thematic analysis allowed me to bring my perspective as a researcher who has conducted QRT which has likely sensitised me to issues which may be relevant to others in this position. The involvement of a trialist and qualitative researcher who may have slightly different perspectives in coding and theme building may also have increased the relevance of findings.

However, the narrative synthesis does have some limitations which need to be accounted for when considering reported findings. A limitation was that the narrative synthesis is a secondary analysis of data that focuses on the interpretations presented by the authors of the original publications and is not based on primary data. Although presented as a strength to the synthesis, bringing my perspectives to the reflexive thematic analysis may have limited the transferability of finding as they represent one interpretation of the data and should be viewed as a such; other interpretations may be produced through different approaches and analysts. Much of the data included in the synthesis was expert opinion or researchers reflecting on their use of QRT in discussion sections of findings publications. This may not be as robust as data collecting through rigorous primary research. Most of the publications included were either reporting on research conducted in the UK or authors were based in the UK. This may limit transferability of findings to contexts outside of the UK. Also, publications included in the narrative synthesis were identified through the search strategy used for the critical

review (reported in chapter 4). Therefore, limitations reported for those publications are relevant here. These include restrictions of including only publications in English and those which explicitly link qualitative research and the trials.

Although a model of how interventions work, why and for whom was not deemed appropriate for this narrative synthesis and not developed, it is possible that having a model of how QRT is used, why and for whom may have helped inform data collection and analysis. Not having a model at the earlier stages may have weakened these aspects and limited insight and understanding of QRT in this narrative synthesis.

Case study of three trials that used qualitative research

A case study approach seeks to provide an in-depth understanding of a case or cases which usually represent complex situations (293). It is a useful approach for addressing how and why questions and understanding phenomena within their natural context. Case study can also help researchers account for the influence of contextual factors on the phenomena being investigated, particularly if boundaries between these are unclear (293, 294). Findings from the narrative synthesis highlighted contextual factors which can influence QRT, and it may be difficult to disentangle the use of QRT from these factors. To understand the use of QRT more fully, I needed to explore the use QRT using examples of its use within a real-life setting. Therefore, I used a case study approach to conduct a piece of primary research that engaged with the people and processes involved in QRT. The aim of this approach was to enhance understanding of the planning, conduct and reporting of QRT in more depth and allow me to test out theories about what influences its use developed from the findings reported in the other components. The conduct of this case study was informed by the approach advocated by Yin (295).

This approach involved using pattern matching to test out study propositions developed based on the findings from the narrative synthesis findings.

Design and methods

I used a multiple case study design using a trial as a single unit of analysis which is considered to be a holistic approach (295).

Units of analysis

The unit of analysis was the trial which was bound by the following eligibility criteria.

The trial must:

- Be a randomised controlled trial where one or more interventions were being assessed against a comparator.
- Have a qualitative component that took place during the pre-trial, the main trial or post-trial phase.
- Be investigating either a behavioural, drug, surgical or medical device intervention.
- Have completed and reported the qualitative component at the time of case study data collection.

Sub-units of analysis were trial documents and interviews with trial team members.

Case Selection

Case selection was based on replication logic (295). I required enough cases to address both literal replication (predicts similar results) and theoretical replication (predicts contrasting results based on anticipated reasons). Based on findings from the other study components I anticipated that the factors that influence the use of QRT would be replicated across cases. However, it was possible that due to lower use of qualitative research in trials investigating drug, surgical and medical device interventions, the challenges, and resistance to conducting QRT may be more pronounced in such trials. Therefore, I decided to use a single case for each of the trial intervention types including behavioural, drug, surgical and medical device (x4 cases). Yin (295) suggested that cases could also be selected based on researcher access to cases as this could be difficult and limit the amount of data collected. I, therefore, used convenience sampling to identify potential trials to be included. These included trials that I was aware of and for which I knew the trial Chief Investigator or knew a key person who could facilitate contact.

Data collection

Semi-structured interviews

I conducted semi-structured interviews with trial teams to explore their views and experiences of conducting QRT. This included how the qualitative research was planned, conducted, and reported. Interviews also explored the roles and working practices of the trial team. I used a flexible topic guide developed based on the case study objective and QRT literature to ensure key areas of questioning were addressed across all interviews, but which also allowed interviewees to discuss views and experiences important to them not already covered in the topic guide. Figure 17 outlines the key areas of discussion, and the full topic guide can be found in Appendix VI. All interviews were audio-recorded and transcribed verbatim by a professional transcription service (The Typing Works - http://www.thetypingworks.com/). Transcripts were then checked against the audio-recordings for accuracy.

Interview topics for discussion

Overview of the trial

- Overview, aims and objectives, intervention and funding

Qualitative component

- Purpose, aims objectives
- Design and methods
- Funding and resources
- Planning and conduct (relative to trial)

Trial team

- Composition, roles and background
- History of collaboration

Interviewee role in trial and team

- Roles and responsibilities
- Knowledge, experience and training

Integration of qualitative members within trial team

- Communication, meetings, working practices and relationships

Trial oversight

- Role of trial oversight committees and stakeholders in qualitative research
- Meetings and reporting

Ethics and governance

Conduct of qualitative research

- Sampling and recruitment
- Set up and conduct
- Data collection and analysis
- Systems/software used
- Timing with trial
- Expectations and issues arising

Integration of qualitative and quantitative data

- Barriers and facilitators

Reporting

- How reported
- Integration in reporting
- Barriers and facilitators

Final reflections

Figure 17 Summary of case study interview topic guide

Sampling for interviews

To ensure I interviewed members of the trial teams who could contribute valuable information to address the case study objective I used key informant sampling which is a form of purposive sampling (133). Purposive sampling is a non-probabilistic approach that is used to select participants who are best placed to provide appropriate and useful information about the topic of interest. Key informant sampling selects participants based on their positions or roles, skills, experiences, and willingness to take part. I identified key people who had a role in the design, conduct and reporting of the qualitative research within the trial and who would be able to provide key insights to inform the case study objective. These included the Chief Investigator (CI), trials methodologist (trialist), trial manager, qualitative lead, and qualitative researcher.

I aimed to interview up to five trial team members for each case trial (a total of twenty across four trials). This sample size was guided by information power; *"information power indicates that the more information the sample holds relevant for the actual study, the lower the number of participants is needed" (296). (p.1759)* To determine how many participants were needed I considered the following criteria; how broad the study aim was and whether an established theory was being applied. The specificity of the sample and the quality of dialogue within the interview were also considered.

I reflected on each of the criteria within the context of my study aims and objectives and the likelihood of high-quality interview dialogue and established that:

a) I had a specific aim in the case study (to test propositions relating to factors influencing QRT),

b) I would be using interviewees who had specific characteristics (high specificity),

c) I was using a set of propositions to guide analysis, and

d) the quality of dialogue was likely to be high due to me being an experienced qualitative researcher who had established rapport with the interviewees beforehand. Interviewees were also going to be either academics or clinicians who were likely to be articulate in interviews.

Each of these points indicated a small sample size would be required. Therefore, I determined that up to five interviewees per trial would be enough. I determined the

sample size before starting data collection and then assessed information power once the analysis was completed (295, 296).

Trial documentation

To corroborate the interview data and gain insight into discussions, decisions and processes involved in the conduct and reporting of qualitative research in trials, I identified and aimed to collect key trial documents (295) (listed in Figure 18). These documents were chosen because they could cover several different settings and events such as different types of meetings over the course of the trial and the different stages of the trial (e.g., planning and reporting). These documents would also help me to understand the roles and responsibilities of members of the trial team including qualitative researchers and how they were integrated into the trial. I requested the documentation below from each trial which was provided by the trial manager. It was possible that other documents may be discovered during interviews deemed to be useful to gaining insight into the study objectives and therefore further documents, if appropriate, were also requested.

For each trial the documents to be collected included:

- Funding application
- Ethics application
- Trial development and management meeting documents
- Trial protocol
- Update report
- Trial team organisational chart
- Gantt Chart (trial timeline)
- Final study report and publications

Figure 18 Case study trial documentation collected

Permission for trial access and informed consent

I requested permission to use the trial as a case, which included obtaining trial documentation and inviting trial team members for an interview, from the trial Chief Investigator via email.

Based on the key roles identified for sampling I asked the Chief Investigator for information on who had that role in the trial and for their contact information. In each trial, I was directed to the trial manager who provided me with the information required. Using this information, I invited selected members of the trial team to participate in the interviews via email, which included the participant information leaflet and consent form (Appendix VII and VIII). Participants were given the option of conducting the interview face-to-face at their place of work or via telephone.

Informed consent was obtained before the interviews started. Written consent was taken for face-to-face interviews and verbal consent for telephone interviews. When verbal consent was taken, I reiterated the key points of the consent form and audio recorded agreement to statements before commencing the interview. These statements can be viewed in the interview topic guide in Appendix VI.

Ethical considerations

Risks, burden, and benefit to participants

I determined the risks and burdens for participants to be minimal. Interviews would be conducted at a time and place convenient for participants and they would have a minimal time impact (1 hour in total). The interview topics were considered non-sensitive, and it was unlikely that participants would experience any pain, discomfort, or distress during or after the interviews. Participants were free to decline to answer any questions and free to withdraw at any time. The potential benefits to participants included the opportunity to contribute to improving the use of QRT. This study would also give voice to those who may not usually have a say in the way research is conducted.

During interviews, it was possible that inappropriate or harmful activity within the trials could be identified. To address this a safety protocol was put in place to protect

participants (within the trials and this study) and included a process to alert the appropriate people should this issue arise and me attend Good Clinical Practice training. See Appendix IX for more information on this process.

Maintaining confidentiality

Identifiable information for potential and actual participants was stored on a password-protected computer. All email correspondence was sent using the confidential function. Interviews were recorded on an encrypted digital audio-recorder which only I had the passcode to. After each interview, I downloaded the recording onto a password-protected computer and deleted the original recordings from the recorder. Recordings were transferred to the professional transcription service using a secure file transfer uplink facility. I obtained a statement of confidentiality from the transcription company. Following transcription, I removed all identifiable data and replaced it with pseudonyms. Transcripts were kept separately to any identifiable data and only I had access to both sets of information. Participants were informed that direct quotes from interviews may be included in publications but would not be associated with any identifiable information and only pseudonyms would be used.

The trial documents were considered 'sensitive' documents and transferred to me using secure transfer. In one case I was granted secure access to the university file store. In another case I was required to sign a confidentiality agreement. Only I had access to these documents and any identifiers were removed prior to reporting to maintain the anonymity of those involved in the trial.

All hard-copy data and study information were kept secured in locked filing cabinets. All electronic data were kept secured on a password-protected computer.

Participant brief and debrief

Following the interviews, I emailed the participants to thank them for taking part and provided them with details about how to contact myself and my supervisors should they wish to discuss anything further. I also informed them that I would send them a summary of findings when the study was completed.

Safeguarding the researcher

Risks to myself within the study were minimal. To ensure my safety all interviews were conducted at the participant's place of work or over the telephone. I also followed the Swansea University lone worker policy.

Ethics permission

I obtained institutional permission to undertake the study from the Swansea University Joint College of Human and Health Sciences and College of Medicine Research Ethics Committee [reference 11214].

Analysis

I used a pattern matching technique which is a strategy for matching an empirical (observed) pattern with a predicted (theoretical) one and also to explain why certain components of the data may not match (293, 295). Pattern matching requires the development of theoretical propositions which are then compared with research findings (295). These propositions can be developed from the literature, a theoretical framework or the researcher's ideas (293, 297). The propositions in this case study were developed based on the key findings from the narrative synthesis. I chose to use pattern matching as it has been described by Yin (293) as an appropriate and *'desirable technique' (p.132)* for use in case study analysis. Using pattern matching can be an important technique for enhancing the quality of case study research and strengthening the internal validity of findings (295, 298). Figure 19 provides a visual outline of the pattern matching process used.

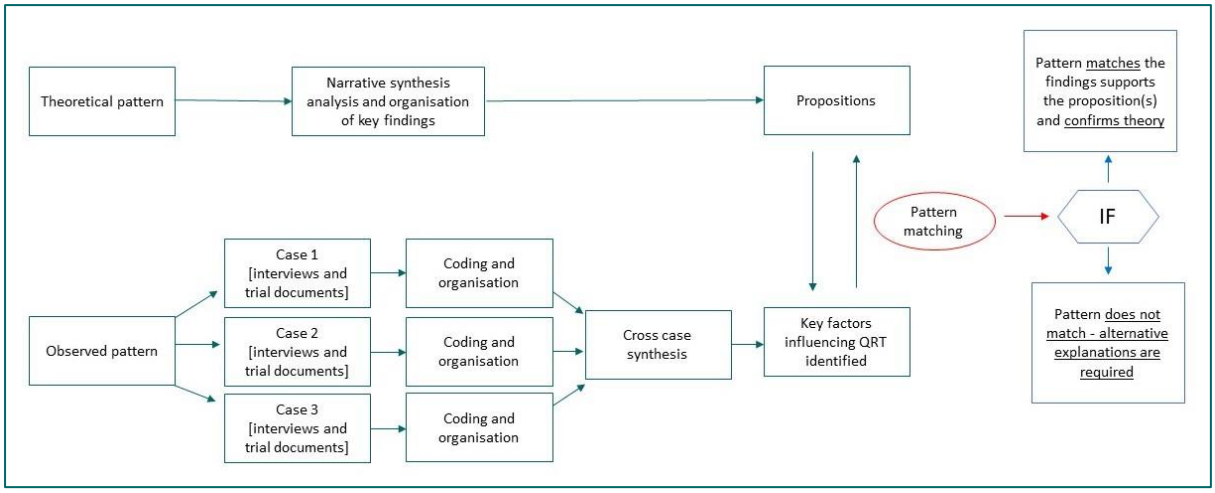

Figure 19 Pattern matching process

Stage 1: Proposition development

Using the themes developed within the narrative synthesis and key findings I developed four propositions to be being tested in this study. These were:

P1. The use of QRT depends on people understanding its value and having positive views and experiences of QRT.

P2. Tensions arising from methodological differences between qualitative and quantitative approaches (perceived or actual) and prioritisation of one set of methodological aims and outputs over the other will be ameliorated if the means to integrate processes and findings are negotiated and established a priori.

P3. Having researchers with qualitative expertise work collaboratively within multidisciplinary trial teams will lead to qualitative research being designed, planned, and implemented well.

P4. Reporting conventions that favour quantitative research and limited words and space for research articles will lead to a lack of or poor reporting of QRT.

Stage 2: Inductive and deductive coding and pattern matching

I used a combination of deductive and inductive coding to analyse the interview transcripts and trial documents (299). I first familiarised myself with all the data by re-listening to the interview recordings and reading through the transcripts and trial

documents. I made notes of key areas relating to the propositions through annotations within NVivo Pro version 10/11 (284). I initially coded and analysed the data deductively according to categories relating to the four propositions (see example Appendix X) (299, 300). Any data that did not fit with the categories were coded inductively. This was useful to help me understand the data relating to the overall case study objective that was not readily explained by the propositions. Interview transcripts and trial documents were analysed sequentially (interview transcripts then trial documents) within each case (295). Each case was analysed separately, and I created narrative memos outlining preliminary findings from each of the cases. Using these narrative memos and data excerpts from the cases I did a cross-case synthesis of all the cases and developed narrative descriptions of the findings to represent the observed pattern. This observed pattern was then compared against the propositions.

Study Database and data management

To increase reliability and rigour I created a case study database using NVivo Pro Version 10 and later 11 (284). This was a way of documenting and organising the data collected and managing the analysis and ensuring all data were accounted for.

Findings

Seven trial Chief Investigators were approached. One did not respond and six gave permission for the trial to be used as a case study. Initially, I approached and received permission for the trial to be used in four cases (one trial evaluating each of a behavioural, drug, surgical and medical device intervention). I had permission to include two trials evaluating medical devices, however, both trials were stopped prematurely and could not be included. Despite further attempts to include other medical device trials, I was unable to source one which could be included which met the inclusion criteria within the study period. Therefore, a total of three trials were included in the study (one behavioural, one drug and one surgical).

To protect confidentiality and reduce the likelihood of the trial and its team members being identified I have provided a general overview of each case and the data collected. I have not provided an individualised breakdown of interviewee roles within each case. To support findings, I have included anonymised quotations and excerpts from documents. However, some details have been omitted and document segments have been summarised or paraphrased in places. Omissions are indicated by … and paraphrasing is indicated by [].

Case descriptions

Case 1

The case 1 trial was a cluster RCT that used a stepped wedge design and compared a behavioural intervention with a usual practice comparator. The trial was funded through the National Institute for Health and Care Research (NIHR) (formally National Institute for Health Research). The trial was conducted over four years within the UK. Qualitative research was conducted throughout the trial (during the main trial phase). The qualitative research aimed to investigate how the intervention was understood and used by key stakeholders. Focus groups, interviews and a supplementary questionnaire were used to capture the views and experiences of healthcare professionals, National Health Service (NHS) managers and policymakers. Data were analysed using thematic analysis and a theoretical framework was used to interpret the qualitative data and present findings. Most of the team had worked together before on mixed method trials.

Case 2

The case 2 trial was a two-arm, open label pragmatic RCT which compared the effectiveness of two different drugs. The trial was funded by the NIHR. The trial was conducted over four years within the UK. Qualitative research was conducted throughout the trial (during main trial phase). The qualitative research aimed to investigate the views and experiences of patients and healthcare professionals of using and receiving the two drugs through interviews. Data were analysed using thematic analysis. The team had worked together on mixed methods studies before.

Case 3

The case 3 trial was a three arm (surgical vs. drug vs. drug placebo) parallel group RCT. The trial was funded by the NIHR. The trial was conducted over five years in the UK. Pre-trial research was also conducted over eight months. Qualitative research was conducted as part of the pre-trial research and in the pilot phase of the trial to help inform the main trial. The pre-trial qualitative research aimed to explore patient and healthcare professionals' views of current treatment pathways and explore the design of the trial using interviews. The qualitative research in the pilot trial aimed to understand and address recruitment issues using audio recordings of trial discussions between healthcare professionals and patients and interviews. Data were analysed using thematic analysis and conversation analysis. Some of the team had worked together on mixed methods trials before.

Each of the cases was considered by those involved to have successfully used qualitative research in the trial and trial team members felt they *"had done it well" (Case 2, Interviewee 3).*

Interviews and trial documentation

Interviews

Across the three cases, I conducted interviews with two Chief Investigators, one trialist (who was involved in two of the cases), two qualitative leads, one qualitative researcher and one trial manager who was also the qualitative researcher. I interviewed two more trial managers (total of nine interviews). Interviews lasted between 33 and 62 minutes with an average length of 50 minutes. The interviews took place between March and October 2017 for case 1, March and September 2017 for case 2 and between January and February 2019 for case 3. Three of the interviews were face to face and six were conducted over the telephone. In two of the three trials (case 1 and case 2), I was known to the interviewees having either collaborated with them on trials or by working in the same office space. For the third trial (case 3) I was not known to the interviewees

beforehand but had spoken with them on several occasions before the interview and had built up a rapport.

Trial documents

I analysed a total of 149 trial documents from the three cases (n=38 case 1, n=84 case 2 and n=27 case 3). Table 14 provides a complete list of all documents from the three cases.

Table 14 Case study trial documents collected and analysed

Trial documents	Case 1	Case 2	Case 3
Funding application (stage 2)	✓	✓	✓
Detailed project description (for funder)	✓	✓	×
Trial protocol	✓	✓	✓
Ethics application	✓	✓	✓
Trial Steering Committee (TSC) meeting documents	✓ *(n=5 over 3 years)*	×	✓ *(n=2 over 2 years)*
Data Monitoring Committee (DMC) meeting documents	✓ *(n=2 over 1 year)*	✓ *(n=8 over 6 years)*	×
Trial Management Group (TMG) meeting documents	✓ *(n=16 over 6 years)*	✓ *(n=63 over 7 years)*	✓ (n=15 over 3 years)
Qualitative sub-group meeting documents	✓ *(n=3 over 3 years)*	×	×
Gantt Chart (trial timeline)	✓	✓	✓
Trial team organisation chart	✓	✓	×
Trial data analysis plan	✓	✓	×
Trial publication and policy plan	✓	✓	×
Final funders report	✓	✓	×

Trial update report for funder*	✗	✗	✓
Publications	✓ (n=3)	✓ (n=4)	✓ (n=4)
Site Initiation Visit (SIV) slides	✗	✗	✓

** Trial update report for funder was collected and analysed as the final report was not yet available*

Pattern Matching

For each of the propositions, a statement for whether the proposition was supported by case study findings is presented, followed by a summary of those findings and coded data excerpts that support the findings (in tables). Within the tables, the coded data has been colour coded for each of the case trials. Case 1 is green, case 2 is blue, case 3 is orange and where excerpts refer to multiple cases, data are presented in purple.

Proposition 1: The use of QRT depends on people understanding its value and having positive views and experiences of QRT.

This proposition was largely supported by findings from the case study. However, one alternative reason for the use of QRT was proposed; that QRT is used because there is an expectation to use it.

The use of QRT did appear to be associated with people's understanding of what qualitative research was and whether they had positive views and experiences of it. QRT was used in the case study trials because it was perceived to be valuable. Positive views about QRT and its perceived value stemmed from people's previous experience of using it and seeing the benefits of QRT. This included optimising the trial (e.g., addressing recruitment issues), interpreting quantitative findings and understanding their applicability to practice. Both cases 1 & 2 referred to QRT being used because of these reasons.

When people did not understand qualitative research or see its value, they were less likely to engage with QRT. For example, in case 3, it was difficult to engage trial site staff with the QRT which it was believed stemmed from surgeons generally having less understanding of QRT and its value.

Through raising the profile of qualitative research within the trial, engaging team members in qualitative research activities, informing people about its importance and demonstrating its value, interviewees believed perceptions about QRT could be changed and engagement with it increased. Site initiation Visits (SIVs) were believed to be key points where the qualitative research could be introduced, and its value explained to trial site staff.

However, it may not be the perceived value of QRT which leads to its use but an expectation that it *should* be used. Interviewees believed that this expectation could lead to some trial teams automatically including qualitative research in trial designs and funding applications. This could be problematic if a clear rationale for including qualitative research in the trial was not established. For example, in case 1 a lack of clarity for why the qualitative research was included, what it was meant to achieve, and how this linked to the quantitative research components led to difficulties with reporting later in the trial. (See Table 15 for coded excerpts)

Table 15 Proposition 1 supporting/contradicting evidence

Themes	**Coded data excerpts**	
	Interviews	**Trial documents**
Perceived value, understanding and experience of QRT	*"It was never in any doubt in our original application I think that we would need a qualitative element… we were conscious we couldn't get all of that information just through quantitative questionnaires, and a qualitative element was essential." (Case 2, Interviewee 1)*	*"As part of the programme of research, CRS patients' attitudes to and acceptability of treatment options will be explored through the qualitative workstream (WS1c) and will be key in shaping the trial design including enabling optimisation of recruitment, retention and implementation." (Case 3, Trial documents)*
	"So I got aware of the contribution qualitative methods could make early on… I was aware of it from another study and was always open to it because I had seen what it contributed to that other study...	

	where the qualitative methods led to substantial improvement in the understanding of policy rules." (Case 1&2 Interviewee 1) *"I think if you're going to sort of achieve a trial that's going to deliver something meaningful… we wanted something that's going to be applicable [to practice], getting that qualitative work with surgeons and the patients involved had been important." (Case 3, Interview 7)* *"Surgical teams are less used to doing qualitative research and lack knowledge and understanding of what it is and its value… Felt like it was a required aspect and not necessarily engaged as they didn't understand its value." (Case 3, Interviewee 9)*	
Increasing understanding and perceived value	*"I think as time's gone on they realise that firstly it does have a lot to offer rather than it purely being something that you have to do… I think maybe they don't put the weight or the emphasis on what the qualitative work can do and what it actually means to them… but now we're coming into the second phase of the qualitative work, I think they've bought into it and I think they realise we're going to get some quite useful information out of it." (Case 3, Interviewee 7)* *"The trial team on the whole [were] very welcoming and can see the value of it… I think something that we did, I say helped, we did the analysis with the group… where various members of the team who were not qualitative specialists got involved… just raising the profile but involving people in the qualitative research and helping them to understand [qualitative research]." (Case 2, Interviewee 6)* *"I think that at the SIV (Site Initiation Visit) it's really important that a section of the SIV is dedicated to the qualitative work, and really*	*The SIV presentation slides for case 3 included dedicated slides which informed sites about the qualitative research. Why the qualitative*

	explaining what its aims are." (Case 3, Interviewee 7)	*research was being conducted, what the benefits to the trial were and its value were presented. Value appeared to be demonstrated through discussion of how qualitative research had benefitted other trials. (Case 3, Trial documents)*
Use based on the expectation of QRT use	*"Because it's like there's this assumption there'll be a qualitative element and it's like 'Yeah here we go again, the design qualitative part… Be really clear about why you are doing the qualitative, what's it for. And it's not just a sort of add on because you think you ought to." (Case 1, Interviewee 3)*	

Proposition 2: Tensions arising from methodological differences between qualitative and quantitative approaches (perceived or actual) and prioritisation of one set of methodological aims and outputs over the other will be ameliorated if the means to integrate processes and findings are negotiated and established a priori.

This proposition was supported in part; integrated processes and findings did help to ameliorate some methodological tensions. However, the integration of quantitative and quantitative approaches was not always believed to be appropriate or feasible. In some cases, even if integration was achieved, tensions still arose when more importance was placed on the quantitative findings than the qualitative findings.

Case study trial teams recognised the importance of the qualitative research being integrated into the wider trial during planning, conduct and reporting and there was evidence to demonstrate how this was achieved. Trial documents and interviewees indicated that cases had integrated qualitative research objectives, methods, and processes into the wider trial framework. Qualitative research was included with the quantitative research within the trial protocols, ethics and Health Research Authority (HRA) approval applications, data management processes, patient flow diagrams, data analysis plans and publication plans. However, the level of integration varied across the cases.

It appeared that aligning trial aims and objectives, processes and methods would lead to more confidence in qualitative findings and help to encourage more meaningful triangulation of the two approaches and sets of findings. Integration of methods such as sampling was believed to strengthen the quality of the trial and reliability of findings. Presenting the qualitative research as an integral part of the trial and as important as quantitative components were believed to have helped change the perceptions of trial site staff who saw the qualitative research as an additional, optional activity that was not as important as the quantitative components. This helped to improve engagement with the QRT.

Although the importance of using both approaches within the trials was recognised, not all interviewees believed integration was appropriate or possible. One interviewee (case 1 & 2) believed that to maintain the rigour of both approaches qualitative and quantitative research needed to remain separate but complementary components of the trial. Some believed integration was not always feasible, particularly integrating data and findings. This was in part due to the timing of data collection and analysis as quantitative results are often not revealed until late in the trial timeline. It can also be difficult to triangulate and integrate contradictory findings.

There was evidence to suggest that a lack of integration or consideration for how qualitative and quantitative approaches related to each other could create tension within the trial and difficulties triangulating and reporting findings. In case 1 it was believed that the purpose of the qualitative research in relation to the quantitative research lacked clarity and the two components were largely kept separate. This led to the collection and analysis of qualitative data which held little relevance to the trial endeavour. This resulted in the qualitative findings not being seen as useful and disregarded. Difficulties also arose when trying to triangulate findings meaningfully and a lot of time and effort was needed to achieve cohesive and comprehensive reporting. A lack of integration could also lead to the qualitative research not being perceived as important and trial teams appeared to struggle with trial site staff engagement.

However, planning for and the integration of quantitative and qualitative research and achieving this throughout the trial did not always alleviate methodological tensions. More importance still appeared to be placed on quantitative research, particularly when reporting findings and considering their significance and implications. Case 2, for

example had integrated qualitative research into the overall trial aims, objectives and methods and had a matrix approach that aimed to facilitate triangulation of these aspects. However, tensions still arose when reporting findings with the rigour of qualitative research approaches being questioned. Findings from the qualitative research aspect of data triangulation were not always welcomed, and results were, at times challenged.

Integration of approaches could still lead to methodological tensions if quantitative standards were being expected of the qualitative research. In case 2, the importance of ensuring the qualitative participant characteristics were 'representative' of the wider trial cohort led to quantitative sampling techniques, which were devised by the trial statistician, being used for interviews. Aligning the qualitative and quantitative cohort characteristics, it was believed, would increase the rigour and validity of the overall trial. However, this proved problematic as it was difficult to align the statistical sampling approach with the purpose of the qualitative research and the practicalities of conducting interviews. See Table 16 for coded excerpts.

Table 16 Proposition 2 supporting/contradicting evidence

Themes	Supporting coded data	
	Interviews	Trial documents
Recognition of the importance of aligning/integration of approaches	*"It's important for the qualitative and the quantitative [research] to complement each other… one wants them to be consistent, one doesn't want conflicts between them because they've been run in totally different ways… to know which participants had qualitative interviews and to be able to check their personal attributes… so that… somebody said… you've picked some very strange people for the qualitative interviews and they can't possibly throw any light on the quantitative." (Case 2, Interviewee 1)*	*"We confirmed that the demographic characteristics [of the qualitative sample] matched those of the overall study participation." (Case 2, Trial documentation)* [Statement of study strengths when reporting QRT.]
		"Qualitative team to explore mapping on the pathway of change required to ensure qualitative work feeds into the whole

		programme." (Case 3, Trial documents) *"[Chief Investigator] agreed the qualitative work does need to flow through [the trial] and it has been designed so that it does." (Case 3, Trial documents)*
How integration was demonstrated	*"The aims and objectives were set out and, methods, clearly spelt out and how they related to these objectives." (Case 1, Interviewee 2)* *"With regards to the qualitative bit within the trial that was also included in the ethics application we put through for the trial." (Case 3, Interviewee 9)*	*"Qualitative requirements meeting with [database and quality assurance manager] … for [trial database] … confirm with IS [Information Science] team what will be required from the trial database for sampling." (Case 2, Trial documents)* *"[Chief Investigator] commented that data management should include qualitative data." (Case 1, Trial documents)*
Integration overcoming methodological tensions	*"So with any mixed method study it's important but difficult to integrate findings and conclusions that arise from different approaches because those findings may sometimes be concordant and they may sometimes be discordant and we used the matrix approach to try and find a way to present this sort of complexity in a way that a reader can assimilate, so the idea was to identify research questions, the methods that were used to answer them and the conclusions that derived from that and use that to show how certain methods might come up." (Case 2, Interviewee 6)* *"The impact that it [qualitative research] has on the trial site staff, they're very busy anyway… which is why it's so crucial that from the moment you set up the trial you introduce the qualitative work and it's non-negotiable." (Case 2, Interviewee 7)*	*Site Initiation Visit (SIV) slides indicated that the qualitative research was presented as an integrated part of the trial through linking qualitative and quantitative objectives and using qualitative research to optimise recruitment pathways and processes. Information about the qualitative research was included in the main study information leaflets and consent forms. (Case 3, Trial documents)*

Question the need and feasibility of integration	*"So there was a nice balance to strike between ensuring that these two are distinct and independent because they are looking at different aspects of these two drugs… ensuring some sort of balance but without, for example saying that the quantitative side dominates the qualitative side… drawing it together could be harmful to a qualitative component." (Case 2, Interviewee 1)* *"How do you integrate it earlier on? You can't because you're not getting the results to integrate as you go along… it's always delayed." (Case 1, Interviewee 2)* *"We were trying to write up the [qualitative] results… when we had no information about the quantitative results at all. Quantitative results for all sorts of reasons were very, very delayed… All the quantitative results came in at the last minute. So, we had some qualitative results that really we wanted to put into context, and we couldn't because we didn't know the wider context of the trial findings." (Case 1, Interviewee 3)*
Lack of integration leading to challenges	*"There was much more of a gap in [trial 1] between the two elements and… there was less discussion about how the bits fitted together… for the most part the two elements, quantitative and qualitative operated separately… the data were kept quite separately and there were many more meetings which were quantitative only." (Case 1, Interviewee 1)* *"There was a sort of after the event rationalisation for why we were doing the qualitative side of things… So there was quite an interesting process of teasing out what value the qualitative work could add to the quantitative… And there was quite an interesting*

	discussion going on in the write up… so when we wrote it up [Chief Investigator] was going you know, 'why is this in here?' She did cross it out… If it's a different type of qualitative study, it's sort of justified to go 'Oh all this stuff in the data… But when it's a trial it's got to be much more focussed on how does this contribute to the main question you're asking." (Case 1, Interviewee 3) *"There's a feeling that the qualitative results are… being undervalued, they're being devalued, they're being dismissed because they contradict the quantitative results so therefore, they must be wrong, rather than the other way around… the figures are the things that are the most important, got to be the figures and nothing else." (Case 1, Interviewee 3)** *"It's an additional thing for them to remember… Sites are finding their feet. Here's a poor guy that doesn't even know if he's coming or going, it's a completely new process for them… there's loads to remember and loads of other equipment and outcome assessments. It takes people a while to get into the swing of things… All of these sites say to me on their first one because I'm so nervous about everything else." (Case 3, Interviewee 9)*	*"[Name] stated [healthcare professionals] not taking part in focus groups so delay… [Name] suggested that when inviting [healthcare professionals] we be clear to say this is part of what they signed up for." (Case 1, Trial documents)*
Integration does not always ameliorate methodological tensions	*"There was a little pushback from the [clinicians] who reviewed it [final report] who did feel that we were giving undue weight to some of the qualitative findings… Some of them felt it was inappropriate to give such emphasis on a few interviews." (Case 2, Interviewee 6)*** *"I know that there were some quite heated debates… that sense that she [qualitative lead] felt she was*	

	*having to really push to get some of the conclusions that she had drawn included [in reporting]." (Case 2, Interviewee 5)***	
	"There was a very specific sampling method that I think it was [trial statistician] had suggested… that was a challenge… that sampling didn't really work because by the time you have sufficient patients to sample from, so the fifth person recruited… some hospitals didn't recruit anywhere near that… I think there's something about being more flexible in sampling… It was devised on the basis that you're not getting any bias in there… realistically it didn't work… We ended up using a more flexible and purposive approach." (Case 2, Interviewee 6)	*"[Qualitative researcher] to liaise with [trialist] and [statistician] how to randomise patients based on [statistician] sampling idea [for qualitative interviews]." (Case 2, Trial documents)*
		"If possible [oversight committee] would like to see a pair of patients from the same hospital interviewed… If not then one [drug] and one [drug] from each site to ensure representativeness. [Qualitative researcher] suggested that the overall views of patients rather than a comparison of [the two drugs]." (Case 2, Trial documents)

* Note: A lack of integration of qualitative research within the trial was highlighted for case 1.
** Note. Case 2 demonstrated integration throughout the trial, but issues remained when reporting

Proposition 3: Having researchers with qualitative expertise work collaboratively within multidisciplinary trial teams will lead to qualitative research being designed, planned and implemented well.

This proposition was largely supported by the case study. However, there was evidence to suggest that even if researchers with qualitative expertise did work collaboratively within trial teams, there was not always adequate planning for QRT. This led to challenges when conducting the qualitative research.

All the cases had researchers with qualitative expertise integrated into the wider multidisciplinary trial team. Each case had a similar trial team composition where a qualitative lead oversaw the qualitative research and a qualitative researcher or researchers who were responsible for the day-to-day conduct of the qualitative research, including collecting and analysing data and preparing reports. These researchers worked collaboratively with other trial team members. In two of the cases, the qualitative team were based within the same institution as the wider trial team. This proximity was believed to have helped communication between the team and planning and conduct of the QRT in relation to the wider trial. Being in separate institutions was not seen to be an issue in the third case as they still met and communicated regularly.

The opportunity to have a team-based approach to conducting QRT was welcomed as it was believed to ensure successful planning and delivery of the QRT. This included the overall integration of both qualitative and quantitative approaches within the trial. Having good working relationships and open communication helped to keep the whole team informed about the QRT and involve team members in resolving issues. Having qualitative researchers within the trial team and having them attend meetings and provide update reports to the team was believed to raise the profile of the QRT and ensure it was considered throughout the trial.

Sharing the progress of the QRT and any issues arising with oversight committees was useful for trial teams to consider any implications for the overall trial and discuss potential solutions and advice for improving QRT conduct. Engagement with the QRT could lead to committee members having a better understanding of the QRT and how it relates to other trial components. Having members of oversight committees who were knowledgeable about or, who had experience of QRT was welcomed and believed to be valuable. Although oversight committees may not be considered part of the trial team, they were perceived to play a key role in overseeing and advising on trial conduct including QRT.

Even if researchers with qualitative expertise did collaborate within multidisciplinary trial teams, this did not always lead to well designed, planned, and conducted QRT. A lack of adequate planning in one case led to difficulties managing the analysis process and completing the analysis within the planned timeframe. It was highlighted how some aspects of QRT tend to be planned better (e.g., data collection) than others (e.g., data

analysis). Interviewees recognised that qualitative researchers needed to take responsibility and be clearer and more focussed when planning QRT. Two of the cases needed to bring in additional qualitative researchers as the planned level of staffing was insufficient. This was supported by the CTUs who provided qualitative researchers to carry out the QRT. Bringing in additional qualitative researchers who were not well integrated into the team at a late stage had a negative impact on the analysis, interpretation, and reporting findings. Also, even if the QRT was well planned, the challenging nature of obtaining funding for trials and conducting them as planned meant the QRT could be difficult to deliver as planned. See Table 17 for coded excerpts.

Table 17 Proposition 3 supporting/contradicting evidence

Themes	**Supporting/contradictory coded data**	
	Interviews	**Trial documents**
Embedding qualitative expertise into the multidisciplinary trial team	*"I think it's really important that the qualitative element is run by people who are qualified and experienced to do that, which we did. I think it was conducted with rigour and analysed with rigour." (Case 2, Interviewee 5)*	*"The qualitative lead… will lead and oversee the qualitative aspects of the study and give guidance on the planning and facilitation of the [data collection], devising interview schedules and analysis of qualitative data. The… qualitative research officer will carry out [data collection] and lead analysis of the qualitative data under the direction of the qualitative lead… The project and data manager will also… support the research officer in qualitative data collection." (Case 1, Trial documents)*
	"[Whole trial team] met regularly both face-to-face and over the telephone." (Case 3, Interviewee 7)	*Team organisational charts for case 1 and case 2 demonstrated how qualitative teams were integrated into the wider trial team. In each case, the team was situated in a hierarchy led by the Chief Investigator. The qualitative team were situated alongside other methodological teams, for example, health economics. Each team reported to the TMG who then reported to the trial oversight committees. In case 1, lines of communication were included and linked the qualitative team with other teams such as data management and systematic review teams. (Case 1 & 2 Trial documents)*

	"Because the qualitative work, it sort of spreads into other universities and we're involved with all the different people individually and as part of the wider team, we do feel very involved. I don't feel like we're on the outside." (Case 3, Interviewee 9)	
Benefits of embedding qualitative expertise	*"I'm thinking we were lucky with the people, the qualitative people… I was part of the concept team, we were lucky with qualitative people who were, a, competent and, b, collaborative." (Case 1, Interviewee 1)* *"It [team-based approach] meant that we were able to integrate the qualitative approach into the overall trial approach, we were able to use the findings to inform our assessment of the results and our interpretation of the results. It meant that the whole trial team were aware of what we were doing, how it was going, the timescales and the discussion enabled us to tweak the protocol, the qualitative protocol at one or two points. If I remember rightly things like I think we modified slightly the timing of some of the interviews and we also discussed things like numbers of patients who had [received treatment] so it meant that we kept the qualitative aspects mainstream rather than as an add-on." (Case 2, Interviewee 5)* *"It was nice to have a team whereby there were other people… to have actually that sort of team environment where there's a group of you able to coordinate things, to discuss things and to plan things, particularly from a project management perspective was very useful." (Case 1, Interviewee 4)*	

	"Having [qualitative lead] with such a strong background in qualitative research... having her part of the team… If we hadn't had such a strong lead… I'm sure there would still have been a qualitative arm. Whether it would have been as strong? … She was certainly on board from the word go and was keen to make sure there was a strong qualitative element to the study." (Case 2, Interviewee 6)	
Communication and discussion – good working relationships	*"Although we often sat on different sides of the fence, I can't for example remember any times, which [qualitative lead] and I came to a disagreement. Occasionally there would be a debate and one of us would say, "It would be better like this," and the other would say, "No, I think it would be better like that," but because we were both committed to the complementary aspects of the trial, I think we worked our way through those issues in a sensible way." (Case 2, Interviewee 1)* *"I do think it's absolutely critical to have a really good relationship... and talk to each other about what's going on." (Case 3, Interviewee 9)* *"I used to provide the update report from the qualitative data to show where we were at any given point, and I think that meant that the profile of the qualitative work was always quite high." (Case 2, Interviewee 6)*	*"[CI] and [qualitative lead] have also discussed the possibility of interviewing a [health area] specialist. [qualitative lead] queried if [organisation] held a dedicated mailing list for [health area] specialists, but [TMG member] confirmed that it was best to make contact via the main [organisation] mailing list. [CI] will look into sending out another mailing via [organisation] specifically to staff grade specialists." (Case 3, Trial documents)* *"[Chief Investigator] requests that an update report be completed for each area to provide consistent methods of reporting… [Chief Investigator] discussion and activity should include qualitative data as relevant as it's important it is not forgotten." (Case 2, Trial documents)* *"The purpose of this [qualitative update] report is to update the trial management group on progress of the various sections of the trial of the trial on a monthly basis… Authored by [qualitative lead and qualitative researcher]." (Case 2, Trial documents)*

Oversight committees	*"I think they [trial oversight committee] realise… that it's more than just the trial, it's about all the information about that including the qualitative work." (Case 3, Interviewee 7)* *"We kept the [oversight committee] informed about the qualitative work… They certainly had sight of the conclusions from the findings and indeed offered some feedback on our interpretations of the findings." (Case 2, Interviewee 5)* *"I think having an [oversight committee] chair that is so well versed in qualitative investigation is incredibly helpful." (Case 2, Interviewee 9)*	*"[Oversight committee] have concerns about qualitative data collection contaminating the quantitative data if an interview falls shortly before quantitative data collection. Agree that qualitative interviews should be scheduled after the 3 month and 6-month quantitative data collection." (Case 2, Trial documents)*
Poor/difficulties with planning despite having qualitative expertise	*"Having a bit more understanding of what we would do with the data and how we would apply for instance the theoretical framework…better understanding of where all the data would fit into [the wider trial] would have been beneficial." (Case 1, Interviewee 4)*	*The case 1 trial documents supported the lack of consideration for analysis and use of the theoretical framework. There was little information about how the analysis would be undertaken nor how the theoretical framework would be applied in the funding application, trial protocol, project description or analysis plan. The issue of qualitative data analysis was also presented to the TMG as a study risk. (Case 1, Trial documents)*
	"[Planning] very much so in terms of data collection, less so in terms of analysis. I think we have a tendency to plan data collection in enormous detail, and then we get loads of transcripts and then go, 'look at all this'. Yes, so plan in more detail from the start… and I would be more, even more tight about why we're collecting different bits of information and what we're going to do with it… but we hadn't necessarily planned to or had a clear outline… It's probably better to	*"[Name} confirmed a fourth person will be supporting the qualitative component who will be funded through the [CTU]." (Case 2, Trial documents)*

	start off much more focussed… and have a clear understanding." (Case 1, Interviewee 3) *"One of the issues, you have an approach to research which kind of values flexibility and all the rest of it, and you have to fit it into a regulatory structure, which looks to fixedness." (Case 1, Interviewee 3)* *"The way you should do it and the way you do do it; it doesn't always happen. So partly the whole timing of everything, you put your bid in, long silence, you put your outline in, long silence, you put your full bid in, long silence, everyone is busy working and even the process of being awarded the grant just takes so long… you haven't really got your head in the whole thing and you haven't recruited all the staff to start the study and you're still finishing off something else… It's really difficult to do that [planning and preparing] properly." (Case 1, Interviewee 2)*	
Issues with staffing	*"I think partly the workload meant that particularly with these [additional interviews] … we needed help with that… I think that just shows that the work involved with qualitative research can sometimes be so… 'Oh you'll go and do these many interviews and then it will be analysed.' … The expectation wasn't fulfilled because we needed more help with it [qualitative research]." (Case 2, Interviewee 6)*	*"[Risk for discussion] Staffing for qualitative interviews/analysis." (Case 1, Trial documents)* *"[Admin assistant] to transcribe interviews… [qualitative lead/qualitative researcher] to look into costs of sending interviews to a transcription service and anything else required to help support the qualitative side… [qualitative researcher] confirmed a third person*

needs to be identified to help with analysis." (Case 1, Trial documents)

Proposition 4: Reporting conventions that favour quantitative research and limited words and space for research articles will lead to a lack of or poor reporting of QRT

This proposition was not supported by the findings from the case study. There was evidence to suggest that a preference for reporting quantitative research and word limits and space do have an impact on the 'manner' QRT is reported. However, it did not lead to 'a lack of' reporting of the QRT.

Journal limitations due to word counts and a reluctance by some journals to publish qualitative research were believed to be instrumental in how the qualitative and quantitative trial findings were published. The qualitative and quantitative trial findings were reported substantially within the main reports for the case trials; the main reports did not have any word limits. However, for all cases, the qualitative and quantitative research findings were published separately. This appeared to be due to limited word counts and a reluctance to publish qualitative research in medical journals. The need to link the publications in some way was however recognised to be important. In most of the publications, the trial or QRT were cross-referenced, however, the balance did differ between the two. Within the qualitative research publications, the QRT was always presented comprehensively within the context of the wider trial framework. However, the quantitative findings publications did not always refer to the qualitative research that had been conducted or had minimal reference to it (1-2 sentences). However, having separate publications did not always indicate poor reporting. Having the qualitative research within its own separate paper could enable a more comprehensive presentation of the research and its findings. Difficulties publishing the QRT was also attributed to some journal reviewers lacking understanding of qualitative research. See Table 18 for coded excerpts.

A revised proposition considering these findings would be

Reporting conventions that favour quantitative research and have limited words and space for research articles will lead to QRT findings being published separately from the quantitative trial findings.

Table 18 Proposition 4 supporting/contradicting evidence

Themes	**Supporting/contradictory coded data**	
	Interviews	***Trial documents***
Difficulties publishing qualitative research	*"I think the qualitative isn't in there [main trial paper] at all…we had a lot of to-ing and fro-ing about whether to publish the combined paper or to split them…and it's much harder to get quali papers published, as you know, in things like the BMJ [British Medical Journal]." (Case 1, Interviewee 2)*	
Restrictions leading to integration or separate publications	*"We did have separate chapters for the data outcomes for the quantitative side and then we had chapters that related specifically to [qualitative findings]. But I think if my memory serves me right that the discussion did draw together the various elements, it wasn't just focusing on the quantitative, it did draw, you know, the discussion stream from all elements of the study." (Case 2, Interviewee 6)*	
	"The [journal] wanted the qualitative findings to be published separately." (Case 2, Interviewee 5)	*"Request from journal editor to remove qualitative components…"I would recommend that qualitative outcomes be removed from this paper and reported separately so that more detail around that sub-protocol methodology and a full description of findings can be provided." (Case 2, Trial documents)*
	"I think there was a very brief comment about the qualitative [in the main trial paper], but I think that that was very, kept to a minimum because of the fact that we would be publishing separate papers." (Case 2, Interviewee 6)	

	"I think it [qualitative research] was referred to but not in a great depth and again that's partly because I suppose of word limits and so on but the main paper did concentrate on the quantitative analysis, but I think it was, there was a brief statement or comment… I think it would be very difficult to make statements in a predominantly quantitative paper, the word limit is such that you, to make, to start trying to report too much of the qualitative, you wouldn't be able to, I don't think you'd be able to do it justice." (Case 2, Interviewee 5)	
	We wouldn't be able to get all of the data into it [main trial paper], because of the word limit… we wouldn't be able to do justice to the qualitative work." (Case 1, Interviewee 4)	
Lack of understanding of qualitative research	*"I think my experience generally with trying to get qualitative work published is that… particularly if you go to the [clinical] journals, often people don't understand qualitative research and you start getting comments back about well it's only a small sample size and well, you know, how does that represent the wider body of patients and then you have to go back and sort of explain why qualitative work is different and you don't need large sample sizes." (Case 3, Interviewee 8)*	

Summary of findings

This case study has examined the use of qualitative research in three case trials and has tested findings from the cases against theoretical propositions to help explain why QRT was used and what influenced how it was planned, conducted, and reported.

The use of QRT appeared to be associated with people's understanding of what qualitative research is and believing QRT to be valuable. Engagement with QRT can be increased through the promotion of its value and activities which facilitate understanding of what it is and why it is being used in the trial. However, there is a risk that researchers may include qualitative research in trial designs because there is a perceived expectation to do so. This can lead to issues with planning and linking the qualitative research with other trial components, particularly when reporting findings.

The integration of qualitative research processes and findings appeared to help overcome methodological tensions which could arise between the qualitative and quantitative approaches. Presenting the qualitative research as an integral part of the trial helped trial site staff to recognise its importance and increase engagement with it. The integration of processes, methods and data and findings was believed to increase people's confidence in the quality of the qualitative research and the reliability of trial findings. However, this integration may not always be possible or required and conducting them separately may ensure the rigour of both approaches is safeguarded. A lack of planning for the integration of qualitative and quantitative research could create tensions between the approaches and can lead to difficulties bringing the different data sets together and reporting findings. Even if the integration of the two approaches was planned and achieved within the trial, this may not always alleviate methodological tensions. Tensions could arise if more importance was placed on quantitative research methodology and findings when reporting trial findings. This appeared to be more pronounced if findings were discordant.

Having researchers with qualitative expertise work collaboratively within multidisciplinary teams was believed to be important for ensuring that the QRT was successfully planned and conducted and integrated into the trial. Regular and open communication where the whole team was kept updated helped raise the profile of the qualitative research and overcome any issues. Keeping oversight committee members informed about the QRT and having members with qualitative knowledge and experience was believed to be valuable for understanding the QRT and how it related to

other trial aspects. Having researchers with qualitative expertise involved in the trial may not always lead to well designed, planned, and conducted QRT. Issues with the level of staffing for the conduct of QRT, a lack of consideration for all the qualitative research aspects and the challenging nature of trials research can be problematic and have a negative impact on the delivery of the research. This appeared to be more of an issue when analysing and reporting the QRT.

A perceived reluctance of some journals to publish qualitative research and restrictive words limits for journal articles appeared to lead to qualitative and quantitative trial findings being published separately. However, publishing separate articles was not always seen as a negative outcome but it was believed that linking them in some way was important. Having journal reviewers who lack knowledge and understanding of qualitative research could present a challenge to trial teams trying to publish qualitative research, whether integrated with the quantitative or on its own.

Strengths and limitations

Strengths of this case study include the collection and triangulation of different types of data (interviews and trial documents) from multiple case trials which were used to corroborate findings. This is likely to have increased construct validity (295).

Being flexible with how the interviews were conducted and offering telephone or face-to-face interviews has likely led to greater engagement and more people participating (301-303). Face-to-face interviews were not always feasible due to limited resources and some people found telephone interviews more convenient. Telephone interviews can also reduce concerns about anonymity which may have helped overcome social desirability to an extent and enabled more focussed communication (301, 302).

The use of trial documents allowed me to verify information from the interviews but also discover new information (295). The documents covered a wide range of different meetings, aspects of trial conduct, and reporting over the course of the trials. This allowed me to track activity, issues and decision making over the course of the trial. This may have compensated for some of the limitations of the interviews (discussed below).

I have also provided a chain of evidence whereby the circumstances of data collection have been outlined and data from each of the cases has been presented alongside a discussion of whether and how the case study data supported the study proposition. This has likely strengthened the construct validity and reliability of the case study (295). However, it should be noted that I did not have key informants review the draft case study report and it is possible that others may have different interpretations of the data.

Case study steps and procedures and how these related to the case study objective were outlined in a case study protocol and have been transparently reported within this thesis. I have also created and maintained a study database within NVivo which is available (within reasonable request) for inspection. These are likely to facilitate understanding of the research processes and how I arrived at my interpretation of the data. This therefore further increases the reliability of the case study.

The use of pattern matching whereby the patterns developed from the analysis of the case study data largely matched that of the theoretical propositions. Where the pattern did not match, other explanations were provided as in the case for why QRT is used, or a revised proposition was provided (as in proposition four). This strengthens the internal validity of the case study findings.

The use of interviews with members of trial teams has enabled an in-depth exploration of how QRT is understood and experienced from the perspectives of people who have used it. Interviewees held different roles within trials teams which provided a range of views and experiences from different perspectives. This has resulted in a more reliable understanding of QRT and is likely to make findings more relevant and useful to others considering the use of, or who are conducting and reporting, QRT. I also used replication logic to include trials that evaluated different types of intervention which has provided a more comprehensive understanding of whether factors influencing QRT differ across them. This increases the transferability of the case study findings to the use of qualitative research in other trials. Assessment of information power indicated the interview data held sufficient information power to address the objective which supports the strength of the findings (295).

It is possible that by conducting telephone interviews, the rapport between me and the interviewee was limited and the absence of any visual observation of body language and situational information may have negatively affected the amount and quality of insight gleaned (301, 304). In six of the nine telephone interviews, I was known to the interviewees and had an existing rapport. In the remaining interviews, I spent time building rapport through general conversation before starting the interviews. This is likely to have negated some of the potential limitations of the interviews. I compared the length and detail of the discussion between the telephone and face-to-face interviews and found no notable difference.

There are also limitations to this case study. As interviews were conducted a few months after the trials ended and interviewees had moved onto other interests, it is possible that recall bias may have affected the accuracy and amount of information provided. Social desirability may also have been present as knowing me (the researcher) and being aware that the study was exploring the best way to conduct QRT they may have wanted to present themselves and their research positively. As interviewees did discuss issues they encountered and limitations of their work it is likely that this effect is minimal.

The trial documents may also have resulted in limitations to the study. The trial documents may not have reflected an accurate account as they would have been influenced by the author and intended audience. This may have led to reporting bias and cannot, therefore, be considered literal recordings of events (295). I did encounter some difficulty obtaining all the intended documents from all the trials, with some providing more than others. This may be the result of selectivity bias (295) and limited my insight and understanding.

Observations have been recommended in a case study (295) as they can enable researchers to capture actual rather than reported behaviour and allow insight into how people interact with each other and enact practices and processes (133). Conducting observations of QRT being planned and undertaken would have been a useful data collection tool and provided a third form of data to triangulate. As trials had already been completed, I was unable to undertake observations that may have enhanced understanding and strengthened construct validity and provided more evidence for pattern matching and therefore strengthened internal validity.

All the case trials were non-commercial trials funded by the NIHR led by academic institutions or the NHS. Commercial trials led by pharmaceutical or industrial companies may be designed and conducted differently to trials included in this case study (305, 306). Non-commercial trials are likely to be later phase, multi-centre national trials, use an active control arm and be limited by a lack of adequate funding (305, 306). Commercial trials are more likely to have adequate funding, be multi-centre international trials and are less likely to use active controls (305, 306). These differences are likely to influence how the trials are conducted and whether and how they use QRT. However, I was unable to explore this which limits insights from this case study.

All the case study trials were conducted in the UK which may have again limited insight and transferability of findings. Trials outside the UK may be conducted in different contexts and have varied factors influencing QRT. In the US, for example, there is no nationalised health service and healthcare is largely delivered through private practice. As a result, clinical research is mostly conducted outside of patients' usual healthcare settings. This and financial disincentives for private practitioners can lead to recruitment challenges (307).

Reflexive account

As a researcher who conducts QRT and is part of the community I am researching, I could be considered to have 'insider status' (308-310). This I believe, has influenced several areas of the case study conduct and interpretation. Being known to the trial teams and being part of the same institution for two of the case trials helped facilitate access to the trial teams and trial documents. This is reflected in more documents being retrieved for these cases. Due to my familiarisation with trial conduct and its associated documentation, I was able to understand the terminology used and easily navigate the documents. This helped to facilitate clarity and understanding. It also made me aware that some information may have been omitted in the documents to present a more favourable picture of the trial. Being known to the interviewees, having rapport, and being seen as part of the QRT community may have led to interviewees being more open about their views and experiences (309, 311). However, it is possible that this 'insider status' may have enhanced concerns about confidentiality and social

desirability (311). As some of the interviewees were senior members of the research community and in positions of authority to me, I was aware that I may not have prompted too hard to elicit any negative information or shed a negative light on the trial through any discussion (prior to or during the interviews). Also, although my insider status is an advantage when sensitising me to information that may be useful to others in my position this may have limited my interpretation. Other people with different perspectives may have been able to appreciate a wider perspective and make connections and inferences which I did not (311).

Interpretation (Narrative Synthesis and Case Study)

A key factor identified in the narrative synthesis and case study (referred to as this/the study onwards) for engagement with QRT was the level of understanding people, such as healthcare professionals, had about QRT and seeing its value. There have been reports that healthcare professionals generally lack familiarity with qualitative research and are uncertain about its credibility and usefulness (118, 312). This can lead to them being ambivalent about or unwilling to use qualitative research (313). This indicates the issues highlighted in this study go beyond QRT to wider use of qualitative health research.

This study highlighted how career aspirations and the way academic and research achievements are considered could influence whether people engage with and use and report QRT. When evaluating academic progress and research impact within the UK, attention has been given to the number of publications that have been published in high impact journals (314). These assessments have important financial and reputation implications for institutions and individuals (315). As noted within this study, and in previous literature it can be difficult to publish qualitative research in these high impact journals (316-318). Therefore, it is unlikely that researchers will engage with QRT but will focus their efforts on conducting quantitative research components of trials to further their careers. Changes to the Research Excellence Framework (REF) criteria in 2021 (315) indicate that a greater account of different forms of evidence to demonstrate impact will be taken and will offer equal opportunities for

interdisciplinary research (319). This may change the perceptions of qualitative research and encourage more people to be open to and engage with QRT in the future.

Not publishing in high impact or medical journals can also have further implications. Findings from this study indicate that QRT findings are more likely to be published separately from the 'main' quantitative trial findings in low impact, non-medical journals. As well as implications for assessment, it is likely that QRT findings are less likely to be read and used by those people in practice and therefore have any meaningful impact. It is also possible that the perception that QRT is unlikely to be published in high impact journals may put people off submitting for fear of rejection (318). Although the proportion of qualitative research is low (320), qualitative research does get published, in high impact, medical journals such as the BMJ (British Medical Journal) (321, 322). This is likely because of the high profile letter to the BMJ which drew attention to their rejection of qualitative research and called for more recognition of its value to the medical community (316) and subsequent change in policy (318, 323). Indeed a higher proportion of qualitative research articles have been found in journals that refer to qualitative research in their policies and author guidelines (320). Therefore, researchers should not let challenges with publishing in high impact, medical journals deter them from engaging with QRT.

The integrated reporting of both qualitative and quantitative trial components may be beneficial for drawing attention to the overall study and their relationship to each other (133). It can also maximise the benefits of using the mixed methods approach. However, there may also be benefits to publishing qualitative and quantitative findings from trials separately but linking them in some way (133, 170). Separate publications can result in more detail and consideration of findings and can draw the reader's attention to information more relevant to them (170). Findings from this study support this and suggest that reporting separate findings may not necessarily be considered a negative outcome. What is important is that separate publications are linked in some way to alert the reader to the wider context of the study and findings. This would help them consider the implications of this.

Findings indicated that a lack of sufficient resources could lead to difficulties conducting QRT. Insufficient resources appeared to be the result of poor planning and a belief that funding organisations prefer to fund quantitative research. Securing funding for

qualitative research has been reported to be an ongoing challenge (324, 325). However, there is an indication that this situation is improving over time, with applied qualitative research being conducted in conjunction with quantitative research being viewed more favourably (325, 326). The NIHR, a major funding body within the UK, and the funder for the case study trials are open to and encourage funding for qualitative and mixed method research (327, 328). Difficulties securing funding were also attributed to limited space on funding applications and researchers not clearly articulating what the value of the QRT was and what it would involve. Issues with available space on funding applications have been highlighted to be problematic more generally in mixed methods research (280, 329). Findings from this study suggest these issues can be overcome by researchers being clear about what the QRT entails and demonstrating its value within applications. This supports previous guidance for obtaining qualitative research funding (325). This study further adds that emphasising the value of qualitative research in funding for trials applications can increase the perceived usefulness of qualitative research and elevate its importance in relation to quantitative research. Difficulties with funding reviewers not having the appropriate skills and knowledge to assess QRT funding applications identified within this study has also been highlighted in the wider mixed methods literature (330). Training for people who review multidisciplinary team funding applications has been recommended (331). Guidelines have been produced for those reviewing applications for mixed methods research for the National Institutes of Health (NIH) (332). Such training and guidelines may be useful for other funding panels and could be adapted for assessing trials that include QRT.

Findings from this study indicate that early planning and the consideration and integration of qualitative and quantitative trial components are important for overcoming the negative impact of favouring quantitative research can have on QRT. This has also been reported to be the case in the wider mixed methods literature (170, 333). One area of planning which appeared to be particularly problematic in this study was the qualitative data analysis. This led to issues with its conduct and was challenging for researchers who felt that having qualitative data analysis plans may help facilitate planning and understanding of how the analysis would be conducted and when. Having a data analysis plan for qualitative research has been advocated (334) and guidance has been produced to help researchers plan and execute these plans (334, 335). The use of qualitative data analysis plans in the case study trials suggests that it is feasible to

develop and use qualitative data analysis plans within trials. Teams conducting QRT may want to consider the use of qualitative data analysis plans which document the analysis approach to be used, who will be involved and when and how it will be conducted. To help researchers develop and use these plans in trials guidance could be developed. However, qualitative data analysis plans may not be appropriate for some types of QRT, and it is important to maintain flexibility when conducting QRT analysis.

This study highlighted the importance researchers place on the integration of qualitative and quantitative research processes, data, and findings for maximising the value of using both approaches within a trial. However, integration was not always welcomed and can be difficult to achieve when considering both data sets and findings, particularly when findings provided mixed messages. Difficulties integrating data sets which can lead to the dismissal of qualitative data and findings has been reported in the wider mixed methods literature (336, 337). Advice on how to integrate different data sets including several techniques for integrating or triangulating data has been provided (28, 41, 135). There has also been discussion about how conflicting findings can be managed and reconciled (337, 338). Despite this, the integration of qualitative data with other trial data sets still appears to be problematic and may be the result of a lack of awareness for such techniques (41). There are examples of how qualitative and quantitative data sets can be integrated within trials (41, 339). However, these are limited, and more examples and guidance are needed to help support researchers conducting mixed methods trials. Such techniques may not always be appropriate and the potential for the different approaches addressing different research questions and using different theoretical approaches needs to be considered (333).

Having an infrastructure that supports multidisciplinary research was found to be conducive to conducting QRT in this study. The role of infrastructure in supporting or inhibiting mixed methods research has been reported on previously (340-342). Having researchers split across different institutions could be challenging (341) and research institutes may not always be favourable environments to conduct mixed methods research (342). Findings from this study suggest these challenges could be overcome through frequent communication among team members and research networks, institutions, and organisations encouraging multidisciplinary collaboration. One such organisation highlighted in this study was that of CTUs. CTUs are specialist units that

provide expert methodological advice and resources to help coordinate and undertake successful trials. They have been recognised for the important role they play in designing and delivering trials and those considering conducting a trial have been recommended to consult with a CTU (343). At the time of writing, there were 53 registered CTUs (344). Thirty of these units (57%) offered qualitative research support (344). This demonstrates that CTU support for qualitative research is available. However, the extent and nature of this support are not clear. Given their crucial involvement in trials and influence over how trials are designed and conducted, CTUs are well placed to advocate a strategic commitment to the use of QRT.

Findings from the case study indicated a role for trial oversight committees in QRT and the value of having members with an understanding of qualitative research. Trial oversight is key to ensuring trials are conducted rigorously and collecting robust data while adhering to good clinical practice (345). They oversee trial progress and provide advice on the trial protocol, recruitment, retention, possible threats to the validity of the trial, and data quality (345, 346). These committees usually include members with statistical backgrounds and lay members and do not usually include members with other methodological expertise, such as qualitative research (346). Considering the increasing use of QRT and the integration of processes, data, and findings, trial oversight committees may wish to consider involving members with qualitative expertise.

This study has highlighted the importance of embedding researchers with qualitative expertise within multidisciplinary trial teams. This is not new and has been widely recommended within the QRT and wider mixed methods literature (22, 42, 332, 333). However, this study has added insight into how qualitative researchers can best be embedded in trial teams and good collaborative relationships fostered. It has also highlighted issues with embedding qualitative researchers into trial teams and how this can be challenging for them. Conducting qualitative research has been found to have an impact on the researcher's wellbeing (332, 347, 348). Those conducting trials with qualitative research need to be aware that the environment can be challenging for qualitative researchers conducting QRT. They need to ensure that they are integrated into teams through meetings and open lines of communication and ensure they have a supportive environment in which to carry out their role.

The importance of increasing knowledge and skills for qualitative research within teams conducting mixed methods research has been previously highlighted (133). Findings from this study support this and indicate several ways in which this could be achieved for QRT. These include involving trial team members in qualitative research activities such as analysing data and the interpretation of findings. Shared learning has also been recommended for multidisciplinary teams undertaking implementation research and can enhance trust between team members (349). This may be particularly useful for QRT where a level of scepticism for the usefulness of qualitative research is present. Formal and on the job training may also be useful for those engaged with QRT. People considering conducting QRT should consider attending training courses aimed at a range of people such as researchers (qualitative and others) and healthcare professionals (for example 'Qualitative Research for Randomised Controlled Trials' - https://www.sheffield.ac.uk/scharr/modules/designing-qualitative-research-randomised-controlled-trials, and 'Qualitative Research to Optimise Design and Conduct of Randomised Trials' - https://www.bristol.ac.uk/medical-school/study/short-courses/biennial-non-active-courses/qualitative-research-to-optimise-design-and-conduct-of-randomised-trials/). Flemming et al. (15) voiced concerns that the lack of training and expertise in teams conducting QRT could lead to it being carried out poorly. This study suggests that involving people with qualitative expertise can improve the conduct of QRT and ensure it is positioned well within the trial. However, this may not always be the case and even if qualitative researchers are involved in the planning and conduct of QRT issues can still arise.

Some of the challenges encountered when conducting QRT have also been reported when conducting trials more generally. Difficulties with delivering trials within restrictive budgets have also been reported for conducting trials (193, 350). Many of the challenges faced when conducting trials are also attributed to a lack of knowledge and understanding of trials and their methodology, not seeing the value or importance of trials in informing practice and difficulties engaging healthcare professionals with trial activities (13, 85, 193, 351). Having cohesive multidisciplinary teams with good communication and trial meetings that are inclusive of all disciplines have also been reported to help reduce professional barriers within trials and help to increase the engagement of all parties when optimising recruitment to trials (352, 353). Having supportive colleagues and research infrastructure has also been reported to facilitate

the conduct of trials (350, 354). Therefore, some of the issues highlighted for QRT may be reflective of the wider trial context.

Many of the influences affecting QRT, particularly the challenges faced, have been reported in the wider mixed methods literature. Findings from this study indicated that the context in which trials are conducted can influence the way QRT is conducted. Trials have additional regulatory requirements compared with other types of studies for example (355), which can affect QRT. Given the prominent and important role that trials play in addressing important healthcare practice questions, it is likely that they are under more scrutiny (356, 357). It is, therefore, possible that the challenges reported in mixed methods research in addition to the challenges faced by those conducting trials may make those encountered in QRT more pronounced.

Conclusion

There are several factors that appear to interact and influence the use of QRT and how it is planned, conducted, and reported. Challenges to using QRT appear to persist over time but are not insurmountable. Key stakeholders, including researchers, healthcare professionals, funding organisations and those involved in publishing QRT need to understand what qualitative research is and the benefits it can bring to trials. Implementing and reporting QRT requires a supportive environment where qualitative researchers are embedded in multidisciplinary teams and where all trial components and how qualitative research can be integrated within the wide trial framework are considered. This requires adequate resources, good planning, flexibility, and activities that foster shared understanding and good working relationships.

The next chapter presents the development and piloting of two reporting quality appraisal checklists.

Chapter 6 Development and piloting of a quality appraisal checklist for publications reporting QRT

To help ensure findings from research can be effectively implemented it is crucial that details regarding how the research was conducted and the research findings are fully and transparently reported (358-360). However, issues with variation in the quality of the information provided when reporting research have been highlighted and information provision is often incomplete (280, 361-363). Selective or inadequate reporting can reduce the usefulness of information for decision makers and lead to research waste (362, 364). Without complete and transparent reporting, it is not possible to assess the methodological robustness of research, for example, to identify any flaws or biases (359, 360). It also limits the clinical usefulness of findings as relevance to practice can be difficult to determine (360).

To help ensure evidence provided by QRT is useful for decision makers, it is therefore, important to report it well. There have been concerns voiced about the lack of visibility of qualitative findings when reporting QRT (22, 37). There is also evidence to suggest that the quality of QRT reporting is poor (26). When reviewing publications reporting QRT, Lewin et al. (26) found most were unclear on sampling, data collection and analysis approaches and conduct. Some publications did not even report any of these aspects. Nineteen publications of trials using qualitative methods were reviewed. Of these 19 publications, 13 failed to adequately describe sampling procedures and 14 did not provide information on data analysis approaches. Publications also provided limited information on links between the qualitative research and the trial. Only nine of the 19 made explicit links between the two and most (13 publications) did not show any evidence of integrating findings from each component. Lewin et al. (26) also attempted to review the methodological quality of the publications. However, 10 of the publications did not provide enough data to allow adequate assessment. The most common weakness reported was a lack of clear justification for use of qualitative methods in the trial. There was also insufficient evidence presented for claims made within the publications. The Lewin et al. review (26) was based on 19 publications that were published between 2001 and 2003. In chapter 4, however, I reported on 3,343

publications reporting the use of qualitative methods between 1999 and 2016 which highlights the low number of publications reviewed by Lewin et al (26). Lewin et al's. (26) review, therefore, is based on a very small number of studies at a time when the conduct of QRT was limited. No other reviews have systematically addressed the quality of the reporting of QRT. Therefore, a review of reporting quality is needed to provide insight into reporting quality and identify potential areas for improvement.

Reporting guidelines aim to improve the quality of reporting of different types of research. A reporting guideline can take different forms including checklists, flow diagrams or descriptive text to guide authors on how to report specific types of research (365). They usually contain the minimum set of information necessary to allow readers to clearly understand what was done and what was found in a study. This can help readers make assessments about the reliability of its findings, the usefulness of this information and whether and how knowledge gleaned from the reports can be applied in practice (359, 366). Guidelines can also help researchers know what is expected from them when writing reports (366). Complete reporting also allows the replication of study methods and processes (359). There is evidence to suggest that the use of reporting quality checklists can lead to improved reporting quality (363, 367). Therefore, the use of reporting guidelines including appraisal checklists can improve reporting transparency and the validity of findings.

A review of appraisal tools highlighted several frameworks and checklists for qualitative research and mixed methods research. Qualitative checklists included the Critical Appraisal Skills Programme (CASP) qualitative checklist (368), the COnsolidated criteria for Reporting Qualitative research (COREQ) checklist (366), McMaster's critical review form for qualitative research (369) and, the Qualitative research review guidelines – RATS (370). Guidelines for reporting mixed methods studies included the Good Reporting of A Mixed Methods Study (GRAMMS) (280) and the Mixed Method Appraisal Tool (MMAT) (371). However, none of these tools accounted for the use of QRT or provided a way of assessing reporting quality in QRT. Ideally, QRT would be conducted and reported as a mixed methods study. However, findings from the narrative synthesis and case study indicated that qualitative research is often likely to be seen as a separate or 'added on' piece of research rather than part of a mixed method study. Also, qualitative research components of trials are often reported separately as a

piece of qualitative research that is linked to a trial but not reported as a mixed methods study. Therefore, researchers may not consider the use of mixed methods guidelines useful. Using a qualitative tool would not account for the linkage to the trial or integration of data and findings from mixed data sets. In theory, qualitative research will contribute to addressing trial questions and be used to provide additional knowledge and a more comprehensive understanding of the intervention being evaluated (15, 23, 165, 179). For research findings to be useful, it is important to understand the wider research context and fuller understanding of all aspects of investigation and outcomes assessed (361, 370). Therefore, it is important to link the qualitative research to the trial within which it was conducted. The context of the trial may have an impact on the reason the qualitative research was conducted, how it was conducted (for example, sampling from the trial population), what research questions it addresses and how findings are interpreted. A reporting tool that specifically addresses QRT may appear more relevant to researchers, can help facilitate good reporting practices and help those considering the evidence to assess its quality.

A rudimental keyword search of the critical review publications (reported in chapter 4) in NVivo (n=2,343) found only 104 (4.4%) publications that reported using a qualitative (n=103) or mixed methods (n=1) appraisal/reporting tool. Although this is not a rigorous examination of tool use, it does suggest that few researchers are using quality appraisal tools when reporting QRT and those researchers who do use tools tend to rely on qualitative research appraisal tools.

I, therefore, aimed to develop a tool to support good reporting and quality assessment of QRT.

Objective

- To develop a tool to assess the quality of reporting for QRT.

Checklist development

Using the existing appraisal tools listed above I produced a checklist for appraising the reporting of QRT. I read and compared the items in the existing appraisal tools for key areas of assessment. I then synthesised the questions and items into common categories and questions (see Appendix XI for an example of appraisal tools questions that led to a checklist question). All aspects of reporting covered by the existing checklists and guidelines used were included in the new checklist. Findings from the narrative synthesis and case study indicated linkage of the qualitative research to the wider context of the trial and discussion of the integration of data sets within analysis, results and findings sections was important. I, therefore, added items that addressed the linkage of the qualitative research and the trial.

I tested the checklist on a random sample of 10 of the critical review publications. From the results of the initial testing, I refined the checklist to clarify and streamline questions. I also became aware that when applied to the protocol publications many of the items were either worded inappropriately or were not applicable. Therefore, I refined the checklist using a sub-set of questions to use for appraisal of the protocol publications. This resulted in two final checklists; one for the appraisal of reported findings from the use of qualitative research in trials i.e., publications reporting on findings, reports and theses, the: Evaluating Qualitative Research In Trials and their Yields (EQUITY) checklist. The second checklist was for the appraisal of published protocols of trials using qualitative research, the: Evaluating Qualitative Research In Trials and their Yields – Protocol (EQUITY-P) checklist.

EQUITY checklist

The EQUITY checklist comprised 6 sections each with guiding questions and a total of 36 items of information to be included in the publication. Table 19 presents the main sections and the number of items for each section. To see the full EQUITY checklist with all questions and items see Appendix XII.

Table 19 Sections and number of items of information for inclusion for the EQUITY checklist

Section	No. items
A. Research question(s)	3
B. Methodological approach	1
C. Appropriateness and transparency of data collection	15
D. Appropriateness and transparency of analysis and reported findings	9
E. Researcher(s) roles and reflexivity	4
F. Discussion and implications	4
Total items	**36**

Section A: Research question(s)

The first section addresses whether the research question is presented clearly, is relevant and is linked to the trial. Clearly stating the research question sets the scene for the study and enables the reader to link and assess the other criteria throughout the publication. Ensuring the question is relevant and justified allows readers to assess whether the study, its findings and implications are relevant to their practice. See Table 20 for the main questions and supplementary information relating to the research question(s) that should be included in the publication.

Table 20 EQUITY checklist section A: Research question(s) questions and items

Questions to ask of the publication about the qualitative research	Information to be included in the publication
Is the research question clear, relevant and linked to the trial?	Clearly stated research question.
	Research question to be justified including stated relevance. Research question should be linked to existing knowledge base (this may be research, practice guidelines, theory, or policy)
	Is the research question linked to the trial?

Section B: Methodological approach

Section B addresses the design and justification of using a qualitative research approach. This helps the reader to assess whether using QRT was appropriate for

addressing the research question(s). See Table 21 for questions and supplementary questions for the methodological approach section.

Table 21 EQUITY checklist Section B: Methodological approach questions and items

Questions to ask of the publication about the qualitative research	Information to be included in the publication
Is a qualitative approach appropriate?	Clearly described study design and justification for why qualitative research was used.

Section C: Appropriateness and transparency of data collection

Section C addresses the approaches to study data collection. There are many approaches to collecting qualitative data and it should be made clear which method(s) were used and why. A clear and transparent description of how data were collected and a rationale for why they were collected this way can help readers evaluate the validity and robustness of the study and its findings. It can also help readers to determine whether the methods used are appropriate for the research question(s). It can help readers to understand links between the research question(s), the approach taken and the results. This can inform readers about the relevance of findings and implications. Clear and transparent descriptions can also help others replicate the study. See Table 22 for the questions and information which should be included in this section.

Table 22 EQUITY checklist Section C: Appropriateness and transparency of data collection questions and items

Questions to ask of the publication about the qualitative research	Information to be included in the publication
Is enough information about the study/trial context provided?	Description of study context including information about the trial. Reference to the trial should be made explicit.
Are the participants selected appropriate to provide data relevant to study questions?	Description of how participants were selected and why.

Was recruitment conducted using appropriate methods?	Description of how the participants were approached.
	Description of how many participants took part and did not take part.
	Description of sample characteristics.
	Clarify links between qualitative sample and trial participants.
Was data collection appropriate and clearly reported?	Clearly stated data collection method.
	Details of data collection materials and outline of content. e.g., interview, focus group, observation topic guides, questions.
	Description of how data is captured. e.g., audio or visual recordings, field notes.
	Description of the number and duration of data sets. e.g., number and duration of interviews, focus groups, observations.
	Description of when and why data collection was stopped. e.g., was data saturation or other approach discussed.
	Description of when data collection was conducted in relation to the trial and outcome measures. E.g., before, after trial, baseline trial outcomes, final trial outcomes.
Have ethical issues been taken into consideration?	Clearly described informed consent processes.
	Discussion of how confidentiality and anonymity have been considered.
	Details of ethical approval.

Section D: Appropriateness and transparency of analysis and reported findings

Section D addresses the appropriateness and transparency of the analytical approaches used for the QRT and how results/findings are reported. As with data collection methods, it is important to clearly describe approaches to data analysis to enable

readers to determine the appropriateness of analysis approaches, the robustness of the analysis and implications of findings. A comprehensive description of the extent of the analysis can provide the reader with a sense of how data were organised and interpreted. It can help with the evaluation of the depth and quality of findings. This along with clearly reported interpretations of the data which is supported with evidence can help readers assess the credibility of interpretations and reported findings. See Table 23 for questions and information items for section D.

Table 23 EQUITY checklist Section D: Appropriateness and transparency of analysis and reported findings questions and items

Questions to ask of the publication about the qualitative research	**Information to be included in the publication**
Was the analysis approach appropriate and justified?	Clearly stated analysis approach.
Are findings clearly reported and supported with appropriate evidence?	Description of how themes were derived from the data. E.g., Deductive, or pre-determined, inductive.
	Adequate evidence to support reported findings.
	Description of when the analysis was undertaken in relation to data collection.
	Description of when the analysis was undertaken in relation to the trial e.g., was the data analyses before or after trial results were known?
	Description of how data and analysis was managed. E.g., use of software.
Has reliability and rigour of analysis and interpretations been addressed?	Discussion of whether and how analysis has been evaluated for reliability and rigour as appropriate to analysis approach. E.g., member checking, double coding, how disagreements were resolved?
Is there evidence of consideration for both qualitative and other trial data sets together?	Is there evidence of integration of qualitative and other data sets during analysis? E.g., use of triangulation protocol, joint displays, matrix approach

	Discussion of the qualitative data set in relation to other data sets (quantitative etc.). This may be within the findings or discussion sections. E.g., qualitative findings are used to interpret/explain trial findings (or vice versa).

Section E: Researcher(s) roles and reflexivity

Qualitative research usually involves researchers directly engaging with participants within the research process. Researchers and participants can be influenced by this relationship. Personal characteristics of the researcher and their relationship with participants can influence participant responses and the researchers understanding of the phenomena and interpretation of findings. It is therefore important to be transparent about researcher characteristics and their relationship with participants. This can help readers understand the implications of these factors and evaluate the credibility and confirmability of findings. See Table 24 for the questions and information to be included for section E.

Table 24 EQUITY checklist Section E: Researcher(s) roles and reflexivity questions and items

Questions to ask of the publication about the qualitative research	**Information to be included in the publication**
What are the characteristics of the researcher(s)?	Details of which author(s) conducted the study procedures. E.g., recruitment, data collection, analysis.
	Details of the researcher(s) experience or training.
	Details of potential influences of the researcher(s) on the study. E.g., bias, assumptions, interest in the study.
What is the researcher's relationship with participants?	Description of any relationship established with participants prior to data collection.

Section F: Discussion and implications

Section F addresses the discussion of findings and implications for stakeholders. This includes consideration of findings in relation to the existing evidence base, addressing the value of the research and its limitations and what the implications of findings are. Clear consideration of these aspects can help readers assess the transferability of findings. That is whether findings can be applied to or be useful in other contexts. It can also allow readers to assess whether findings are important and whether they can make a meaningful contribution to understanding the phenomena being investigated. See Table 25 for the questions and information to be included for section F.

Table 25 EQUITY checklist Section F: Discussion and implications questions and items

Questions to ask of the publication about the qualitative research	**Information to be included in the publication**
Have findings been considered within the existing evidence base?	Is there adequate discussion about the existing evidence base and how the findings contribute?
Has the trustworthiness and validity of the study been considered?	Discuss the limitations and strengths of the study.
Has the potential influence of the trial on the interpretation of qualitative findings been discussed?	Discussion of the potential influence of the trial on qualitative findings. E.g., are there any limitations resulting from conducting the qualitative research within the trial context? This may be timing, sampling of trial participants, participant burden.
Are study implications considered and made clear?	Clearly state the implications for different stakeholders. E.g., researchers inc. trialists, intervention developers, service providers, patients.

Integration of qualitative research with the trial criteria

The aim of using a mixed method approach in trials is to provide a more comprehensive understanding and enhance the usefulness of knowledge for informing practice. Integration of processes, data and findings can help to maximise these benefits. Therefore, it is important to include how integration occurred and when. This can help

facilitate understanding of how the study was conducted and evaluate its rigour. It can also help to understand findings and how they were arrived at and determine their usefulness. To assess the level of integration of the qualitative research and the trial in the findings publications, I embedded integration criteria throughout the relevant sections. The integration criteria comprised 7 items. Table 26 presents these items.

Table 26 Integration quality assessment criteria for EQUITY checklist

Items for integration criteria in the EQUITY checklist
Is the research question linked to the trial?
Description of study setting including information about the trial.
Clarify links between qualitative sample and trial participants.
Description of when data collection was conducted in relation to the trial and outcome measures.
Description of when the analysis was undertaken in relation to the trial.
Discussion of the qualitative data set in relation to other trial data sets.
Discussion of the potential influence of the trial on qualitative findings.
Total number of items = 7

EQUITY-P checklist

The EQUITY-P checklist comprised four sections each with guiding questions and a total of 21 items of information to be included in the publication. Table 27 presents the sections and number of items for each section. To see the full EQUITY-P checklist with all questions and items see Appendix XIII.

Table 27 Sections and number of items of information for inclusion for EQUITY-P checklist

Section	No. items
A. Research question(s)	3
B. Methodological approach	1
C. Appropriateness and transparency of data collection	11
D. Appropriateness and transparency of analysis	6
Total items	**21**

Sections A-D were similar to those of the EQUITY checklist and were included for the same reasons. These include helping readers to assess whether the study, including the research question(s), is relevant and useful to their practice and evaluating whether methods are appropriate for addressing questions. Clear and comprehensive reporting of these items within protocol publications can also help readers to evaluate the study and its future findings in terms of validity, robustness, reliability, and transferability. It also allows other researchers to replicate the study.

Differences in the sections included changing the tense of questions and information to be provided, as protocols provide information about what is planned rather than what has been done. They are usually reporting before or shortly after a study starts. Parts of section D and sections E and F from the EQUITY checklist were not included in the EQUITY-P checklist as these were not relevant. Although some protocols may report on baseline or preliminary findings, it is likely that reporting of findings and implications would not be relevant for the protocol reporting checklist. It is also unlikely that, as the study has not yet been conducted, the role of the research and reflexivity may not be known yet and would not be relevant for a protocol publication.

Integration in protocol publications.

To assess the level of integration of the qualitative research and the trial in the protocol publications, I embedded integration criteria throughout the relevant sections. The integration criteria comprised of six items. Table 28 presents these items.

Table 28 Integration quality assessment criteria for EQUITY-P checklist

Integration criteria (protocol publications)
Is the research question linked to the trial?
Description of study setting including information about the trial.
Clarify links between qualitative sample and trial participants.
Description of when data collection is planned to take place in relation to the trial and outcome measures
Description of when the analysis is planned to take place in relation to the trial
Discussion of whether and how analysis will be evaluated for reliability and rigour.
Total number integration criteria = 6

Checklist scoring

To help make judgements about the quality of the reporting in the publications I dichotomised each question to yes (1 point) or no (0 points). If a criterion was NOT present or it was unclear whether a criterion was present within the publication, the reviewer selects no (0 points). If the reviewer deemed that a criterion was present, a score of 1 is given.

The responses for each of the questions were summed to give a score between 0 and 36 for the EQUITY checklist and 0 and 21 for the EQUITY-P checklist, with a higher score representing better quality. For the EQUITY checklist, those scoring 0-18 were considered low quality with those scoring 19-36 as high quality. The EQUITY-P checklist was scored between 1-21; those scoring 0-10 were considered low quality with those scoring 11-21 as high quality.

Piloting the checklists

I piloted the checklists on a sample of the publications identified through the critical review (reported in chapter 4). I assessed a 5% random sample of the publications (n=121) published between 2011-2017 using the two checklists as appropriate. Eighty (66.1%) publications were categorised as findings publications and assessed using the EQUITY checklist. Forty-one (33.9%) publications were categorised as protocol publications and assessed using the EQUITY-P checklist.

A second reviewer independently assessed 10% (n=12) of the publications using the appropriate checklists. Discrepancies in scoring were discussed and a final score was agreed upon between the two reviewers.

Findings from quality assessment

Overall scores

There was a large range of total scores for findings publications (4-35) with an average score of 20. Thirty-two (40%) of the findings publications were categorised as low quality and 48 (60%) as high quality. See Table 29.

Table 29 Quality of reporting scores for findings publications

Total score range (1-36)	4-35
Average score	20
Number (%) of low quality (score 0-18)	32 (40%)
Number of high quality (score 19-36)	48 (60%)
Total number of publications	80

There was a large range of total scores for protocol publications (4-18) with an average score of 11. Sixteen (39%) of the protocol publications were categorised as low quality and 25 (61%) as high quality. See Table 30.

Table 30 Quality of reporting scores for protocol publications

Total score range (1-21)	4-18
Average score	11
Number (%) of low quality (score 0-10)	16 (39%)

Number (%) of high quality (score 11-21)	25 (61%)
Total	41

Integration criteria scores

For the 8 integration criteria, findings publications had a wide range of scores (1-7) with an average integration score of 4. Most findings publications reported well in criteria for the description of the study setting including information about the trial (92.5%), describing the timing of qualitative data collection with the trial (67.5%), and linking qualitative sampling to trial participants (65%). However, they reported poorly in the criteria for discussion of the integration of data sets during analysis (12.5%), discussion about the qualitative data sets in relation to other trial data sets (36.3%) and when the qualitative analysis was conducted in relation to the trial (13.8%) (Table 31 displays these scores).

Table 31 Number and percentage of findings publications reporting on integration quality assessment criteria

Integration criteria (findings papers)	**Number**	**Percentage**
Is the research question linked to the trial?	55	68.8%
Description of study context including information about the trial.	74	92.5%
Clarify links between qualitative sample and trial participants.	52	65%
Description of when data collection was conducted in relation to the trial and outcome measures.	54	67.5%
Description of when the analysis was undertaken in relation to the trial	11	13.8%
Discussion of integration of data sets during analysis stages.	10	12.5%
Discussion of the qualitative data set in relation to other trial data sets	29	36.3%
Discussion of the potential influence of the trial on qualitative findings.	25	31.3%

From the 6 integration criteria, protocol publications had a wide range of scores (1-6) with an average integration score of 4. Protocol publications reported well on most of the integration criteria including providing information on the study setting including the trial (95.1%) and linking the qualitative research questions with the trial (75.6%).

However, they reported poorly on the description of when the analysis was planned in relation to the trial (7.3%) (Table 32).

Table 32 Number and percentage of protocol publications reporting on integration quality assessment criteria

Integration criteria (protocol publications)	Number	Percentage
Is the research question linked to the trial?	31	75.6%
Description of study setting including information about the trial.	39	95.1%
Clarify links between qualitative sample and trial participants.	24	58.5%
Description of when data collection is planned to take place in relation to the trial and outcome measures	28	68.3%
Description of when the analysis is planned to take place in relation to the trial	3	7.3%
Discussion of whether and how analysis will be evaluated for reliability and rigour.	20	48.8%

The quality of reporting was consistent over time for both findings and protocol publications (Figure 20).

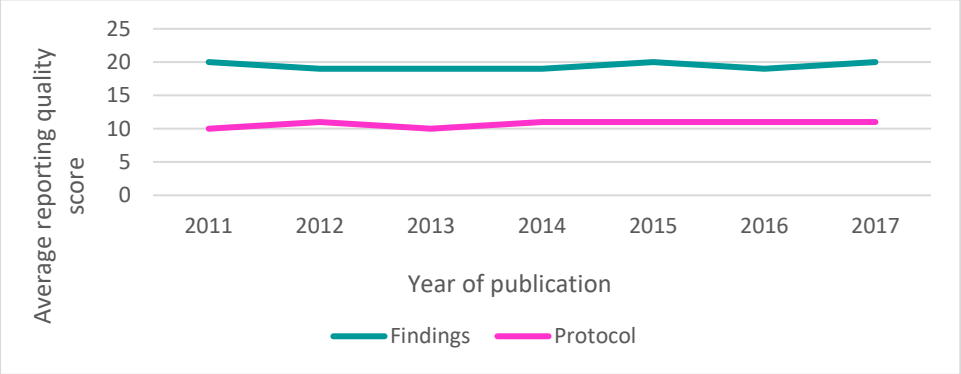

Figure 20 Average reporting criteria scores over time

Discussion

I have developed two checklists to aid good reporting practice for QRT and to assess the quality of reporting. The two checklists address the reporting of findings and protocols

(EQUITY and EQUITY-P checklists). The checklists consist of items specific to the reporting of QRT. Items of information that should be reported on within the publications relate to the research question(s), study design and data collection and analysis approaches. Additionally, the EQUITY checklist addresses the reporting of findings and their implications and the role of researchers. Embedded throughout the checklists are items relating to the integration of qualitative research with the trial and other forms of data.

Findings from the quality assessment of 121 publications using the two checklists developed (EQUITY and EQUITY-P) reported that most of the publications were of high quality. However, there was a large range of scores and average scores were close to the cut off score for high quality. This occurred for both findings and protocol publications. An assessment of quality over time indicated this was consistent over the seven years of publications. Total scores for integration criteria were also high quality. Publications consistently scored better on providing information on the context of the trial and linking the timing of the qualitative research and participant sampling with the trial. However, they reported poorly on the integration of data sets during analysis and reporting findings.

Previous reviews have reported poor quality in reporting QRT. Lewin et al. (26) highlighted issues with lack of clarification for methods used and not enough information being provided to support claims made. They also reported a lack of explicit links within the trial and integration of findings. My findings support Lewin et al.'s (26) findings to an extent. I did find a lack of reporting for the analysis approach used for the QRT. I also found a lack of integration of trial and qualitative findings. However, my findings indicated that overall reporting was high quality. Further to this, integrated reporting was also mostly high quality. This is inconsistent with reports from Lewin et al. (26). I assessed the quality of a much larger number of publications over a longer period than Lewin et al. (26) which supports the strength of my findings. Although overall reporting quality was high, average scores for reporting indicate room for improvement in future publications of QRT. The quality assessment indicated that publications performed better in some areas than others. This has also been reported when assessing the quality of qualitative (363) and mixed methods research reporting (280, 333). Mixed methods papers tend to lack integration of components (280).

Qualitative and quantitative components of mixed methods studies for example tend to be either reported in separate papers or each component is presented in parallel with a lack of integration (333). Using an integrated approach to reporting allows for explicit attention to be paid to the overall study design as well as the individual methods (133). However, there are challenges to achieving this, including a lack of knowledge and understanding of how this can be achieved (41).

Strengths and limitations

The checklists provide a comprehensive list of information that should be included in publications reporting on QRT. They offer specific criteria for reporting QRT when reporting findings and publishing protocols that may not be found in other appraisal tools. The checklists were developed through a synthesis of existing checklists and reporting guidelines for qualitative research and mixed methods research which strengthens its validity. Piloting of the checklists demonstrated useability. However, criteria may be open to interpretation and this should be considered when using the results of the checklists. Further testing of the checklists on a larger number of publications needs to be conducted to test their validity. The use of the checklists by a wider range of users (e.g., authors from different disciplines, reviewers from different disciplines and types of journals) could also help further explore usefulness and validity.

There is an ongoing discussion about whether checklists should be used in the quality appraisal of research reporting (363, 370, 372). Some have argued that, although checklists can be useful, caution should be taken when using them in the appraisal of qualitative research (370, 372, 373). Checklists can be used too prescriptively to ensure 'technical fixes' are addressed which can be counterintuitive and lead to 'the tail wagging the dog' (373). This can stifle the flexibility and adaptability of qualitative research which is one of its key strengths (370). However, the EQUITY and EQUITY-P checklists are designed not to be prescriptive about technical aspects of conducting studies including which qualitative approaches or methods researchers should use. Rather they emphasise the explicit and transparent reporting of information about the approaches used.

There has been discussion about whether publications should be scored in terms of quality rather than using a descriptive approach (363, 372). Some argue that scoring criteria can inhibit reporting flexibility and encourage cookbook reporting (372). Some have queried the level of adherence to quality criteria and questioned the subjective nature of what good quality in reporting may be (358, 359). Some authors have argued that 100% of reporting criteria is required for good quality, for example, in systematic reviews (358).

Within this study, I used a scoring system that has been useful to evaluate the reporting quality in QRT. However, many of the publications scoring as high quality were close to the cut off level. It may be the cut off level is not appropriate and may need reconsideration. It also became apparent when using the EQUITY and EQUITY-P checklists that some items may not be applicable to all publications reporting QRT. For example, some papers only reported on the qualitative data and while consideration of trial results was discussed, it may not have been appropriate to integrate data during analysis. Therefore, including this in the publication may not have been appropriate. While these checklists do encourage integration, it may not always be appropriate and not reporting these aspects may still result in a good quality publication. Other reporting checklists have included a not applicable option when assessing criteria (370). The checklists could benefit from further piloting which could involve consensus work where stakeholders agree whether a cut off level of quality is appropriate and what this should be and whether all criteria need to be included. This may lead to further development and refinement of the checklists.

Conclusion

Those authoring or reviewing QRT publications could use the EQUITY and EQUITY-P quality checklists as a guide to what should be included in such publications. They may be particularly useful for those who are unfamiliar with or new to QRT. The use of the EQUITY and EQUITY-P checklists may help to improve the quality of reporting and therefore the usefulness of the publications. Further work needs to be done to validate the checklists and establish whether and how publications can be scored for quality.

The next chapter presents the triangulation of findings from all the study components.

Chapter 7 Triangulation of findings from different components

Design and methods

To bring together the findings from all the study components and draw overall conclusions I triangulated findings using a triangulation protocol approach (172, 374, 375). This approach has been recommended for and applied when integrating findings from quantitative and qualitative data and findings in mixed methods studies (172, 374, 376). I identified the key findings from each study component: systematic review, critical review, narrative synthesis, case study and the findings from the piloting of the quality checklists I developed. Statements representing these key findings from each data set were then compared with those of the other data sets. I then identified the meta-themes that cut across the findings from the different components (374, 375). Within each meta-theme I considered the relationships between the data against four categories: convergence, contradiction, dissonance, and silence (172, 375). Agreement represented convergence in the data, partial agreement reflected complementarity across data sets, dissonance represented conflicting findings and silence reflected instances where findings were present in some data sets but absent from others. The final convergence coding including meta-themes, key findings from the quantitative and qualitative data sets, and categories (convergence, contradiction, dissonance, and silence) are presented within a joint display (377-379). I then drew conclusions within each theme (380) and added these to the joint display.

Results

A total of 14 meta-themes were developed through the triangulation protocol. Note that numbering does not reflect any order of priority or prevalence in the datasets but has been added to ease the discussion of convergence (see below).

1. Prevalence of QRT over time.

2. The use of qualitative research methods in trials.
3. Understanding what qualitative is and seeing the value of QRT.
4. Researchers include qualitative research in trials based on expectations it should be used.
5. QRT is mainly conducted during the main trial and feasibility or pilot stages of trials.
6. Multidisciplinary teamworking where qualitative researchers are embedded in the trial team.
7. Methodological tensions and maintaining rigour and validity.
8. Qualitative analysis in QRT is not always planned, conducted, or reported well.
9. Integration of processes, data, and findings from qualitative and quantitative approaches.
10. Sufficient resources.
11. The role of research organisations/networks.
12. A place for QRT expertise on trial oversight committees.
13. Reporting quality.
14. Problematic journal reporting conventions.

The meta-themes, relevant key findings from each data set relating to these themes, the convergence categories and conclusions are displayed in Table 33.

Instances of convergence

Instances of silence were most common and occurred across all meta-themes and datasets; there were no meta-themes to which all datasets contributed. There were also 4 meta-themes to which only one dataset contributed (4, 5, 12 and 13). Most meta-themes had instances of either agreement or partial agreement (n=10, 1, 2, 3, 6, 7, 8, 9, 10, 11 and 14). There were instances of agreement in 5 meta-themes (1, 7, 8, 9 and 10) and of partial agreement in 5 meta-themes (2, 3, 6, 9 and 14) where different datasets helped to explain or enhance data from others. Most agreement occurred between narrative synthesis and case study (7, 10 and 11). For one meta-theme (8) four of the datasets contributed with only the systematic review not contributing. There were no instances of dissonance.

Table 33 Joint display of triangulation protocol results

No.	Meta-themes	Systematic Review (SR)	Critical Review (CR)	Narrative Synthesis (NS)	Case Study (CS)	Quality checklists (QC) (findings from piloting)	Convergence category for meta-theme	Conclusions
1	Prevalence of QRT over time.	Compared with the number of overall trials, the proportion of trials reported to use qualitative research is low. 0.24% of registered trials reported using qualitative research. The use of QRT has increased over time (from 1.2%-8.4% ISRCTN/0.03%-0.59% ClinicalTrials.com/0.0-0.06 WHO ICTRP).	The number of publications reporting on QRT has increased over time (n=243 publications in 2011 to n=1096 publications in 2020).				Agreement (SR and CR) Silence (NS, CS and QC)	The use of QRT has continued to increase over time. But the proportion of trials using qualitative research compared to the large number of trials being conducted is low.
2	The use of qualitative research methods in trials.	Use of QRT is more prevalent in trials being conducted in Western countries with a higher gross national income (38.2% UK/28.5% US).	Use of QRT is more prevalent in trials evaluating behavioural interventions (57.7%) with few trials evaluating drug, surgical and medical device trials				Partial agreement (SR and CR) Silence (NS, CS and QC)	Qualitative research is used in a range of trials evaluating a range of interventions. However, it is mainly used within trials conducted in rich Western countries, those evaluating behavioural

			(8.3%, 2.7%, 0.8% respectively).					interventions and trials being conducted in populations with co-morbidities, and in mental health and oncology.
		The use of QRT is limited to trials evaluating behavioural interventions (39%). Surgical, drug and medical device trials each accounted for less than 6% of registered trials reported to use qualitative research (drug – 5.5%, medical device – 4.6% and surgical – 3.8%)	Most publications reporting on QRT were for trials evaluating interventions in the areas of co-morbidity (14.8%), mental health (13.7%), oncology (9.9%) or infectious diseases (8.3%). All other healthcare areas each accounted for less than 5.0% of the publications reviewed.					
3	Understanding what qualitative research is and seeing the value of QRT.			Non qualitative trial team members may not understand what qualitative research is and why it is	Interviewees indicated that QRT was used because the trial team had previously used QRT, found it to be useful and		Partial agreement (NS and CR) Silence (SR, CR and QC)	The use of QRT is dependent on people understanding what qualitative research is and seeing its value in trials. However,

				important to the trial. Facilitating a shared understanding within the trial team about why the QRT is being conducted can help encourage engagement with the qualitative research and consideration of the qualitative and quantitative research in the trial.	believed it would be valuable within the case trial.			some researchers may use it because it is expected.

				Involving non qualitative team members in qualitative research activities could help enhance understanding of the qualitative research.	Interviewees described difficulties with engaging trial site staff with the qualitative research activities because they did not see them as important as the quantitative components. They believed that people's perceptions could be changed by increasing their knowledge about why the QRT was being conducted and demonstrating its value.			
				Increasing knowledge, understanding and perceived value of QRT can help challenge negative assumptions about QRT and promote its use.				

				A belief that qualitative research is not valued for career development (unlikely to attract prestigious funding or be published in high impact journals) and therefore there is less incentive to engage with it.				
				Those who had experienced the benefits of QRT were more open to its use.				
4	Researchers include qualitative research in trials based on expectations it should be used.				Interviewees believed that expectations that QRT should be used can lead to its automatic inclusion in trial designs and funding applications.		Silence (CS only)	Qualitative research may be used in trials because there is an expectation to do so.

5	QRT is mainly conducted during the main and feasibility or pilot stages of trials.		Most of the QRT reported took place during the main trial period (69.1%) and the feasibility/pilot stage (17.4%).				Silence (CR only)	The use of QRT is mainly found in the main trial phase, with few publications indicating its use before or after the trial.
6	Multidisciplinary teamworking where qualitative researchers are embedded in the trial team.			Having a collaborative multidisciplinary team-based approach can help to ensure the needs of the overall trial and the qualitative research are considered. This can help ensure the qualitative research is integrated into the wider trial framework. Having a researcher with qualitative expertise to lead on the development and delivery of	Interviewees liked having a team-based approach to the QRT where the wider team worked with qualitative researchers who regularly attended meetings and communicated with the wider team about the QRT. This was believed to raise the profile of the qualitative research and ensure it was considered throughout the trial alongside		Partial agreement (NS and CS) Silence (SR, CR and QC)	It is important to include researchers with qualitative expertise to help ensure QRT is planned, conducted, and reported well. Working with the wider trial team and taking a team-based approach to QRT can help facilitate shared understanding of all trial components. This can help raise the profile of QRT and ensure it is considered. Tensions can arise in trial teams which can lead to QRT being

				QRT could help ensure the qualitative research was considered and help with planning and conducting it well.	other trial components.			dismissed or devalued and this can be challenging for qualitative researchers. Even if qualitative researchers are involved in the QRT, other factors may mean adequate planning can be difficult. Delays or difficulties with the trial can make QRT difficult to conduct as planned.
				Not having qualitative expertise or disjointed working practices can lead to qualitative research being poorly conducted.	Having the multidisciplinary team (including qualitative researchers) based within the same institute was believed to have helped communication between the team. This helped to foster effective working relationships that facilitated the planning and conduct of the QRT. If team members were based at separate institutions, good and frequent			

					communication could still maintain effective working relationships.			
				Publications discussed how a lack of qualitative expertise, or lack of staff continuity when conducting QRT can lead to poor data collection and analysis.	Even when researchers with qualitative expertise were part of the trial team, the QRT was poorly planned in one of the case trials. This led to difficulties with the analysis process and interpretation of findings and reporting.			
				Tensions within the team can arise and lead to qualitative research and its findings being challenged, devalued, or dismissed. Good relationships and working practices could				

				be facilitated through frequent communication and meetings where updates on the qualitative research were provided.				
				Meetings and open and frequent communication about the qualitative research and the wider trial could also help raise the profile of the qualitative research, enhance mutual understanding of trial components, and engage the wider team in decision making about the QRT.				
7	Methodological tensions and maintaining rigour and validity.			Perceived and actual differences between	Methodological tensions arose in one trial when trial		Agreement (NS and CS)	Methodological tensions can arise when using two different

				qualitative and quantitative approaches, including epistemological and paradigmatic differences can lead to a perceived dichotomy between them. It can be challenging to use both qualitative and quantitative approaches within a trial without compromising the validity and rigour of one or both approaches. More importance is often placed on the experimental approach in the trial which can lead to the qualitative research being assigned a	teams attempted to use statistical approaches to participant sampling for the qualitative research. It was difficult to align this approach with the flexible purposive approach of the qualitative research and practicalities of conducting interviews.		Silence (SR, CR and QC)	approaches within a trial. This can be challenging and lead to more importance being placed on one component by trial team members. Concerns with trying to maintain the rigour and validity of both qualitative and quantitative approaches can be difficult and constraints and inappropriate standards can be applied to the qualitative research component.

				lower status or priority within the trial. Trialist's fears about the negative impact the qualitative research can have on the experimental trial components (including contamination of trial arms, unintended changes to the intervention, unblinding of investigators) were highlighted. These concerns could lead to constraints being placed on the QRT or its methodological integrity being compromised.				
8	Qualitative analysis in QRT is not always planned, conducted, or reported well.		Many of the publications reviewed did not describe the type of qualitative	Publications indicated that a lack of qualitative expertise can lead to QRT	Interviewees and trial documents indicated that planning for the qualitative data	Reporting of when the analysis was conducted in relation to the trial was low in	Agreement (CR, NS, CS and QC) Silence (SR)	Analysis of qualitative data in QRT appears to be a neglected area of QRT and may require greater

			analysis used in the QRT (33.8%).	being poorly conducted and highlighted how a lack of continuity can negatively impact qualitative analysis and interpretation.	analysis was poor.	findings publications (13.8%) and protocol publications (7.3%).		consideration when planning and reporting QRT. Sufficient time and staff resources are required to adequately undertake qualitative analysis and interpretation well.
9	Integration of processes, data, and findings from qualitative and quantitative approaches.			Integration of the qualitative and qualitative elements was believed to enhance the benefits of using QRT including providing greater insight into the trial research questions for investigators. Key areas where integration could occur include qualitative sampling, data collection, analysis and the	Integrating the qualitative research into the wider trial framework was believed to be important within the case trials. It could help to encourage more meaningful integration of the components and instil greater confidence in the qualitative research. The qualitative research aims/objectives, methods and		Partial agreement (NS and CS) Silence (SR, CR and QC)	The integration of qualitative processes, data and findings with other trial sets is believed to be important for maximising the benefits of using a mixed methods approach in trials. Trial teams do appear to be trying to integrate or align components. However, it can be challenging to achieve meaningful integration and it may not always be appropriate of feasible.

				interpretation and reporting of findings.	processes were integrated into the wider trial framework. This was documented within trial protocols, data management processes and planning documentation. Presenting the qualitative research as an integral part of the trial was believed to elevate the perceived importance of the qualitative research and improve engagement with it. A lack of integration or consideration for how the components relate to each other could create tensions within the trial team and			

					difficulties triangulating and interpreting findings. This can lead to qualitative findings being disregarded. Even if integration was planned and achieved throughout the trial, challenges were still encountered when interpreting and reporting findings from both components. Qualitative findings were not always welcomed and sometimes challenged.			
				Achieving integration can be difficult and authors believed it could often be	Not all interviewees believed the qualitative and quantitative research should be integrated			Achieving integration of qualitative data, and findings may not always be appropriate or feasible. It is

				overlooked or avoided. Reasons for lack of integration included - lack of knowledge and awareness of how to integrate data and findings - the timing of when data and findings are available - whether qualitative findings are perceived to be useful - journal reporting conventions - time and resources.	and conducting them as separate but complementary trial components could ensure the rigour of both approaches.			important to plan for how qualitative and quantitative components relate to each other and how they can best be integrated to maximise the benefits of using QRT. More information/guidance which includes examples of integration is needed to help enable researchers to better plan for and be able to integrate qualitative and quantitative data sets and findings.
10	Sufficient resources.			To enable qualitative researchers to contribute to	Case trials did not have enough qualitative staff		Agreement (NS and CS)	Researchers need to ensure sufficient resources are available for the

				the trial most effectively their role needs to be appropriately resourced.	resources and needed to bring in additional researchers to undertake data collection and analysis.		Silence (SR, CR and QC)	feasible conduct of the QRT. Inadequate resources can result from a lack of reviewer's understanding about qualitative research, not having enough information about what the QRT entails, and what its value is to the trial, and researchers not requesting enough resources. Applicants for QRT need to request enough time and funding to support qualitative researcher(s) for the duration of the trial.
11	The role of research organisations/networks.			Research hubs and CTUs can be key organisations to support and actively encourage QRT. CTUs can benefit from	CTUs supported the QRT research in two trials when staffing issues were encountered.		Agreement (NS and CS) Silence (SR, CR and QC)	Research organisations such as CTUs have a role in QRT and can support trial teams delivering QRT.

				hosting trial qualitative researchers as they can bring in funding. CTUs can help to develop qualitative expertise for trials and provide a supportive environment for QRT.				
12	A place for QRT expertise on trial oversight committees.				Sharing progress about the QRT and being able to highlight and discuss qualitative research issues with the oversight committee was believed to be useful. It could help them have a better understanding of the qualitative research and how it related to the other trial components.		Silence (CS only)	Keeping trial oversight committees informed about QRT and having members with qualitative research understanding could help promote understanding of QRT and ensure its role within the trial is considered.

					Having oversight committee members who understood qualitative research or who had qualitative expertise was seen to be valuable by trial teams.			
13	Reporting quality.					Overall, quality of reporting was categorised as high (findings publications – 60%, protocol publications – 61%). There was a wide range of total scores (4-35 for findings publications and 4-18 for protocol publications) which suggests variability in quality.	Silence (Only QC)	Overall reporting quality for QRT appears to be good but is variable with some areas of reporting being poorer.

						QRT publications reported well on some reporting criteria. These included - providing a description of the study setting including a description of the trial (findings publications – 92.5%, protocol publications – 95.1%). - describing data collection in relation to the trial (findings publications – 67.5%, protocol publicatio		

						ns – 68.3%). - Linking qualitative research questions to the trial (findings publications – 68.8%, protocol publications – 75.6%) Areas where publications reported less well included - description of the integration of data sets during analysis (findings – 12.5%) - information about data analysis (protocols – 7.3%).		

14	Problematic journal reporting conventions.			Journal editors and reviewers were believed to play a role in whether QRT was reported. A preference for publishing quantitative research and persistent resistance to publishing qualitative research in some journals can reinforce the perception that qualitative research is inferior to quantitative research. Small word limits can be problematic for researchers publishing in-depth and rich findings from qualitative research. Due to these challenges and lack of time and	Word counts and a reluctance by some high impact medical journals were believed to influence whether and how QRT was published. Qualitative and quantitative research was reported together in the case trial main reports with one trial using a matrix approach to integrate data and findings (case 2). In all trial cases, the qualitative and quantitative research findings were reported in separate publications and journals. This appeared to be because		Partial agreement (NS and CS) Silence (SR, CR and QC)	Traditional journal reporting conventions which include a preference for quantitative research, small word counts, and limited space can lead to qualitative research either not being reported or being reported separately to the quantitative trial findings. Journal editors and reviewers need to understand QRT to enable appropriate review. If the trial components are published separately, they should be linked in some way to alert readers to the wider study context, findings, and implications.

				staff resources, QRT may not be published. Having QRT publications reviewed by people with qualitative research expertise could ensure QRT publications were appropriately reviewed. If the qualitative and quantitative trial components are reported separately, a link should be established between them to alert readers to the wider context of the study and its findings.	the qualitative research could be more fully reported within its own separate publication. Also, some reviewers did not appear to understand what qualitative research was and dismissed its value. Trial teams attempted to link the qualitative and 'main' (quantitative) trial findings publications in some way which mainly involved cross referencing the two outputs or providing a description of the complementary components in some way. This was more noticeable in			

					the qualitative papers where the trial was often described in detail and reference to quantitative findings was made. This was not always the case for quantitative publications that tended to only refer to the qualitative research within a few sentences.			

Discussion

As this triangulation protocol represents the final phase of the research which aimed to provide a final set of key findings, a summary of the key findings and discussion of implications are presented in the next (final) chapter (chapter 8).

Strengths and limitations

The strengths of using a triangulation protocol are that it allowed a systematic comparison of findings from the different methods and data sets that enhanced rigour and understanding. The development of meta-themes allowed me to move beyond individual data sets and findings to understand the wider picture and consider the interpretation of all the study findings in relation to each other that provided an enhanced overall understanding and interpretation at a higher level to inform the study's overarching aim.

The level of agreement/partial agreement and silence also need to be considered. Others have used a triangulation protocol when addressing a single aim or research question using different data collection methods (22). Convergent designs can also be conducted using the same measures of assessments in the qualitative and quantitative datasets and results are then compared and integrated (376) (28). In these studies convergence for meta-themes could be assessed across all data sets (e.g., (376) and convergence was used to determine the strength of findings (374, 376). This may be misleading if applied to this study. In this study I have used different methods to address different objectives with some methods addressing the same objectives (e.g., the systematic review and critical review both addressed objective 1 and the narrative synthesis and case study both addressed objective 5 (see table 1 in chapter 1). Therefore, it was expected that some data sets would not contribute to all meta-themes and there would be a high level of silence and partial agreement as different methods were used to supplement and inform each other with some elements (e.g., narrative synthesis and case study building on each other). Silence largely occurred between the

systematic review/critical review and narrative synthesis/case study datasets. This was expected as they were addressing different objectives.

Even when only one dataset contributed to a theme, this was not interpreted as a limitation of the study but as a strength in that the dataset provided additional insight into the overall aim. There was also a high level of agreement (complete or partial) across the dataset which also demonstrates how using multiple methods helped contribute to a greater understanding.

Limitations of the conduct of the triangulation protocol include only using one investigator to conduct the convergence coding. The use of investigator triangulation whereby the convergence coding is performed independently with analysts coming together to discuss the coding and agree on final meta-themes has been recommended (172, 375). Not doing this in this study may have limited insight that may have been provided by multiple analysts that may have yielded multiple perspectives and different interpretations and convergence coding.

Chapter 8 Discussion

Summary of key findings

This study aimed to explore the use of QRT and identify what influences the planning, conduct, and reporting of QRT. To address this aim I conducted five study components (systematic review, critical review, narrative synthesis, case study, and development and piloting of quality checklists for the reporting of QRT) and triangulated findings from these components. Key findings from this study are that the use of QRT has increased over time, but overall usage remains low. The use of QRT is limited to trials investigating behavioural interventions, those conducted in rich Western countries, and those being conducted in co-morbidity conditions, oncology, and mental health. The overall reporting quality for QRT appears to be good but is variable with some areas of reporting being poorer. Engagement with and use of QRT depends on people understanding what it is and having positive views about its value. Having adequately resourced qualitative expertise embedded within multidisciplinary trials teams and good collaborative relationships is important. This can help raise the profile of the QRT and ensure it is well planned, conducted, and reported. The consideration of all qualitative research aspects and how these relate to other trial components, whilst remaining flexible, can help to ensure QRT is conducted and reported well. An area that appears to be considered less and can be poorly planned and conducted is the qualitative analysis and how to integrate qualitative data and findings with other trial data sets and findings. Presenting qualitative research as an integral part of the trial and implementing processes and activities that encourage this can help to overcome methodological tensions and ensure the validity and rigour of all approaches. Meaningful integration of methodological approaches, data and findings is believed to be important but may not always be appropriate or feasible. This may be due to the timing of findings being available, resource constraints, level of importance placed on the QRT and journal reporting conventions. Having supportive colleagues and research infrastructure can help facilitate qualitative research and its integration into the trial.

Study contributions within the context of the wider literature

The findings from each of the study components have been discussed in relation to the wider literature at the end of each chapter. Here I will present the contribution this study has made to the wider literature. Findings have updated knowledge and added to the research community's understanding of the prevalence of use over time and of the characteristics of trials using qualitative research (15, 22, 26). They have further highlighted healthcare areas where QRT is used more and have identified areas where it could be increased. I have provided an in-depth and nuanced understanding of the factors that influence the planning, conduct, and reporting of QRT by identifying and bringing together and synthesising existing publications that discuss the implementation of QRT which has created new insights. I have also added to this knowledge using primary research data within the case study and tested propositions developed from the narrative synthesis findings. Using both existing and new knowledge I have identified strategies for overcoming challenges faced by researchers when planning, conducting and reporting QRT.

Based on these findings I have made recommendations for a range of stakeholders for the conduct and reporting of QRT (presented at the end of this chapter). These practical recommendations support and add to the existing guidance and recommendations for QRT (22, 28, 37, 38, 43, 144, 232) and should be used alongside them. Areas where my recommendations support others include the importance of appropriate use of QRT across the phases of trials and early comprehensive planning (22, 28, 42, 43). Also, the need for adequate funding, time and qualitative researcher expertise when conducting and reporting QRT (22, 37). The importance of teamworking and embedding qualitative researchers within trial teams has been recommended (22, 37, 42) which my recommendations also support, and I provide ways that this can be facilitated. Previous recommendations have also encouraged the promotion of QRT and the enhancement of skills and knowledge in QRT (22). Previous guidance has also highlighted the role of CTUs in planning and conducting QRT (37, 38). I further this by recommending CTUs and other research infrastructures make a strategic commitment to support QRT and

researchers in the field. My recommendations also encourage the consideration of qualitative research with the wider trial framework (28) but also provide ways of doing this. These include using SIVs to engage trial site staff and embedding QRT in trial documentation and processes. My recommendations also add to existing guidance by highlighting the role of trial oversight committees in QRT and the benefit of having qualitative expertise on these committees. I also make recommendations for guidance for funding application reviewers and journal reviewers with the quality appraisal checklists.

I have highlighted the role of multidisciplinary teamwork when planning and delivering QRT. The role of multidisciplinary teamwork in research has been gathering more interest recently with the emergence of 'team science' (319, 331, 349). Team science has been defined as *'output-focused research involving two or more research groups – to address increasingly complex and multifaceted research challenges'* (319). (p.6) The concept of team science has been developed and applied within the fields of biomedical and implementation research (331) (319, 381) but not trials. This study has provided insight into how multidisciplinary teams can work together to implement two different approaches to research in a complementary manner and overcome tensions and challenges that can arise when one component is deemed more important than another. This has not been addressed widely in the team science literature and findings and recommendations may also apply to people engaged in team science.

Findings from this study are also relevant to the ongoing quantitative-qualitative-mixed methods research debate (30, 382, 383). The stance of this study has been a pragmatic one and has largely accepted that to address important healthcare questions and inform practice, a mixed methods approach to evaluating interventions is most appropriate. Findings from this study demonstrate that this is largely the view of researchers using QRT and that integration should be achieved to maximise its benefits. Indeed, its use depends on people seeing the value of QRT. This aligns with arguments made by supporters of mixed methods research (27, 54, 60, 380). This study has also demonstrated that both qualitative and quantitative approaches are successfully used together within trials and highlighted ways to do this. However, others have taken a different stance on the use of mixed methods research and believe it is not possible to reconcile the different paradigmatic underpinnings of qualitative and quantitative

approaches (382). This includes within trials (384). This study identified that some people involved in QRT believed that because of their underlying assumptions qualitative and quantitative research should remain separate but complementary trial components. I do not attempt to resolve this debate within this study, but it is important to be mindful that it is ongoing and is reflected in the implementation of QRT.

Poor quality reporting of QRT and a lack of integration when reporting qualitative and quantitative trial components have been previously highlighted (26). Prior to this study, there was limited guidance for reporting QRT, and no quality appraisal tools were available. The development of the EQUITY and EQUITY-P quality appraisal checklists provides new tools which can support people wanting to publish QRT and those reviewing QRT.

Reflections on the future of QRT

Although it appears that further QRT has been published, I am not aware of any methodological papers discussing the use of QRT or its implementation since 2021 (the end of the narrative synthesis review). However, researchers do appear to be continuing to discuss QRT and how it can best be used and conducted. Within the MRC/NIHR Trials Methodology Research Partnership (TMRP) trial conduct working group (385) a subgroup for qualitative methods in trials has been formed. Within this group, several priorities for QRT have been identified and researchers are collaborating on ways to build capacity to address these.

The COVID-19 pandemic has had a major impact on the way trials are conducted and changes implemented are likely to continue beyond the pandemic period (386, 387). The importance of having well designed and conducted trials has been highlighted as the increased number of trials and speed with which they were completed and reported during the pandemic has led to a lack of methodological rigour and poor planning (387). Attention has been drawn to the use of adaptive platform trial designs and master trial protocols (387). Trials have also faced recruitment and resource issues, have had to be flexible with data collection processes and timelines, and be adaptive with how treatments being assessed are delivered (375, 386, 388). These changes and challenges

will likely have an impact on the role and conduct of QRT. Within this study I have highlighted how issues being faced by trials can have implications for QRT and it is likely that the ongoing impact of COVID-19 on trials will also create challenges for those conducting QRT. However, there is also an opportunity here to use QRT to address some of these challenges. QRT for example could be used to help optimise recruitment, evaluate how master protocols are being implemented across different sites and countries, and help determine optimum and acceptable trial designs.

Qualitative research is an evolving field that is responsive to new technologies, changing societal priorities, and the demands placed on it by the wider research field (389). As a result of the COVID-19 pandemic, more people are turning to digital, remote means of communicating as restrictions have been placed on society (390, 391). For a discipline that has valued and relied upon face-to-face data collection, qualitative researchers have had to rapidly adapt and evaluate the way data is collected, analysed, and disseminated (390, 391). Qualitative research has increasingly involved data collection through remote digital means and the use of online data such as internet forums for example (144, 389). This is likely to continue and influence the way QRT is used. As the need for rapid answers to important questions was required there has also been a spotlight cast on rapid research methods including rapid qualitative reviews and evaluations (392, 393). This has highlighted the benefits of rapid qualitative approaches, including their use in trials (394-396) and they will likely be increasingly used in trials. It will be interesting to see whether and how the way QRT is conducted throughout the pandemic and beyond it changes.

The new guidance framework for developing and evaluating complex interventions from the MRC (171) is also likely to have an impact on the use of QRT in the future. In chapter 3 I highlighted how an uptick in the use of QRT was likely the result of the MRC guidance supporting the use of qualitative research in the evaluation of complex interventions (19, 25). At the time the framework limited its discussion of interventions to those that aimed to change behaviour (behavioural interventions). The new framework broadens its description of what a complex intervention is to consider not just the components of the intervention, but the context and processes needed to implement the intervention. Examples they use included vaccines and robot assisted surgery. Given this widened perspective more people may consider the use of QRT in

trials other than those evaluating behavioural interventions. The framework also states that

> *'a purely quantitative approach, using an experimental design with no additional elements such as a process evaluation, is rarely adequate for complex intervention research, where qualitative and mixed methods designs might be necessary to answer questions beyond effectiveness' (171). (p.7)*

This endorsement of qualitative research and mixed methods designs will likely enhance the perceived value and acceptance of these approaches and increase the meaningful use of QRT. Given the attention paid to process evaluations within the guidance, QRT is likely to take this form.

Strengths and limitations

In this study I used multiple methods that included the collection, analysis, and triangulation of qualitative and quantitative data from multiple sources. Therefore, this study provides a strong approach to gaining an in-depth and comprehensive understanding of QRT which wouldn't have been achieved if I only used one strategy. The strengths and limitations of each approach used in this study have been discussed in their respective chapters. Using a mixed methods approach with both quantitative and qualitative methods has enabled me to approach the aim from different perspectives and understand the different aspects of QRT. This has enabled greater insight and a broader more comprehensive understanding. The use of multiple methods has allowed some of the limitations of the individual approaches to be addressed. I was able to both explore and explain the use of QRT. Findings from the different approaches were able to supplement and inform each other with findings from earlier components used to inform later ones, for example, findings from the narrative synthesis informed the propositions to be tested in the case study. However, not all the limitations were able to be overcome for the different components and readers should be mindful of these when considering findings and recommendations.

There have been challenges when conducting this study through a methodological lens rather than a clinical one. As discussed in chapter 1 research contexts are complex and although processes can appear tangible, they can be influenced by different factors when being implemented (46, 47). Within this study this has been difficult on two levels, one investigating a methodology (QRT) that has many facets and complex contexts has required multiple research components which has been time and resource intensive and has been challenging. Using a pragmatic approach that allowed flexibility and a focus on what would be useful to researchers in the field has helped with this challenge. Secondly, using methodologies that have largely been designed and used to investigate clinical activities and contexts has also been challenging and required modified approaches to be used. It has also been difficult to interpret and apply methods such as the critical review and narrative synthesis. Usually, critical reviews use a narrative approach and use qualitative data (251, 253, 396). When using the critical review approach, I focussed on its purpose of synthesising a body of data to identify problems or gaps that needed addressing in QRT rather than building a model or theory. It was difficult to interpret guidance for using a critical review approach (253) in this manner. I also encountered difficulties with the use of the narrative synthesis and related guidance (281). As discussed in chapter 5 I used a modified approach that did not develop a model of how the intervention work (see chapter 5) as this study was not investigating an intervention. I also encountered difficulties with the application of parts of the guidance and the processes recommended. Issues were related to the adaptation of the guidance to the exploration of the implementation of a research methodology. The application of the guidance to the exploration of the use of a research methodology rather than an actual intervention meant that some recommendations could not be adhered to. For example, the guidance recommends that *"for reviews focussing on implementation it would be important to extract detailed data on the design of the intervention, the context in which it was introduced, and the factors and/or processes identified as impacting on implementation." (281) (p. 18)*

Conclusion and recommendations

Conclusion

The use of QRT has continued to increase over time, however, there are areas of trials research that do not use QRT. Several key factors influence the implementation of QRT and it can be challenging to ensure it is planned, conducted, and reported well. However, challenges are not insurmountable, and people must be aware of the benefits of QRT and how they can increase its use and plan, conduct and report QRT well. The following recommendations are aimed at key stakeholders involved in QRT. These recommendations should be used as a supplement to existing guidance for QRT.

Recommendations for practice

Researchers

Considering the use of QRT

Researchers and healthcare professionals in all health areas need to recognise the benefits of using QRT and how it can be used to optimise trials. They should consider using existing frameworks and guidelines for how QRT can be used and its value maximised.

Be clear about why QRT is being used and that it is appropriate. If there is no clear rationale for why QRT is being used, then researchers should not use it. Using QRT without a clear rationale and an understanding of how it complements the trial can lead to challenges with data interpretation and reporting and lead to qualitative findings being devalued or dismissed.

Planning QRT

When planning QRT, researchers should be clear about the objectives of the qualitative research, and how they relate to the overarching trial research question(s). It is also important to consider what data will be collected and why and researchers may want to ensure data collection and analysis are focussed on informing the trial research questions.

Researchers should consider the wide range of qualitative methods available and consider how best they can address trial research questions and objectives. Researchers should consider being flexible with the approach they use, adapting traditional methods and consider using more innovative methods including online qualitative research methods.

When planning QRT, researchers need to consider ALL aspects of data collection, analysis, interpretation and reporting and how this relates to the other trial components. Qualitative analysis appears to be an area that is often poorly planned in QRT. This can lead to difficulties conducting the analysis in a meaningful way and producing useful insights. Researchers may wish to use a data analysis plan but be mindful it may not always be appropriate and needs to remain flexible to align with the nature of qualitative research.

Ensure sufficient time and staff capacity is available to consider the qualitative research findings in relation to other trial data sets to maximise learning opportunities and a more comprehensive interpretation of all aspects of the trial research question(s).

Be aware of the iterative and flexible nature of qualitative research and the potential for delays or challenges to trial progress that may impact the QRT. Consider building in time and resources to account for changes or delays.

Researchers should ensure they request sufficient funding to enable enough staff and time to carry out good quality research. Taking a minimalist approach to funding for QRT could lead to challenges with not enough staff and time and lead to difficulties conducting and reporting the QRT and poor-quality research. When completing funding applications, researchers should make it clear what the value of the QRT is and what it will entail to help reviewers make informed decisions.

Include researchers with qualitative research expertise in trial teams for the duration of the trial from the design/planning stages through to reporting stages.

Consider a complementary or integrated trials design where the needs of both the qualitative and quantitative research are considered. This can help to ensure the rigour and quality of all components. Considering how methods, data and findings can be integrated can help maximise the benefits of using QRT and provide a more informed understanding of trial outcomes and their implications.

Conducting QRT

Ensure qualitative research is presented as an integral part of the trial to collaborators early in the trial. Consider using Site Initiation Visits (SIVs) to introduce the purpose of the qualitative research and its value in the trial to the trial site staff. Where possible have the qualitative researcher(s) attend investigator meetings such as SIVs.

Embedding the qualitative research into trial documentation and processes can help ensure it is visible and the consideration of how it relates to other trial components. Trial teams should consider including the qualitative research within trial protocols, data management processes and plans, trial documentation (including participant facing documents), standard operating procedures (SOPs) or working instructions, analysis plans and publications plans.

Qualitative researchers should be embedded within the wider multidisciplinary trial team and work collaboratively with team members. This can help the team consider all the trial components and how they relate to each other. It is important to foster good working relationships and a shared understanding of trial components. This can be achieved through open and frequent communication that values input from all team members. Having the qualitative researcher(s) attend and contribute to team meetings such as TMGs, having a standing agenda item for qualitative research and qualitative researchers providing update reports for the team can also ensure the visibility of the QRT and encourage consideration of its contribution. Engaging non-qualitative team members in qualitative data analysis and interpretation activities can also enhance understanding of the QRT and produce more meaningful insights into findings and their wider implications for the trial.

Trial teams should consider sharing the QRT progress, potential issues, and findings with trial oversight committees to provide members with a more complete understanding of the trial. They may also consider the benefits of having trial oversight committee members with qualitative expertise to facilitate understanding of the QRT and provide more informed advice.

Reporting QRT

Consider using the EQUITY and EQUITY-P quality appraisal checklists developed within this study to aid the reporting of QRT.

Consider integrating reporting of the qualitative research findings with those of other trial components. Publishing separate qualitative publications may enable a more detailed and nuanced account of the qualitative research findings. But may also lose the benefits of presenting an integrated report of all the trial findings. If separate papers are published, researchers should ensure they are linked in some way and that readers are aware of the wider study context and the implications this may have. Researchers should consider adding the trial registration number to any separate qualitative papers. They could also consider publishing paired papers in the same journal.

Promotion of QRT and training

Researchers with experience and knowledge and skills in QRT need to continue to advocate its use where appropriate and report the benefits it can bring to answering important healthcare practice questions. They should be aware that QRT may need to be explained or promoted in some areas more than others. This study has highlighted how surgeons may be one group of healthcare professionals who are more likely to not understand QRT and not believe it to be useful.

Those who intend to undertake trials with qualitative research should consider enhancing their understanding and skills in QRT through formal and on the job training.

Funders

Funding organisations should consider the value of QRT for decision making in practice and how they can encourage applicants to apply for sufficient funding to support QRT. Funders may want to consider providing guidance for funding panel reviewers about how to review QRT and have people with the appropriate expertise review applications. Funders may also want to provide applicants with guidance on what needs to be included in applications to enable reviewers to make informed decisions about whether to fund QRT.

Journal editors and reviewers

Journal editors should consider the benefits of QRT and its value to the healthcare and research community. They could consider including qualitative research in author guidelines and policies. Journal reviewers should have a sufficient understanding of qualitative research and its use in trials and may want to consider using the EQUITY and EQUITY-P checklists to assist their decision making about the appropriate inclusion of information and the quality of submissions.

Clinical Trials Units (CTUs)/Research organisations

Research organisations, such as CTUs, who provide infrastructure to support trials should consider how they can support research teams with the use of QRT and develop QRT expertise. This may involve hosting researchers with QRT expertise and a strategic commitment to supporting the use of QRT.

Future Research

This study has highlighted the role of CTUs in QRT and has suggested they can increase the use of QRT and support good practice. Further exploration of the roles CTUs have in QRT, the extent to which they do or can support QRT and how this may be enhanced is needed. This could be achieved through conducting a mapping exercise which may involve a survey to scope; the current involvement of CTUs in QRT, how many CTUs have researchers with qualitative expertise embedded within them or who collaborate with them, what level of involvement they advocate or provide for supporting/conducting QRT and how qualitative researchers are funded (e.g., core or grant funded), and the types of trials for which qualitative research is used and which type of trials CTUs may recommend qualitative research in. Interviews or focus groups with CTU staff such as CTU directors and qualitative researchers (embedded within or who collaborate with CTUs) could explore these topics in more depth including the processes and mechanisms involved in CTU involvement with QRT. Outputs could

include guidance or recommendations for CTUs for engaging with QRT and how to maximise their role in enhancing QRT.

This study has highlighted the potential benefits of integrating qualitative and quantitative data and findings within trials. However, it has also highlighted potential issues with this integration including whether it is appropriate and feasible. It has also highlighted a lack of examples and guidance for how it can be achieved. Further research is therefore needed to investigate what the added value of integrating qualitative and quantitative data and findings in trials may be and how this can be optimised. Potential areas to be explored include when might integration be appropriate or beneficial and possible. The extent of techniques and how and why these may be used; understanding the processes and practices involved in integrating qualitative and quantitative data and findings in trials and the experiences of members of trial teams (e.g., qualitative researchers, trial managers, clinicians, trialists, health economists, statisticians). Outputs could include recommendations for trial teams conducting mixed methods trials. This could be achieved through a mixed method study which involves a systematic mapping review, focus groups and a consensus activity (such as a Delphi survey and/or stakeholder workshop).

As discussed in chapter 6, the reporting quality checklists could benefit from further piloting. The checklists could be applied to a much larger sample of publications by a wider group of reviewers with different disciplinary backgrounds to assess their validity. Consensus work through stakeholder workshops would allow further and wider discussion of the criteria and to agree on whether a cut off level for the quality is appropriate and if so, what this should be. If appropriate the checklists could be refined or developed further.

Further research is also needed to understand how QRT is conducted outside of the UK setting (such as trials conducted in the US) and explore what may influence its use and conduct and whether this differs from QRT conducted in the UK. There are clearly many trials using qualitative research in the US. However, most of the research addressing its implementation has largely been UK centric (including this study). More research is needed to explore whether the different context of healthcare and research delivery in the US influences whether and how QRT is used. Potential areas to be explored include; an exploration of the context of trial design and conduct in the US and whether this

differs substantially to the US; how does QRT factor into trials in the US and do the reasons for using it differ to the UK; do trial teams or research organisations or infrastructures differ when supporting the conduct and reporting of QRT and what can be done to optimise this, and how does the different models of healthcare delivery influence the use of QRT in the US. This could be achieved through conducting exploratory interviews with people involved in the conduct of trials in the UK including those who conduct QRT. These findings could then inform more explanatory case studies which include further interviews, observations (e.g., planning meetings, trial team meetings) and the use of trial documents with findings then triangulated.

What is next for me

Moving forward I would like to continue to build on this research and use what I have learnt from it within my role as a researcher in QRT. I am currently leading the development of funding applications to address some of the future research recommendations I have made. I also plan to submit publications for the research presented in this thesis including, the quality reporting checklists and a paper discussing researcher vulnerability in QRT developed from the presentation accepted for the Bath Qualitative Symposium. I also plan to submit abstracts from the different study components to the International Clinical Trials Methodology Conference (ICTMC) 2022. I also plan to deliver a webinar for the MRC-NIHR-TMRP webinar series.

References

1. Sackett DL, Rosenberg WMC, Gray JAM, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isnt. BMJ. 1996;312(7023):71.
2. Dawes M, Summerskill W, Glasziou P, Cartabellotta A, Martin J, Hopayian K, et al. Sicily statement on evidence-based practice. BMC Medical Education. 2005;5(1):1.
3. Cochrane AL. Effectiveness and efficiency: random reflections on health services: Nuffield Provincial Hospitals Trust; 1972.
4. Research Excellence Framework. CUtLASS: Changing attitudes and prescribing practice: Cost effectiveness of first versus second generation antipsychotic drugs in people with schizophrenia. [Case study 28074] 2014 September 14, 2020. Available from: http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=28074.
5. Morales DR, Donnan PT, Daly F, Staa TV, Sullivan FM. Impact of clinical trial findings on Bell's palsy management in general practice in the UK 2001–2012: interrupted time series regression analysis. BMJ Open. 2013;3(7):e003121.
6. Research Excellence Framework. Curing chronic granulomatous disease in children through early bone marrow transplant. [Case study 21717] 2016 September 14, 2020. Available from: http://impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=21717.
7. Sullivan FM, Swan IRC, Donnan PT, Morrison JM, Smith BH, McKinstry B, et al. A randomised controlled trial of the use of aciclovir and/or prednisolone for the early treatment of Bell's palsy: the BELLS study. 2009;13:47.
8. Campbell M, Snowdon C, Francis D, R Elbourne D, McDonald A, Knight R, et al. Recruitment to randomised trials: Strategies for Trial Enrolment and Participation Study (STEPS)2007.
9. Britton A, McKee M, Black N, McPherson K, Sanderson C, Bain C. Choosing between randomised and non-randomised studies: a systematic review. Health Technol Assess. 1998;2(13):i-iv, 1-124.
10. Brueton VC, Tierney JF, Stenning S, Meredith S, Harding S, Nazareth I, et al. Strategies to improve retention in randomised trials: a Cochrane systematic review and meta-analysis. BMJ open. 2014;4(2):e003821-e.
11. Glasgow RE, Nelson CC, Kearney KA, Reid R, Ritzwoller DP, Strecher VJ, et al. Reach, engagement, and retention in an Internet-based weight loss program in a multi-site randomized controlled trial. J Med Internet Res. 2007;9(2):e11.
12. Mills N, Donovan JL, Smith M, Jacoby A, Neal DE, Hamdy FC. Perceptions of equipoise are crucial to trial participation: a qualitative study of men in the ProtecT study. Controlled Clinical Trials. 2003;24(3):272-82.
13. Potter S, Mills N, Cawthorn SJ, Donovan J, Blazeby JM. Time to be BRAVE: is educating surgeons the key to unlocking the potential of randomised clinical trials in surgery? A qualitative study. Trials. 2014;15(1):80.
14. Johnson R, Evans M, Cramer H, Bennert K, Morris R, Eldridge S, et al. Feasibility and impact of a computerised clinical decision support system on investigation and initial management of new onset chest pain: a mixed methods study. BMC medical informatics and decision making. 2015;15:71-.
15. Flemming K, Adamson J, Atkin K. Improving the effectiveness of interventions in palliative care: the potential role of qualitative research in enhancing evidence from randomized controlled trials. Palliative Medicine. 2008;22(2):123-31.

16. Mulder R, Singh AB, Hamilton A, Das P, Outhred T, Morris G, et al. The limitations of using randomised controlled trials as a basis for developing treatment guidelines. Evid Based Ment Health. 2018;21(1):4-6.
17. Lenney W, Perry S, Price D. Clinical trials and tribulations: the MASCOT study. Thorax. 2011;66(6):457.
18. Blencowe NS, Blazeby JM, Donovan JL, Mills N. Novel ways to explore surgical interventions in randomised controlled trials: applying case study methodology in the operating theatre. Trials. 2015;16:589.
19. Campbell M, Fitzpatrick R, Haines A, Kinmonth AL, Sandercock P, Spiegelhalter D, et al. Framework for design and evaluation of complex interventions to improve health. BMJ (Clinical research ed). 2000;321(7262):694-6.
20. Heneghan C, Goldacre B, Mahtani KR. Why clinical trial outcomes fail to translate into benefits for patients. Trials. 2017;18(1):122.
21. Griffiths AHS, Gene F, Estela B, Lee B, Anna D, Farah E-S, et al. Improving the healthcare response to domestic violence and abuse in primary care: protocol for a mixed method evaluation of the implementation of a complex intervention. BMC Public Health. 2018;18(1):971.
22. O'Cathain A, Thomas KJ, Drabble SJ, Rudolph A, Goode J, Hewison J. Maximising the value of combining qualitative research and randomised controlled trials in health research: the QUAlitative Research in Trials (QUART) study – a mixed methods study. Health Technol Assess. 2014;18(38).
23. O'Cathain A, Thomas KJ, Drabble SJ, Rudolph A, Hewison J. What can qualitative research do for randomised controlled trials? A systematic mapping review. BMJ Open. 2013;3(6).
24. Snowdon C. Qualitative and mixed methods research in trials. Trials. 2015;16:558.
25. Medical Research Council. A Framework for Development and Evaluation of RCTs for Complex Interventions to Improve Health. 2000.
26. Lewin S, Glenton C, Oxman AD. Use of qualitative methods alongside randomised controlled trials of complex healthcare interventions: methodological study. BMJ. 2009;339.
27. Creswell JW, Fetters MD, Plano Clark VL, Morales A. Mixed Methods Intervention Trials. In: Andrew S, Halcomb EJ, editors. Mixed Methods Research for Nursing and the Health Sciences2009. p. 159-80.
28. Creswell JW, Clark VLP. Designing and Conducting Mixed Methods Research: SAGE Publications; 2017.
29. Plano Clark VL, Schumacher K, West C, Edrington J, Dunn LB, Harzstark A, et al. Practices for Embedding an Interpretive Qualitative Approach Within a Randomized Clinical Trial. Journal of Mixed Methods Research. 2013;7(3):219-42.
30. Denzin NK, Lincoln YS. The SAGE Handbook of Qualitative Research: SAGE Publications; 2017.
31. Donovan JL, Paramasivan S, de Salis I, Toerien M. Clear obstacles and hidden challenges: understanding recruiter perspectives in six pragmatic randomised controlled trials. Trials. 2014;15:5-.
32. Gikonyo C, Bejon P, Marsh V, Molyneux S. Taking social relationships seriously: lessons learned from the informed consent practices of a vaccine trial on the Kenyan Coast. Social science & medicine (1982). 2008;67(5):708-20.
33. Murtagh MJ, Thomson RG, May CR, Rapley T, Heaven BR, Graham RH, et al. Qualitative methods in a randomised controlled trial: the role of an integrated

qualitative process evaluation in providing evidence to discontinue the intervention in one arm of a trial of a decision support tool. Quality & safety in health care. 2007;16(3):224-9.
34. Jones LL, Calvert M, Moiemen N, Deeks JJ, Bishop J, Kinghorn P, et al. Outcomes important to burns patients during scar management and how they compare to the concepts captured in burn-specific patient reported outcome measures. Burns : journal of the International Society for Burn Injuries. 2017;43(8):1682-92.
35. Abetz L, Rofail D, Mertzanis P, Heelis R, Rosa K, Tellefsen C, et al. Alzheimer's disease treatment: assessing caregiver preferences for mode of treatment delivery. Adv Ther. 2009;26(6):627-44.
36. Berk M, Munib A, Dean O, Malhi GS, Kohlmann K, Schapkaitz I, et al. Qualitative methods in early-phase drug trials: broadening the scope of data and methods from an RCT of N-acetylcysteine in schizophrenia. The Journal of clinical psychiatry. 2011;72(7):909-13.
37. Rapport F, Storey M, Porter A, Snooks H, Jones K, Peconi J, et al. Qualitative research within trials: developing a standard operating procedure for a clinical trials unit. Trials. 2013;14(1):54.
38. Cooper C, O'Cathain A, Hind D, Adamson J, Lawton J, Baird W. Conducting qualitative research within Clinical Trials Units: avoiding potential pitfalls. Contemporary clinical trials. 2014;38(2):338-43.
39. O'Cathain A, Goode J, Drabble SJ, Thomas KJ, Rudolph A, Hewison J. Getting added value from using qualitative research with randomized controlled trials: a qualitative interview study. Trials. 2014;15(1):215.
40. Glenton C, Lewin S, Scheel IB. Still too little qualitative research to shed light on results from reviews of effectiveness trials: A case study of a Cochrane review on the use of lay health workers. Implementation Science. 2011;6(1):53.
41. Richards DA, Bazeley P, Borglin G, Craig P, Emsley R, Frost J, et al. Integrating quantitative and qualitative data and findings when undertaking randomised controlled trials. BMJ Open. 2019;9(11):e032081.
42. O'Cathain A, Hoddinott P, Lewin S, Thomas KJ, Young B, Adamson J, et al. Maximising the impact of qualitative research in feasibility studies for randomised controlled trials: guidance for researchers. Pilot and Feasibility Studies. 2015;1(1):32.
43. O'Cathain A. A Practical Guide to Using Qualitative Research with Randomized Controlled Trials: Oxford University Press; 2018.
44. Thayer HS, Peirce CS. Pragmatism, the Classic Writings: Charles Sanders Peirce, William James, Clarence Irving Lewis, John Dewey, George Herbert Mead: Hackett Publishing Company; 1982.
45. James W. Pragmatism: Dover Publications; 1995.
46. Morgan DL. Pragmatism as a Paradigm for Social Research. Qualitative Inquiry. 2014;20(8):1045-53.
47. Kelly LM, Cordeiro M. Three principles of pragmatism for research on organizational processes. Methodological Innovations. 2020;13(2):2059799120937242.
48. Shaw JA, Connelly DM, Zecevic AA. Pragmatism in practice: mixed methods research for physiotherapy. Physiotherapy theory and practice. 2010;26(8):510-8.
49. Kaushik V, Walsh CA. Pragmatism as a Research Paradigm and Its Implications for Social Work Research. Social Sciences. 2019;8(9).
50. Long KM, McDermott F, Meadows GN. Being pragmatic about healthcare complexity: our experiences applying complexity theory and pragmatism to health services research. BMC Medicine. 2018;16(1):94.

51. Biesta G. SAGE Handbook of Mixed Methods in Social & Behavioral Research. 2010 2020/09/18. Thousand Oaks, California: SAGE Publications, Inc. 2. Available from: https://methods.sagepub.com/book/sage-handbook-of-mixed-methods-social-behavioral-research-2e.
52. Morgan DL. Paradigms Lost and Pragmatism Regained: Methodological Implications of Combining Qualitative and Quantitative Methods. Journal of Mixed Methods Research. 2007;1(1):48-76.
53. Yvonne Feilzer M. Doing Mixed Methods Research Pragmatically: Implications for the Rediscovery of Pragmatism as a Research Paradigm. Journal of Mixed Methods Research. 2009;4(1):6-16.
54. Johnson RB, Onwuegbuzie AJ. Mixed Methods Research: A Research Paradigm Whose Time Has Come. Educational Researcher. 2004;33(7):14-26.
55. Creswell JW. Qualitative Inquiry and Research Design: Choosing Among Five Approaches: SAGE Publications; 2012.
56. Dewey J, Dewey JF, Allen G, Unwin. Logic, the Theory of Inquiry: H. Holt; 1938.
57. Goldkuhl G. Pragmatism vs interpretivism in qualitative information systems research. European Journal of Information Systems. 2012;21(2):135-46.
58. Friedrichs J, Kratochwil F. On Acting and Knowing: How Pragmatism Can Advance International Relations Research and Methodology. International Organization. 2009;63(4):701-31.
59. Denscombe M. Communities of Practice: A Research Paradigm for the Mixed Methods Approach. Journal of Mixed Methods Research. 2008;2(3):270-83.
60. Onwuegbuzie AJ, Johnson RB, Collins KM. Call for mixed analysis: A philosophical framework for combining qualitative and quantitative approaches. International Journal of Multiple Research Approaches. 2009;3(2):114-39.
61. Pearson A, Wiechula R, Court A, Lockwood C. The JBI model of evidence-based healthcare. International Journal of Evidence-Based Healthcare. 2005;3(8):207-15.
62. Jadad AR, Enkin MW, Jadad AR, Enkin MW. Randomized Controlled Trials : Questions, Answers and Musings. Oxford, UNITED KINGDOM: John Wiley & Sons, Incorporated; 2007.
63. Pope C, Mays N. Qualitative Research: Reaching the parts other methods cannot reach: an introduction to qualitative methods in health and health services research. BMJ. 1995;311(6996):42.
64. Sackett DL, Rosenberg WM. The need for evidence-based medicine. Journal of the Royal Society of Medicine. 1995;88(11):620-4.
65. Upshur RE, VanDenKerkhof EG, Goel V. Meaning and measurement: an inclusive model of evidence in health care. Journal of evaluation in clinical practice. 2001;7(2):91-6.
66. Sibbald B, Roland M. Understanding controlled trials: Why are randomised controlled trials important? BMJ. 1998;316(7126):201.
67. Hariton E, Locascio JJ. Randomised controlled trials – the gold standard for effectiveness research. BJOG: An International Journal of Obstetrics & Gynaecology. 2018;125(13):1716-.
68. Dawson J, Doll H, Fitzpatrick R, Jenkinson C, Carr AJ. The routine use of patient reported outcome measures in healthcare settings. BMJ. 2010;340:c186.
69. Saczynski JS, McManus DD, Goldberg RJ. Commonly used data-collection approaches in clinical research. Am J Med. 2013;126(11):946-50.
70. Creswell JW. A Concise Introduction to Mixed Methods Research: SAGE Publications; 2014.

71. Macur M. Quality in health care: possibilities and limitations of quantitative research instruments among health care users. Quality & Quantity. 2013;47(3):1703-16.
72. Jones MM, Kamenetzky A, Manville C, Ghiga I, MacLure C, Harte E, et al. The National Institute for Health Research at 10 Years: An Impact Synthesis: 100 Impact Case Studies. Rand health quarterly. 2017;6(2):13.
73. Johnson S, Nolan F, Pilling S, Sandor A, Hoult J, McKenzie N, et al. Randomised controlled trial of acute mental health care by a crisis resolution team: the north Islington crisis study. BMJ. 2005;331(7517):599.
74. Makris M, Greaves M, Phillips WS, Kitchen S, Rosendaal FR, Preston EF. Emergency oral anticoagulant reversal: the relative efficacy of infusions of fresh frozen plasma and clotting factor concentrate on correction of the coagulopathy. Thrombosis and haemostasis. 1997;77(3):477-80.
75. Lewis S, Davies L, Jones P, Barnes T, R. M. Randomised controlled trials of conventional antipsychotic versus new atypical drugs, and new atypical drugs versus clozapine, in people with schizophrenia responding poorly to, or intolerant of, current drug treatment. Health Technology Assessment. 2006;10(17).
76. Ashton HA, Buxton MJ, Day NE, Kim LG, Marteau TM, Scott RA, et al. The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial. Lancet. 2002;360(9345):1531-9.
77. Research Excellence Framework. A major randomised trial of screening for abdominal aortic aneurysms, and initiation of a UK national screening programme-Thompson2014 August 24, 2021. Available from: https://impact.ref.ac.uk/casestudies/CaseStudy.aspx?Id=19667.
78. Research Excellence Framework. Avoiding harm and evaluating benefit: establishing and implementing an evidence-based policy for prostate cancer screening in the UK2014 August 24, 2021. Available from: https://impact.ref.ac.uk/casestudies/CaseStudy.aspx?Id=40165.
79. Research Excellence Framework. Alternatives to acute hospital admission in adult mental health2014 March 16, 2021. Available from: https://impact.ref.ac.uk/casestudies/CaseStudy.aspx?Id=36445.
80. Raftery J, Powell J. Health Technology Assessment in the UK. Lancet. 2013;382(9900):1278-85.
81. Framework RE. Case Study 4. Improving chemotherapy, radiotherapy and patient outcomes for colorectal cancer through patient-focused integrated clinical trials2014 August 24, 2021. Available from: https://impact.ref.ac.uk/casestudies/CaseStudy.aspx?Id=27417.
82. Roth JA, Etzioni R, Waters TM, Pettinger M, Rossouw JE, Anderson GL, et al. Economic return from the Women's Health Initiative estrogen plus progestin clinical trial: a modeling study. Ann Intern Med. 2014;160(9):594-602.
83. Kao LS, Aaron BC, Dellinger EP. Trials and tribulations: current challenges in conducting clinical trials. Archives of surgery (Chicago, Ill : 1960). 2003;138(1):59-62.
84. Whybrow P, Pickard R, Hrisos S, Rapley T. Equipoise across the patient population: optimising recruitment to a randomised controlled trial. Trials. 2017;18(1):140.
85. Davies G, Mills N, Holcombe C, Potter S. Perceived barriers to randomised controlled trials in breast reconstruction: obstacle to trial initiation or opportunity to resolve? A qualitative study. Trials. 2020;21(1):316.

86. Cook JA. The challenges faced in the design, conduct and analysis of surgical randomised controlled trials. Trials. 2009;10(1):9.
87. Friedberg JP, Lipsitz SR, Natarajan S. Challenges and recommendations for blinding in behavioral interventions illustrated using a case study of a behavioral intervention to lower blood pressure. Patient education and counseling. 2010;78(1):5-11.
88. Kadam RA, Borde SU, Madas SA, Salvi SS, Limaye SS. Challenges in recruitment and retention of clinical trial subjects. Perspect Clin Res. 2016;7(3):137-43.
89. McDonald AM, Knight RC, Campbell MK, Entwistle VA, Grant AM, Cook JA, et al. What influences recruitment to randomised controlled trials? A review of trials funded by two UK funding agencies. Trials. 2006;7:9.
90. Briel M, Olu KK, von Elm E, Kasenda B, Alturki R, Agarwal A, et al. A systematic review of discontinued trials suggested that most reasons for recruitment failure were preventable. J Clin Epidemiol. 2016;80:8-15.
91. Walters SJ, Bonacho Dos Anjos Henriques-Cadby I, Bortolami O, Flight L, Hind D, Jacques RM, et al. Recruitment and retention of participants in randomised controlled trials: a review of trials funded and published by the United Kingdom Health Technology Assessment Programme. BMJ Open. 2017;7(3):e015276.
92. Stensland KD, McBride RB, Latif A, Wisnivesky J, Hendricks R, Roper N, et al. Adult cancer clinical trials that fail to complete: an epidemic? J Natl Cancer Inst. 2014;106(9).
93. Schroen AT, Petroni GR, Wang H, Thielen MJ, Gray R, Benedetti J, et al. Achieving Sufficient Accrual to Address the Primary Endpoint in Phase III Clinical Trials from U.S. Cooperative Oncology Groups. Clinical Cancer Research. 2012;18(1):256.
94. Daykin A, Clement C, Gamble C, Kearney A, Blazeby J, Clarke M, et al. 'Recruitment, recruitment, recruitment' – the need for more focus on retention: a qualitative study of five trials. Trials. 2018;19(1):76.
95. Foster JM, Sawyer SM, Smith L, Reddel HK, Usherwood T. Barriers and facilitators to patient recruitment to a cluster randomized controlled trial in primary care: lessons for future trials. BMC medical research methodology. 2015;15:18-.
96. Harrop E, Kelly J, Griffiths G, Casbard A, Nelson A. Why do patients decline surgical trials? Findings from a qualitative interview study embedded in the Cancer Research UK BOLERO trial (Bladder cancer: Open versus Lapararoscopic or RObotic cystectomy). Trials. 172016.
97. Nelson A, Fenlon D, Morris J, Sampson C, Harrop E, Murray N, et al. QUALZICE: a QUALitative exploration of the experiences of the participants from the ZICE clinical trial (metastatic breast cancer) receiving intravenous or oral bisphosphonates. Trials. 2013;14:325.
98. Sekhon M, Cartwright M, Lawes-Wickwar S, McBain H, Ezra D, Newman S, et al. Does prospective acceptability of an intervention influence refusal to participate in a randomised controlled trial? An interview study. Contemporary Clinical Trials Communications. 2021;21:100698.
99. Paramasivan S, Rogers CA, Welbourn R, Byrne JP, Salter N, Mahon D, et al. Enabling recruitment success in bariatric surgical trials: pilot phase of the By-Band-Sleeve study. International Journal of Obesity (2005). 2017;41(11):1654-61.
100. Peter M, Joy B, Jacqueline F, Jennifer F-J, Alexander M. Receiving or not receiving acupuncture in a trial: The experience of participants recovering from breast cancer treatment. Complementary therapies in clinical practice. 2014;20(4):291-6.

101. Fries JF, Krishnan E. Equipoise, design bias, and randomized controlled trials: the elusive ethics of new drug development. Arthritis Res Ther. 2004;6(3):R250-R5.
102. McCarthy CM. Randomized Controlled Trials. Plastic and Reconstructive Surgery. 2011;127(4):1707-12.
103. Kahan BC, Rehal S, Cro S. Risk of selection bias in randomised trials. Trials. 2015;16:405-.
104. Donovan JL, de Salis I, Toerien M, Paramasivan S, Hamdy FC, Blazeby JM. The intellectual challenges and emotional consequences of equipoise contributed to the fragility of recruitment in six randomized controlled trials. Journal of Clinical Epidemiology. 2014;67(8):912-20.
105. Jepson M, Elliott D, Conefrey C, Wade J, Rooshenas L, Wilson C, et al. An observational study showed that explaining randomization using gambling-related metaphors and computer-agency descriptions impeded randomized clinical trial recruitment. J Clin Epidemiol. 2018;99:75-83.
106. The Health Foundation. Perspectives on Context: A selection of essays considering the role of context in successful quality improvement. London; 2014.
107. Tsukamoto K, Carroll KA, Onishi T, Matsumaru N, Brasseur D, Nakamura H. Improvement of Pediatric Drug Development: Regulatory and Practical Frameworks. Clinical Therapeutics. 2016;38(3):574-81.
108. Sherman RE, Davies KM, Robb MA, Hunter NL, Califf RM. Accelerating development of scientific evidence for medical products within the existing US regulatory framework. Nature Reviews Drug Discovery. 2017;16(5):297-8.
109. Jones PS, Jones D. New regulatory framework for cancer drug development. Drug Discovery Today. 2012;17(5):227-31.
110. Moore GF, Audrey S, Barker M, Bond L, Bonell C, Hardeman W, et al. Process evaluation of complex interventions: Medical Research Council guidance. BMJ : British Medical Journal. 2015;350.
111. Castillo G, Mack DR, Lalu MM, Singleton R, Fergusson DA, Stintzi A, et al. Factors contributing to fidelity in a pilot trial of individualized resistant starches for pediatric inflammatory bowel disease: a fidelity study protocol. Pilot and Feasibility Studies. 2021;7(1):75.
112. Peeters Grietens K, Ribera JM, Erhart A, Hoibak S, Ravinetto RM, Gryseels C, et al. Doctors and vampires in sub-Saharan Africa: ethical challenges in clinical trial research. Am J Trop Med Hyg. 2014;91(2):213-5.
113. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ. 2008;337.
114. Weinberger M, Oddone EZ, Henderson WG, Smith DM, Huey J, Giobbie-Hurder A, et al. Multisite randomized controlled trials in health services research: scientific challenges and operational issues. Medical care. 2001;39(6):627-34.
115. Oakley A, Strange V, Bonell C, Allen E, Stephenson J. Process evaluation in randomised controlled trials of complex interventions. BMJ. 2006;332(7538):413-6.
116. Shahsavari H, Matourypour P, Ghiyasvandian S, Nejad MRG. Medical Research Council framework for development and evaluation of complex interventions: A comprehensive guidance. J Educ Health Promot. 2020;9:88-.
117. Huang W, Howie J, Taylor A, Robinson N. An investigation into the effectiveness of traditional Chinese acupuncture (TCA) for chronic stress in adults: a randomised controlled pilot study. Complementary therapies in clinical practice. 2011;17(1):16-21.
118. Pope C, Mays N. Qualitative Research in Health Care: Wiley; 2013.

119. Curtis K, Fry M, Shaban RZ, Considine J. Translating research findings to clinical nursing practice. Journal of clinical nursing. 2017;26(5-6):862-72.
120. Julian DG. Translation of clinical trials into clinical practice. Journal of Internal Medicine. 2004;255(3):309-16.
121. Runciman WB, Hunt TD, Hannaford NA, Hibbert PD, Westbrook JI, Coiera EW, et al. CareTrack: assessing the appropriateness of health care delivery in Australia. Medical Journal of Australia. 2012;197(2):100-5.
122. Timmermans S, Mauck A. The Promises And Pitfalls Of Evidence-Based Medicine. Health Affairs. 2005;24(1):18-28.
123. Croft P, Malmivaara A, van Tulder M. The Pros and Cons of Evidence-Based Medicine. Spine. 2011;36(17):E1121-E5.
124. Greenhalgh T, Howick J, Maskrey N. Evidence based medicine: a movement in crisis? BMJ : British Medical Journal. 2014;348.
125. Bentley C, Cressman S, van der Hoek K, Arts K, Dancey J, Peacock S. Conducting clinical trials—costs, impacts, and the value of clinical trials networks: A scoping review. Clinical Trials. 2019;16(2):183-93.
126. Ioannidis JPA, Greenland S, Hlatky MA, Khoury MJ, Macleod MR, Moher D, et al. Increasing value and reducing waste in research design, conduct, and analysis. The Lancet. 2014;383(9912):166-75.
127. Hind D, Reeves BC, Bathers S, Bray C, Corkhill A, Hayward C, et al. Comparative costs and activity from a sample of UK clinical trials units. Trials. 2017;18(1):203.
128. Martin L, Hutchens M, Hawkins C, Radnov A. How much do clinical trials cost? Nature Reviews Drug Discovery. 2017;16(6):381-2.
129. Malterud K. The art and science of clinical knowledge: evidence beyond measures and numbers. The Lancet. 2001;358(9279):397-400.
130. Braun V, Clarke V. Successful Qualitative Research: A Practical Guide for Beginners: SAGE Publications; 2013.
131. Aspers P, Corte U. What is Qualitative in Qualitative Research. Qualitative Sociology. 2019;42(2):139-60.
132. Neale J. Research Methods for Health and Social Care: Macmillan Education UK; 2008.
133. Bourgeault I, Dingwall R, de Vries R. The SAGE Handbook of Qualitative Methods in Health Research: SAGE Publications; 2010.
134. Ritchie J, Lewis J, Lewis PSPJ, Nicholls CMN, Ormston R. Qualitative Research Practice: A Guide for Social Science Students and Researchers: SAGE Publications; 2013.
135. Creswell JW. Research Design: Qualitative, Quantitative, and Mixed Methods Approaches: SAGE Publications; 2009.
136. Mačiulienė M, Skaržauskienė A. Emergence of collective intelligence in online communities. Journal of Business Research. 2016;69(5):1718-24.
137. Silverman D. Doing Qualitative Research: A Practical Handbook: SAGE Publications; 2013.
138. Ochieng PA. An Analysis Of The Strengths And Limitation Of Qualitative And Quantitative Research Paradigms. Problems of Education in the 21st Century. 2009;13:13-8.
139. Mason P. Visual data in applied qualitative research: lessons from experience. Qualitative Research. 2005;5(3):325-46.
140. Lynn N, Lea SJ. Through the looking glass: considering the challenges visual methodologies raise for qualitative research. Qualitative Research in Psychology. 2005;2(3):213-25.

141. Nolan-Clark DJ, Neale EP, Probst YC, Charlton KE, Tapsell LC. Consumers' salient beliefs regarding dairy products in the functional food era: a qualitative study using concepts from the theory of planned behaviour. BMC Public Health. 2011;11(1):843.
142. Day M, Thatcher J. "I'm Really Embarrassed That You're Going to Read This …": Reflections on Using Diaries in Qualitative Research. Qualitative Research in Psychology. 2009;6(4):249-59.
143. Donovan JL, Rooshenas L, Jepson M, Elliott D, Wade J, Avery K, et al. Optimising recruitment and informed consent in randomised controlled trials: the development and implementation of the Quintet Recruitment Intervention (QRI). Trials. 2016;17(1):283.
144. Bouchard K, Tulloch H. Strengthening behavioral clinical trials with online qualitative research methods. Journal of health psychology. 2019:1359105319855120.
145. Braun V, Clarke V. Using thematic analysis in psychology. Qualitative Research in Psychology. 2006;3(2):77-101.
146. Gale NK, Heath G, Cameron E, Rashid S, Redwood S. Using the framework method for the analysis of qualitative data in multi-disciplinary health research. BMC Medical Research Methodology. 2013;13(1):117.
147. Riessman CK. Narrative Analysis: SAGE Publications; 1993.
148. Glaser B, Strauss A. The discovery of grounded theory: strategies for qualitative research. New York: Aldine de Gruyter; 1967.
149. Miles MB, Huberman AM. Qualitative Data Analysis: An Expanded Sourcebook: SAGE Publications; 1994.
150. Anderson C. Presenting and evaluating qualitative research. Am J Pharm Educ. 2010;74(8):141-.
151. Popay J, Williams G. Qualitative research and evidence-based healthcare. Journal of the Royal Society of Medicine. 1998;91(Suppl 35):32-7.
152. Thompson WT, Cupples ME, Sibbett CH, Skan DI, Bradley T. Challenge of culture, conscience, and contract to general practitioners' care of their own health: qualitative study. Bmj. 2001;323(7315):728-31.
153. Dawoodbhoy FM, Delaney J, Cecula P, Yu J, Peacock I, Tan J, et al. AI in patient flow: applications of artificial intelligence to improve patient flow in NHS acute mental health inpatient units. Heliyon. 2021;7(5):e06993-e.
154. Anderson K, Foster M, Freeman C, Luetsch K, Scott I. Negotiating "Unmeasurable Harm and Benefit": Perspectives of General Practitioners and Consultant Pharmacists on Deprescribing in the Primary Care Setting. Qualitative health research. 2017;27(13):1936-47.
155. Murphy DJ, Pope C, Frost J, Liebling RE. Women's views on the impact of operative delivery in the second stage of labour: qualitative interview study. Bmj. 2003;327(7424):1132.
156. Barry CA, Bradley CP, Britten N, Stevenson FA, Barber N. Patients' unvoiced agendas in general practice consultations: qualitative study. Bmj. 2000;320(7244):1246-50.
157. Skirbekk H, Nortvedt P. Making a difference: a qualitative study on care and priority setting in health care. Health Care Anal. 2011;19(1):77-88.
158. Tarzia L, Wellington M, Marino J, Hegarty K. "A Huge, Hidden Problem": Australian Health Practitioners' Views and Understandings of Reproductive Coercion. Qualitative health research. 2018;29(10):1395-407.

159. Kang-Yi CD, Grinker RR, Beidas R, Agha A, Russell R, Shah SB, et al. Influence of Community-Level Cultural Beliefs about Autism on Families' and Professionals' Care for Children. Transcult Psychiatry. 2018;55(5):623-47.
160. Stewart DW, Depue J, Rosen RK, Bereolos N, Goldstein MG, Tuitele J, et al. Medication-taking beliefs and diabetes in American Samoa: a qualitative inquiry. Translational behavioral medicine. 2013;3(1):30-8.
161. Johns G. The Essential Impact of Context on Organizational Behavior. The Academy of Management Review. 2006;31(2):386-408.
162. Fahie D. Doing Sensitive Research Sensitively: Ethical and Methodological Issues in Researching Workplace Bullying. International Journal of Qualitative Methods. 2014;13(1):19-36.
163. JMMR. The New Era of Mixed Methods. Journal of Mixed Methods Research. 2007;1(1):3-.
164. Gibson G, Timlin A, Curran S, Wattis J. The scope for qualitative methods in research and clinical trials in dementia. Age Ageing. 2004;33(4):422-6.
165. Maher L, Neale J. Adding quality to quantity in randomized controlled trials of addiction prevention and treatment: a new framework to facilitate the integration of qualitative research. Addiction. 2019;114(12):2257-66.
166. Johnson RB, Onwuegbuzie AJ, Turner LA. Toward a Definition of Mixed Methods Research. Journal of Mixed Methods Research. 2007;1(2):112-33.
167. Sandelowski M. The problem of rigor in qualitative research. ANS Advances in nursing science. 1986;8(3):27-37.
168. Cypress BS. Rigor or Reliability and Validity in Qualitative Research: Perspectives, Strategies, Reconceptualization, and Recommendations. Dimensions of Critical Care Nursing. 2017;36(4).
169. Greene JC, Caracelli VJ, Graham WF. Toward a Conceptual Framework for Mixed-Method Evaluation Designs. Educational Evaluation and Policy Analysis. 1989;11(3):255-74.
170. Bryman A. Barriers to Integrating Quantitative and Qualitative Research. Journal of Mixed Methods Research. 2007;1(1):8-22.
171. Skivington K, Matthews L, Simpson SA, Craig P, Baird J, Blazeby JM, et al. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. BMJ. 2021;374:n2061.
172. Tonkin-Crine S, Anthierens S, Hood K, Yardley L, Cals JWL, Francis NA, et al. Discrepancies between qualitative and quantitative evaluation of randomised controlled trial results: achieving clarity through mixed methods triangulation. Implementation Science. 2016;11(1):66.
173. Barbour RS. The Case for Combining Qualitative and Quantitative Approaches in Health Services Research. Journal of Health Services Research & Policy. 1999;4(1):39-43.
174. Tashakkori A, Teddlie C. SAGE Handbook of Mixed Methods in Social and Behavioral Research. Thousand Oaks, California2010. Available from: https://methods.sagepub.com/book/sage-handbook-of-mixed-methods-social-behavioral-research-2e.
175. Akard TF, Gilmer MJ, Friedman DL, Given B, Hendricks-Ferguson VL, Hinds PS. From qualitative work to intervention development in pediatric oncology palliative care research. J Pediatr Oncol Nurs. 2013;30(3):153-60.

176. Husbands S, Caskey F, Winton H, Gibson A, Donovan JL, Rooshenas L. Pre-trial qualitative work with health care professionals to refine the design and delivery of a randomised controlled trial on kidney care. Trials. 2019;20(1):224.
177. Sheridan R, Martin-Kerry J, Hudson J, Parker A, Bower P, Knapp P. Why do patients take part in research? An overview of systematic reviews of psychosocial barriers and facilitators. Trials. 2020;21(1):259.
178. The Look AHEAD Research Group. The development and description of the comparison group in the Look AHEAD trial. Clin Trials. 82011. p. 320-9.
179. O'Cathain A, Thomas K, Drabble S, Rudolph A, Hewison J. What can qualitative research do for randomised controlled trials? A systematic mapping review. Trials. 2013;14(1):O52.
180. Sekhon M, Cartwright M, Francis JJ. Acceptability of healthcare interventions: an overview of reviews and development of a theoretical framework. BMC Health Services Research. 2017;17(1):88.
181. Joseph PD, Caldwell PHY, Tong A, Hanson CS, Craig JC. Stakeholder Views of Clinical Trials in Low- and Middle-Income Countries: A Systematic Review. Pediatrics. 2016;137(2):e20152800.
182. Clement C, Ridd MJ, Roberts K, Santer M, Boyle R, Muller I, et al. Parents and GPs' understandings and beliefs about food allergy testing in children with eczema: qualitative interview study within the Trial of Eczema allergy Screening Tests (TEST) feasibility trial. BMJ Open. 2020;10(11):e041229.
183. Toye F, Williamson E, Williams MA, Fairbank J, Lamb SE. What Value Can Qualitative Research Add to Quantitative Research Design? An Example From an Adolescent Idiopathic Scoliosis Trial Feasibility Study. Qualitative health research. 2016;26(13):1838-50.
184. Donovan J, Mills N, Smith M, Brindle L, Jacoby A, Peters T, et al. Quality improvement report: Improving design and conduct of randomised trials by embedding them in qualitative research: ProtecT (prostate testing for cancer and treatment) study. Commentary: presenting unbiased information to patients can be difficult. Bmj. 2002;325(7367):766-70.
185. Husbands S, Elliott D, Davis TRC, Blazeby JM, Harrison EF, Montgomery AA, et al. Optimising recruitment to the HAND-1 RCT feasibility study: integration of the QuinteT Recruitment Intervention (QRI). Pilot and Feasibility Studies. 2020;6(1):173.
186. David P-M, Mathiot B, Thiongane O, Graham JE. Under consent: participation of people with HIV in an Ebola vaccine trial in Canada. BMC Medical Ethics. 2021;22(1):42.
187. Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. BMJ. 2016;355:i5239.
188. National Institute for Health Research. NIHR Research for Patient Benefit (RfPB) Programme Guidance on Applying for Feasibility Studies 2017 [Available from: https://www.nihr.ac.uk/documents/nihr-research-for-patient-benefit-rfpb-programme-guidance-on-applying-for-feasibility-studies/20474#Guidance_on_applying_to_RfPB_for_a_feasibility_or_pilot_study.
189. National Institute for Health Research. Supporting Information for Applicants Applying to the HTA Programme 2017 [Available from: https://www.nihr.ac.uk/documents/hta-supporting-information/11929#Feasibility_and_Pilot_studies.

190. Baldeh T, MacDonald T, Kosa SD, Lawson DO, Stalteri R, Olaiya OR, et al. More pilot trials could plan to use qualitative data: a meta-epidemiological study. Pilot and Feasibility Studies. 2020;6(1):164.
191. Deja E, Peters MJ, Khan I, Mouncey PR, Agbeko R, Fenn B, et al. Establishing and augmenting views on the acceptability of a paediatric critical care randomised controlled trial (the FEVER trial): a mixed methods study. BMJ Open. 2021;11(3):e041952.
192. Horwood J, Clement C, Roberts K, Waldron C-A, Irving WL, Macleod J, et al. Increasing uptake of hepatitis C virus infection case-finding, testing, and treatment in primary care: evaluation of the HepCATT (Hepatitis C Assessment Through to Treatment) trial. British Journal of General Practice. 2020;70(697):e581.
193. Varse F, Janani L, Moradi Y, Solaymani-Dodaran M, Baradaran HR, Rimaz S. Challenges in the design, conduct, analysis, and reporting in randomized clinical trial studies: A systematic review. Med J Islam Repub Iran. 2019;33:37-.
194. Elliott D, Husbands S, Hamdy FC, Holmberg L, Donovan JL. Understanding and Improving Recruitment to Randomised Controlled Trials: Qualitative Research Approaches. European Urology. 2017;72(5):789-98.
195. Luker JA, Craig LE, Bennett L, Ellery F, Langhorne P, Wu O, et al. Implementing a complex rehabilitation intervention in a stroke trial: a qualitative process evaluation of AVERT. BMC Medical Research Methodology. 2016;16(1):52.
196. Marzan-Rodriguez M, Varas-Diaz N, Neilands T. Qualitative Contributions to a Randomized Controlled Trial Addressing HIV/AIDS-Stigma in Medical Students. Qualitative report (Online). 2015;20(12):2012-24.
197. Bradt J, Potvin N, Kesslick A, Shim M, Radl D, Schriver E, et al. The impact of music therapy versus music medicine on psychological outcomes and pain in cancer patients: a mixed methods study. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer. 2015;23(5):1261-71.
198. Downs M. The Emergence of the Person in Dementia Research. Ageing and Society. 1997;17(5):597-607.
199. Coast J. Qualitative Methods for Health Economics: Rowman & Littlefield International; 2017.
200. Williams JG, Alam MF, Alrubaiy L, Clement C, Cohen D, Grey M, et al. Comparison Of iNfliximab and ciclosporin in Steroid Resistant Ulcerative Colitis: pragmatic randomised Trial and economic evaluation (CONSTRUCT). Health Technol Assess. 2016;20(44).
201. Clement C, Rapport F, Seagrove A, Alrubaiy L, Williams J. Healthcare professionals' views of the use and administration of two salvage therapy drugs for acute ulcerative colitis: a nested qualitative study within the CONSTRUCT trial. BMJ Open. 2017;7(2):e014512.
202. Cole S, Seale C, Griffiths C. 'The blue one takes a battering' why do young adults with asthma overuse bronchodilator inhalers? A qualitative study. BMJ Open. 2013;3(2):e002247.
203. Berendsen BAJ, Kremers SPJ, Savelberg HHCM, Schaper NC, Hendriks MRC. The implementation and sustainability of a combined lifestyle intervention in primary care: mixed method process evaluation. BMC Family Practice. 2015;16(1):37.
204. Houston L, Yu P, Martin A, Probst Y. Clinical researchers' lived experiences with data quality monitoring in clinical trials: a qualitative study. BMC Medical Research Methodology. 2021;21(1):187.

205. International Conference on Harmonisation (ICH) of technical requirements for registration of pharmaceuticals for human use 2016. E6(R2) Good Clinical Practice 2016 [Available from: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM464506.pdf.
206. Lewis NV, Dowrick A, Sohal A, Feder G, Griffiths C. Implementation of the Identification and Referral to Improve Safety programme for patients with experience of domestic violence and abuse: A theory-based mixed-method process evaluation. Health & Social Care in the Community. 2019;27(4):e298-e312.
207. Cox LB, Antony A, Karen. "Did the trial kill the intervention?" experiences from the development, implementation and evaluation of a complex intervention. BMC Medical Research Methodology. 2011;11(1):24.
208. Bair MJ, Matthias MS, Nyland KA, Huffman MA, Stubbs DL, Kroenke K, et al. Barriers and facilitators to chronic pain self-management: a qualitative study of primary care patients with comorbid musculoskeletal pain and depression. Pain medicine (Malden, Mass). 2009;10(7):1280-90.
209. National Research Council Panel on Race E, Health in Later L. The National Academies Collection: Reports funded by National Institutes of Health. In: Anderson NB, Bulatao RA, Cohen B, editors. Critical Perspectives on Racial and Ethnic Differences in Health in Late Life. Washington (DC): National Academies Press (US)

National Academy of Sciences.; 2004.
210. U.S Food and Drug Administration. Food and Drug Administration Modernization Act of 1997. 1997.
211. Dyer O. GlaxoSmithKline faces US lawsuit over concealment of trial results. BMJ : British Medical Journal. 2004;328(7453):1395-.
212. Organisation WH. Ministerial Summit on Health Research. 2004.
213. Smith PG, Ross DA, Morrow RH. Field Trials of Health Interventions: A Toolbox: Oxford University Press; 2015.
214. Health NIf. ClinicalTrials.gov Background. 2018.
215. Ltd BC. ISRCTN About. 2018.
216. Organisation WH. International Clinical Trials Registry Platform (ICTRP). 2018.
217. Group" WB. World Bank Countries and Income 2018 [Available from: http://data.worldbank.org/country.
218. McCall B. UK implements national programme for surgical trials. The Lancet.382(9898):1083-4.
219. Freedman B. Equipoise and the ethics of clinical research. The New England journal of medicine. 1987;317(3):141-5.
220. Gagliardi AR, Ducey A, Lehoux P, Turgeon T, Ross S, Trbovich P, et al. Factors influencing the reporting of adverse medical device events: qualitative interviews with physicians about higher risk implantable devices. BMJ Quality & Safety. 2017.
221. Neugebauer EAM, Rath A, Antoine S-L, Eikermann M, Seidel D, Koenen C, et al. Specific barriers to the conduct of randomised clinical trials on medical devices. Trials. 2017;18(1):427.
222. Gargon E, Williamson PR, Young B. Improving core outcome set development: qualitative interviews with developers provided pointers to inform guidance. Journal of Clinical Epidemiology. 2017;86:140-52.
223. Drabble SJ, O'Cathain A, Thomas KJ, Rudolph A, Hewison J. Describing qualitative research undertaken with randomised controlled trials in grant proposals: a documentary analysis. BMC Medical Research Methodology. 2014;14(1):24.

224. University of Sheffiled. Maximising the value of combining qualitative research and

randomised controlled trials conference. 2012.
225. Vischer N, Pfeiffer C, Limacher M, Burri C. "You can save time if…"—A qualitative study on internal factors slowing down clinical trials in Sub-Saharan Africa. PLOS ONE. 2017;12(3):e0173796.
226. Toto N, Douglas E, Gmeiner M, Barrett LK, Lindblad R, Makhaza L, et al. Conducting clinical trials in sub-Saharan Africa: challenges and lessons learned from the Malawi Cryptosporidium study. Trials. 2020;21(1):680.
227. Grover S, Xu M, Jhingran A, Mahantshetty U, Chuang L, Small W, Jr., et al. Clinical trials in low and middle-income countries - Successes and challenges. Gynecol Oncol Rep. 2016;19:5-9.
228. Alemayehu C, Mitchell G, Nikles J. Barriers for conducting clinical trials in developing countries- a systematic review. International Journal for Equity in Health. 2018;17(1):37.
229. Franzen SRP, Chandler C, Enquselassie F, Siribaddana S, Atashili J, Angus B, et al. Understanding the investigators: a qualitative study investigating the barriers and enablers to the implementation of local investigator-initiated clinical trials in Ethiopia. BMJ Open. 2013;3(11).
230. Camlin CS, Ssemmondo E, Chamie G, El Ayadi AM, Kwarisiima D, Sang N, et al. Men "missing" from population-based HIV testing: insights from qualitative research. AIDS Care. 2016;28 Suppl 3:67-73.
231. Palinkas LA. Qualitative and mixed methods in mental health services and implementation research. J Clin Child Adolesc Psychol. 2014;43(6):851-61.
232. Davis K, Minckas N, Bond V, Clark CJ, Colbourn T, Drabble SJ, et al. Beyond interviews and focus groups: a framework for integrating innovative qualitative methods into randomised controlled trials of complex public health interventions. Trials. 2019;20(1):329.
233. Gask L, Bower P, Lovell K, Escott D, Archer J, Gilbody S, et al. What work has to be done to implement collaborative care for depression? Process evaluation of a trial utilizing the Normalization Process Model. Implementation Science. 2010;5(1):15.
234. May C, Finch T, Mair F, Ballini L, Dowrick C, Eccles M, et al. Understanding the implementation of complex interventions in health care: the normalization process model. BMC Health Services Research. 2007;7(1):148.
235. Curran JA, Brehaut J, Patey AM, Osmond M, Stiell I, Grimshaw JM. Understanding the Canadian adult CT head rule trial: use of the theoretical domains framework for process evaluation. Implementation science : IS. 2013;8:25-.
236. Davis R, Campbell R, Hildon Z, Hobbs L, Michie S. Theories of behaviour and behaviour change across the social and behavioural sciences: a scoping review. Health Psychol Rev. 2015;9(3):323-44.
237. Davidoff F, Dixon-Woods M, Leviton L, Michie S. Demystifying theory and its use in improvement. BMJ Quality & Safety. 2015;24(3):228.
238. Amico KR, Mugavero M, Krousel-Wood MA, Bosworth HB, Merlin JS. Advantages to Using Social-Behavioral Models of Medication Adherence in Research and Practice. J Gen Intern Med. 2018;33(2):207-15.
239. Hardeman W, Sutton S, Griffin S, Johnston M, White A, Wareham NJ, et al. A causal modelling approach to the development of theory-based behaviour change programmes for trial evaluation. Health Education Research. 2005;20(6):676-87.

240. Giné-Garriga M, Coll-Planas L, Guerra M, Domingo À, Roqué M, Caserotti P, et al. The SITLESS project: exercise referral schemes enhanced by self-management strategies to battle sedentary behaviour in older adults: study protocol for a randomised controlled trial. Trials. 2017;18(1):221.
241. Backman R, Foy R, Michael BD, Defres S, Kneen R, Solomon T. The development of an intervention to promote adherence to national guidelines for suspected viral encephalitis. Implementation Science. 2015;10(1):37.
242. Colquhoun HL, Brehaut JC, Sales A, Ivers N, Grimshaw J, Michie S, et al. A systematic review of the use of theory in randomized controlled trials of audit and feedback. Implementation Science. 2013;8(1):66.
243. Adom D, Hussein E, Agyem JA. Theoretical and Conceptual Framework: Mandatory Ingredients of a Quality Research. International journal of scientific research. 2018;7.
244. Buckingham S, Kendall M, Ferguson S, MacNee W, Sheikh A, White P, et al. HELPing older people with very severe chronic obstructive pulmonary disease (HELP-COPD): mixed-method feasibility pilot randomised controlled trial of a novel intervention. npj Primary Care Respiratory Medicine. 2015;25(1):15020.
245. Morrow GR, Hickok JT, Burish TG. Behavioral aspects of clinical trials. An integrated framework from behavior theory. Cancer. 1994;74(9 Suppl):2676-82.
246. Gruba M. Applying Behavior Change Strategies to Patient Engagement in Clinical Research. Clinical Researcher. 2020;34(4).
247. Murray E, Treweek S, Pope C, MacFarlane A, Ballini L, Dowrick C, et al. Normalisation process theory: a framework for developing, evaluating and implementing complex interventions. BMC Medicine. 2010;8(1):63.
248. May CR, Finch T, Ballini L, MacFarlane A, Mair F, Murray E, et al. Evaluating complex interventions and health technologies using normalization process theory: development of a simplified approach and web-enabled toolkit. BMC Health Services Research. 2011;11(1):245.
249. Green HE. Use of theoretical and conceptual frameworks in qualitative research. Nurse Res. 2014;21(6):34-8.
250. Paré G, Trudel M-C, Jaana M, Kitsiou S. Synthesizing information systems knowledge: A typology of literature reviews. Information & Management. 2015;52(2):183-99.
251. Grant MJ, Booth A. A typology of reviews: an analysis of 14 review types and associated methodologies. Health Information & Libraries Journal. 2009;26(2):91-108.
252. Kirkevold M. Integrative nursing research--an important strategy to further the development of nursing science and nursing practice. Journal of advanced nursing. 1997;25(5):977-84.
253. de Klerk W, Pretorius J. Guideline for conducting critical reviews in psychology research. Journal of Psychology in Africa. 2019;29(6):645-9.
254. Mannell J, Davis K. Evaluating Complex Health Interventions With Randomized Controlled Trials: How Do We Improve the Use of Qualitative Methods? Qualitative health research. 2019;29(5):623-31.
255. Hennessy M, Hunter A, Healy P, Galvin S, Houghton C. Improving trial recruitment processes: how qualitative methodologies can be used to address the top 10 research priorities identified within the PRioRiTy study. Trials. 2018;19(1):584.
256. Borreani C, Miccinesi G, Brunelli C, Lina M. An increasing number of qualitative research papers in oncology and palliative care: does it mean a thorough development of the methodology of research? Health and Quality of Life Outcomes. 2004;2(1):7.

257. Tcheremissine OV, Rossman WE, Castro MA, Gardner DR. Conducting clinical research in community mental health settings: Opportunities and challenges. World J Psychiatry. 2014;4(3):49-55.
258. Patel R, Oduola S, Callard F, Wykes T, Broadbent M, Stewart R, et al. What proportion of patients with psychosis is willing to take part in research? A mental health electronic case register analysis. BMJ Open. 2017;7(3):e013113.
259. Ajithkumar TV, Gilbert DC. Modern Challenges of Cancer Clinical Trials. Clinical Oncology. 2017;29(12):767-9.
260. Lean M, Leavey G, Killaspy H, Green N, Harrison I, Cook S, et al. Barriers to the sustainability of an intervention designed to improve patient engagement within NHS mental health rehabilitation units: a qualitative study nested within a randomised controlled trial. BMC Psychiatry. 2015;15(1):209.
261. Peters S. Qualitative Research Methods in Mental Health. Evidence Based Mental Health. 2010;13(2):35.
262. Goswami ND, Pfeiffer CD, Horton JR, Chiswell K, Tasneem A, Tsalik EL. The State of Infectious Diseases Clinical Trials: A Systematic Review of ClinicalTrials.gov. PLOS ONE. 2013;8(10):e77086.
263. Viergever RF, Terry RF, Karam G. Use of data from registered clinical trials to identify gaps in health research and development. Bull World Health Organ. 2013;91(6):416-25C.
264. Foy R, Ovretveit J, Shekelle PG, Pronovost PJ, Taylor SL, Dy S, et al. The role of theory in research to develop and evaluate the implementation of patient safety practices. BMJ Quality & Safety. 2011;20(5):453.
265. Evans BC, Coon DW, Ume E. Use of Theoretical Frameworks as a Pragmatic Guide for Mixed Methods Studies: A Methodological Necessity? Journal of mixed methods research. 2011;5(4):276-92.
266. Ivers N, Jamtvedt G, Flottorp S, Young JM, Odgaard-Jensen J, French SD, et al. Audit and feedback: effects on professional practice and healthcare outcomes. The Cochrane database of systematic reviews. 2012(6):Cd000259.
267. Fain JA. Reading, Understanding, and Applying Nursing Research. Second ed: F.A. Davis; 2004.
268. Atkins L, Francis J, Islam R, O'Connor D, Patey A, Ivers N, et al. A guide to using the Theoretical Domains Framework of behaviour change to investigate implementation problems. Implementation Science. 2017;12(1):77.
269. May CR, Mair FS, Dowrick CF, Finch TL. Process evaluation for complex interventions in primary care: understanding trials using the normalization process model. BMC Family Practice. 2007;8(1):42.
270. May C, Harrison R, Finch T, MacFarlane A, Mair F, Wallace P, et al. Understanding the normalization of telemedicine services through qualitative evaluation. J Am Med Inform Assoc. 2003;10(6):596-604.
271. May C, Rapley T, Mair FS, Treweek S, Murray E, Ballini L, et al. Normalization Process Theory On-line Users' Manual, Toolkit and NoMAD instrument.2015; (13th June 2021).
272. RE-AIM: Improving Public Health Relevance and Population Health Impact 2021 [Available from: https://www.re-aim.org/.
273. Herlihy JM, Shaikh A, Mazimba A, Gagne N, Grogan C, Mpamba C, et al. Local perceptions, cultural beliefs and practices that shape umbilical cord care: a qualitative study in Southern Province, Zambia. PLoS One. 2013;8(11):e79191.

274. Olstad DL, Ball K, Abbott G, McNaughton SA, Le HND, Ni Mhurchu C, et al. A process evaluation of the Supermarket Healthy Eating for Life (SHELf) randomized controlled trial. International Journal of Behavioral Nutrition and Physical Activity. 2016;13(1):27.
275. Liu H, Lindley R, Alim M, Felix C, Gandhi DBC, Verma SJ, et al. Protocol for process evaluation of a randomised controlled trial of family-led rehabilitation post stroke (ATTEND) in India. BMJ Open. 2016;6(9):e012027.
276. Petticrew M, Egan M, Thomson H, Hamilton V, Kunkler R, Roberts H. Publication bias in qualitative research: what becomes of qualitative research presented at conferences? J Epidemiol Community Health. 2008;62(6):552-4.
277. Toews I, Glenton C, Lewin S, Berg RC, Noyes J, Booth A, et al. Extent, Awareness and Perception of Dissemination Bias in Qualitative Research: An Explorative Survey. PLOS ONE. 2016;11(8):e0159290.
278. Russell J, Berney L, Stansfeld S, Lanz D, Kerry S, Chandola T, et al. The role of qualitative research in adding value to a randomised controlled trial: lessons from a pilot study of a guided e-learning intervention for managers to improve employee wellbeing and reduce sickness absence. Trials. 2016;17(1):396.
279. Bartlam B, Waterfield J, Bishop A, Holden MA, Barlas P, Ismail KM, et al. The Role of Qualitative Research in Clinical Trial Development: The EASE Back Study. Journal of Mixed Methods Research. 2016;12(3):325-43.
280. O'Cathain A, Murphy E, Nicholl J. The quality of mixed methods studies in health services research. J Health Serv Res Policy. 2008;13(2):92-8.
281. Popay J, Roberts H, Sowden A, Petticrew M, Arai L, Rodgers M, et al. Guidance on the conduct of narrative synthesis in systemtic reviews. A product from the ESRC Methods Programme. Lancaster: Institute of Health Research; 2006.
282. Pope C, Mays N, Popay J. Synthesising Qualitative And Quantitative Health Evidence: A Guide To Methods: A Guide to Methods: McGraw-Hill Education; 2007.
283. Braun V, Clarke V. Thematic Analysis: A Practical Guide: SAGE Publications, Limited; 2021.
284. QSR International. What is NVivo? | NVivo 2019 [Available from: https://www.qsrinternational.com/nvivo/what-is-nvivo.
285. Catallo C, Jack SM, Ciliska D, MacMillan HL. Mixing a Grounded Theory Approach with a Randomized Controlled Trial Related to Intimate Partner Violence: What Challenges Arise for Mixed Methods Research? Nursing Research and Practice. 2013;2013:12.
286. Milne H, van der Pol M, McCloughan L, Hanley J, Mead G, Starr J, et al. The use of global positional satellite location in dementia: a feasibility study for a randomised controlled trial. BMC Psychiatry. 2014;14(1):160.
287. Midgley N, Ansaldo F, Target M. The meaningful assessment of therapy outcomes: Incorporating a qualitative study into a randomized controlled trial evaluating the treatment of adolescent depression. Psychotherapy (Chicago, Ill). 2014;51(1):128-37.
288. Presseau J, Hawthorne G, Sniehotta FF, Steen N, Francis JJ, Johnston M, et al. Improving Diabetes care through Examining, Advising, and prescribing (IDEA): protocol for a theory-based cluster randomised controlled trial of a multiple behaviour change intervention aimed at primary healthcare professionals. Implementation science : IS. 2014;9:61.

289. Toye F, Williamson E, Williams MA, Fairbank J, Lamb SE. What Value Can Qualitative Research Add to Quantitative Research Design? An Example From an Adolescent Idiopathic Scoliosis Trial Feasibility Study. Qualitative health research. 2016.
290. Wright P. Maximising Recruitment to Randomised Controlled Trials: The Role of Qualitative Research to Inform Recruitment Challenges. Eur Urol. 2017;72(5):799-800.
291. Rooshenas L, Paramasivan S, Jepson M, Donovan JL. Intensive Triangulation of Qualitative Research and Quantitative Data to Improve Recruitment to Randomized Trials: The QuinteT Approach. Qualitative health research. 2019;29(5):672-9.
292. Simoni JM, Beima-Sofie K, Amico KR, Hosek SG, Johnson MO, Mensch BS. Debrief Reports to Expedite the Impact of Qualitative Research: Do They Accurately Capture Data from In-depth Interviews? AIDS and behavior. 2019;23(8):2185-9.
293. Yin RK. Case Study Research: Design and Methods: SAGE Publications; 2009.
294. Crowe S, Cresswell K, Robertson A, Huby G, Avery A, Sheikh A. The case study approach. BMC Medical Research Methodology. 2011;11(1):100.
295. Yin RK. Case Study Research: Design and Methods: SAGE Publications; 2013.
296. Malterud K, Siersma VD, Guassora AD. Sample Size in Qualitative Interview Studies: Guided by Information Power. Qualitative health research. 2015.
297. Trochim WMK. Outcome pattern matching and program theory. Evaluation and Program Planning. 1989;12(4):355-66.
298. Attard Cortis P, Muir F. Twelve tips for using Pattern Matching in data analysis for qualitative medical education research. Medical Teacher. 2021:1-5.
299. Almutairi AF, McCarthy A, Gardner GE. Understanding Cultural Competence in a Multicultural Nursing Workforce:Registered Nurses' Experience in Saudi Arabia. Journal of Transcultural Nursing. 2015;26(1):16-23.
300. Pearse N. An Illustration of a Deductive Pattern Matching Procedure in Qualitative Leadership Research. Electron J Bus Res Methods. 2019;17(3):143-64.
301. Vogl S. Telephone Versus Face-to-Face Interviews:Mode Effect on Semistructured Interviews with Children. Sociological Methodology. 2013;43(1):133-77.
302. Sturges JE, Hanrahan KJ. Comparing Telephone and Face-to-Face Qualitative Interviewing: a Research Note. Qualitative Research. 2004;4(1):107-18.
303. Opdenakker R. Advantages and Disadvantages of Four Interview Techniques in Qualitative Research. 2006. 2006;7(4).
304. Gillham B. Research Interviewing: The Range of Techniques: Open University Press; 2005.
305. Fuentes Camps I, Rodríguez A, Agustí A. Non-commercial vs. commercial clinical trials: a retrospective study of the applications submitted to a research ethics committee. British Journal of Clinical Pharmacology. 2018;84(6):1384-8.
306. Remuzzi G, Schieppati A, Boissel JP, Garattini S, Horton R. Independent clinical research in Europe. Lancet. 2004;364(9446):1723-6.
307. Institute of Medicine Forum on Drug Discovery D, Translation. The National Academies Collection: Reports funded by National Institutes of Health. Transforming Clinical Research in the United States: Challenges and Opportunities: Workshop Summary. Washington (DC): National Academies Press (US)

National Academy of Sciences.; 2010.
308. Allen D. Fieldwork and Participant Observation. 2010 2019/08/30. In: The SAGE Handbook of Qualitative Methods in Health Research [Internet]. London: SAGE Publications Ltd. Available from: http://sk.sagepub.com/reference/sage-hdbk-qualitative-methods-in-health-research.

309. Breen LJ. The researcher 'in the middle': Negotiating the insider/outsider dichotomy. The Australian Community Psychologist. 2007;19(1):163-74.
310. Smyth A, Holian R. Credibility issues in research from within organisations. In: Sikes P, Potts A, editors. Researching education from the inside. New York: Taylor & Francis; 2008. p. 33-47.
311. Dwyer SC, Buckle JL. The Space Between: On Being an Insider-Outsider in Qualitative Research. International Journal of Qualitative Methods. 2009;8(1):54-63.
312. Kuper A, Reeves S, Levinson W. An introduction to reading and appraising qualitative research. Bmj. 2008;337:a288.
313. Albert M, Laberge S, Hodges BD, Regehr G, Lingard L. Biomedical scientists' perception of the social sciences in health research. Social Science & Medicine. 2008;66(12):2520-31.
314. Research Excellence Framework. Research Excellence Framework 2019 [Available from: https://www.ref.ac.uk/.
315. Research Excellence Framework. Guide for research users 2022 [Available from: https://www.ref.ac.uk/about/guide-for-research-users/.
316. Greenhalgh T, Annandale E, Ashcroft R, Barlow J, Black N, Bleakley A, et al. An open letter to The BMJ editors on qualitative research. BMJ. 2016;352:i563.
317. Duracinsky M, Lalanne C, Rous L, Dara AF, Baudoin L, Pellet C, et al. Barriers to publishing in biomedical journals perceived by a sample of French researchers: results of the DIAzePAM study. BMC Medical Research Methodology. 2017;17(1):96.
318. Clark AM, Thompson DR. Five Tips for Writing Qualitative Research in High-Impact Journals: Moving From #BMJnoQual. International Journal of Qualitative Methods. 2016;15(1):1609406916641250.
319. The Academy of Medical Sciences. From innovation to implementation: team science two years on. 2019.
320. Shuval K, Harker K, Roudsari B, Groce NE, Mills B, Siddiqi Z, et al. Is Qualitative Research Second Class Science? A Quantitative Longitudinal Examination of Qualitative Research in Medical Journals. PLOS ONE. 2011;6(2):e16937.
321. Østengaard L, Lundh A, Tjørnhøj-Thomsen T, Abdi S, Gelle MHA, Stewart LA, et al. Influence and management of conflicts of interest in randomised clinical trials: qualitative interview study. BMJ. 2020;371:m3764.
322. Parker L, Fabbri A, Grundy Q, Mintzes B, Bero L. "Asset exchange"—interactions between patient groups and pharmaceutical industry: Australian qualitative study. BMJ. 2019;367:l6694.
323. Loder E. The BMJ editors respond. BMJ. 2016.
324. Khankeh H, Ranjbar M, Khorasani-Zavareh D, Zargham-Boroujeni A, Johansson E. Challenges in conducting qualitative research in health: A conceptual paper. Iran J Nurs Midwifery Res. 2015;20(6):635-41.
325. Carey MA, Swanson J. Funding for Qualitative Research. Qualitative health research. 2003;13(6):852-6.
326. Galdas P. Revisiting Bias in Qualitative Research: Reflections on Its Relationship With Funding and Impact. International Journal of Qualitative Methods. 2017;16(1):1609406917748992.
327. National Institute for Health Research. Our funding programmes 2022 [Available from: https://www.nihr.ac.uk/researchers/apply-for-funding/how-to-apply-for-project-funding/our-funding-programmes.htm.
328. National Institute for Health Research. Webinar: Discover more about the NIHR Methodology Incubator qualitative workstream 2022 [Available from:

https://www.nihr.ac.uk/events/webinar-discover-more-about-the-nihr-methodology-incubator-qualitative-workstream/29698.
329. Curry L, Nunez-Smith M. Mixed Methods in Health Sciences Research: A Practical Primer. Thousand Oaks, California2015. Available from: https://methods.sagepub.com/book/mixed-methods-in-health-sciences-research-a-practical-primer.
330. O'Cathain A, Murphy E, Nicholl J. The Quality of Mixed Methods Studies in Health Services Research. Journal of Health Services Research & Policy. 2008;13(2):92-8.
331. Academy of Medical Sciences. Improving recognition of team science contributions in biomedical research careers. 2016.
332. NIH Office of Behavioural and Social Sciences. Best Practices for Mixed Methods Research in the Health Sciences. 2nd ed. Bethesda: National Institute of Health; 2018.
333. Bryman A. Integrating quantitative and qualitative research: how is it done? Qualitative Research. 2006;6(1):97-113.
334. Vanover C, Mihas P, Saldana J. Analyzing and Interpreting Qualitative Research: After the Interview: SAGE Publications; 2021.
335. Guest G, MacQueen KM, Namey EE. Applied Thematic Analysis: SAGE Publications; 2012.
336. Halcomb EJ. Mixed methods research: The issues beyond combining methods. Journal of advanced nursing. 2019;75(3):499-501.
337. Moffatt S, White M, Mackintosh J, Howel D. Using quantitative and qualitative data in health services research – what happens when mixed method findings conflict? BMC Health Services Research. 2006;6(1):28.
338. Herman AN, Whitaker RC. Reconciling mixed messages from mixed methods: A randomized trial of a professional development course to increase trauma-informed care. Child abuse & neglect. 2020;101:104349.
339. Hutchings HA, Thorne K, Jerzembek GS, Cheung W-Y, Cohen D, Durai D, et al. Successful development and testing of a Method for Aggregating The Reporting of Interventions in Complex Studies (MATRICS). Journal of Clinical Epidemiology. 2016;69:193-8.
340. O'Cathain A, Murphy E, Nicholl J. Multidisciplinary, Interdisciplinary, or Dysfunctional? Team Working in Mixed-Methods Research. Qualitative health research. 2008;18(11):1574-85.
341. Fernald DH, Duclos CW. Enhance your team-based qualitative research. Annals of Family Medicine. 2005;3(4):360-4.
342. O'Cathain A, Nicholl J, Murphy E. Structural issues affecting mixed methods studies in health research: a qualitative study. BMC Medical Research Methodology. 2009;9(1):82.
343. National Institute for Health Research. Clinical Trials Guide 2020 [Available from: https://www.nihr.ac.uk/documents/clinical-trials-guide/20595.
344. UK Clinical Research Collaboration. Registered Clinical Trial Units 2020 [Available from: https://www.ukcrc.org/research-infrastructure/clinical-trials-units/registered-clinical-trials-units/.
345. Medical Research Council. MRC Guidelines for management of global health trials 2017 [Available from: https://mrc.ukri.org/documents/pdf/guidelines-for-management-of-global-health-trials/.
346. Lane JA, Gamble C, Cragg WJ, Tembo D, Sydes MR. A third trial oversight committee: Functions, benefits and issues. Clinical Trials. 2019;17(1):106-12.

347. Staley K, Abbey-Vital I, Nolan C. The impact of involvement on researchers: a learning experience. Research Involvement and Engagement. 2017;3(1):20.
348. Fenge LA, Oakley L, Taylor B, Beer S. The Impact of Sensitive Research on the Researcher: Preparedness and Positionality. International Journal of Qualitative Methods. 2019;18:1609406919893161.
349. Disis Mary L, Slattery John T. The Road We Must Take: Multidisciplinary Team Science. Science Translational Medicine. 2010;2(22):22cm9-cm9.
350. Duffett M, Choong K, Foster J, Meade M, Menon K, Parker M, et al. High-Quality Randomized Controlled Trials in Pediatric Critical Care: A Survey of Barriers and Facilitators. Pediatr Crit Care Med. 2017;18(5):405-13.
351. Bower P, Brueton V, Gamble C, Treweek S, Smith CT, Young B, et al. Interventions to improve recruitment and retention in clinical trials: a survey and workshop to assess current practice and future priorities. Trials. 2014;15:399-.
352. Strong S, Paramasivan S, Mills N, Wilson C, Donovan JL, Blazeby JM. 'The trial is owned by the team, not by an individual': a qualitative study exploring the role of teamwork in recruitment to randomised controlled trials in surgical oncology. Trials. 2016;17(1):212.
353. Kaur G, Smyth RL, Williamson P. Developing a survey of barriers and facilitators to recruitment in randomized controlled trials. Trials. 2012;13(1):218.
354. Hamm MP, Scott SD, Klassen TP, Moher D, Hartling L. Do health care institutions value research? A mixed methods study of barriers and facilitators to methodological rigor in pediatric randomized trials. BMC Medical Research Methodology. 2012;12(1):158.
355. Tang M, Joensuu H, Simes RJ, Price TJ, Yip S, Hague W, et al. Challenges of international oncology trial collaboration—a call to action. British Journal of Cancer. 2019;121(7):515-21.
356. Lorman AJ. Clinical trials face heightened scrutiny as science and commerce appear to merge. J Biolaw Bus. 2001;4(4):23-32.
357. Mokhtar I. Rapid response to: Indian study sparks debate on the use of placebo in psychiatry trials. BMJ. 2006;332(566).
358. Jin Y, Sanger N, Shams I, Luo C, Shahid H, Li G, et al. Does the medical literature remain inadequately described despite having reporting guidelines for 21 years? - A systematic review of reviews: an update. J Multidiscip Healthc. 2018;11:495-510.
359. Logullo P, MacCarthy A, Kirtley S, Collins GS. Reporting guideline checklists are not quality evaluation forms: they are guidance for writing. Health Science Reports. 2020;3(2):e165.
360. MacCarthy A, Kirtley S, de Beyer JA, Altman DG, Simera I. Reporting guidelines for oncology research: helping to maximise the impact of your research. British Journal of Cancer. 2018;118(5):619-28.
361. Chan A-W, Song F, Vickers A, Jefferson T, Dickersin K, Gøtzsche PC, et al. Increasing value and reducing waste: addressing inaccessible research. The Lancet. 2014;383(9913):257-66.
362. Chalmers I, Glasziou P. Avoidable waste in the production and reporting of research evidence. The Lancet. 2009;374(9683):86-9.
363. de Jong Y, van der Willik EM, Milders J, Voorend CGN, Morton RL, Dekker FW, et al. A meta-review demonstrates improved reporting quality of qualitative reviews following the publication of COREQ- and ENTREQ-checklists, regardless of modest uptake. BMC Medical Research Methodology. 2021;21(1):184.

364. Chan A-W, Song F, Vickers A, Jefferson T, Dickersin K, Gøtzsche PC, et al. Increasing value and reducing waste: addressing inaccessible research. Lancet (London, England). 2014;383(9913):257-66.
365. Moher D, Schulz KF, Simera I, Altman DG. Guidance for Developers of Health Research Reporting Guidelines. PLOS Medicine. 2010;7(2):e1000217.
366. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. International Journal for Quality in Health Care. 2007;19(6):349-57.
367. Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, et al. CONSORT 2010 Explanation and Elaboration: updated guidelines for reporting parallel group randomised trials. BMJ. 2010;340:c869.
368. Critical Appraisal Skills Programme. CASP qualitative checklist [online]. 2018.
369. Letts L, Wilkins S, Law M, Stewart D, Bosch J, Westmorland M. Guidelines for critical review form: qualitative studies (version 2.0). 2007 17.5.2019. Available from: http://www.fhs.mcmaster.ca/rehab/ebp/. .
370. Clark J. How to peer review a qualitative manuscript. Second Edition ed. Godlee F, Jefferson T, editors. London: BMJ Books; 2003.
371. Hong QN, Fàbregues S, Bartlett G, Boardman F, Cargo M, Dagenais P, et al. The Mixed Methods Appraisal Tool (MMAT) version 2018 for information professionals and researchers. Education for Information. 2018;34:285-91.
372. Hannes K, Heyvaert M, Slegers K, Vandenbrande S, Van Nuland M. Exploring the Potential for a Consolidated Standard for Reporting Guidelines for Qualitative Research: An Argument Delphi Approach. International Journal of Qualitative Methods. 2015;14(4):1609406915611528.
373. Barbour RS. Checklists for improving rigour in qualitative research: a case of the tail wagging the dog? BMJ. 2001;322(7294):1115.
374. O'Cathain A, Murphy E, Nicholl J. Three techniques for integrating data in mixed methods studies. BMJ. 2010;341:c4587.
375. Farmer T, Robinson K, Elliott SJ, Eyles J. Developing and Implementing a Triangulation Protocol for Qualitative Health Research. Qualitative health research. 2006;16(3):377-94.
376. Hopf YM, Francis J, Helms PJ, Haughney J, Bond C. Core requirements for successful data linkage: an example of a triangulation method. BMJ Open. 2016;6(10):e011879.
377. Younas A, Pedersen M, Durante A. Characteristics of joint displays illustrating data integration in mixed-methods nursing studies. Journal of advanced nursing. 2020;76(2):676-86.
378. Guetterman TC, Fàbregues S, Sakakibara R. Visuals in joint displays to represent integration in mixed methods research: A methodological review. Methods in Psychology. 2021;5:100080.
379. Guetterman TC, Fetters MD, Creswell JW. Integrating Quantitative and Qualitative Results in Health Science Mixed Methods Research Through Joint Displays. Ann Fam Med. 2015;13(6):554-61.
380. Tashakkori A, Teddlie C, Teddlie CB. Handbook of Mixed Methods in Social & Behavioral Research: SAGE Publications; 2003.
381. Bennett LM, Gadlin H. Collaboration and team science: from theory to practice. J Investig Med. 2012;60(5):768-75.
382. Sale JE, Lohfeld LH, Brazil K. Revisiting the Quantitative-Qualitative Debate: Implications for Mixed-Methods Research. Quality and Quantity. 2002;36(1):43-53.

383. Creswell JW, Creswell JD. Mixed methods research: Developments, debates, and dilemmas. Research in organizations: Foundations and methods of inquiry. 2005;2:315-26.
384. Blackwood B, O'Halloran P, Porter S. On the problems of mixing RCTs with qualitative research: the case of the MRC framework for the evaluation of complex healthcare interventions. Journal of Research in Nursing. 2010;15(6):511-21.
385. MRC Hubs for Trials Methdology Research. MRC-NIHR Trials Methodology Research Partnership (TMRP) 2022 [Available from: http://www.methodologyhubs.mrc.ac.uk/about/tmrp/.
386. Ledford H. The COVID pandemic's lingering impact on clinical trials. Nature. 2021;595(7867):341-2.
387. Park JJH, Mogg R, Smith GE, Nakimuli-Mpungu E, Jehan F, Rayner CR, et al. How COVID-19 has fundamentally changed clinical research in global health. Lancet Glob Health. 2021;9(5):e711-e20.
388. Fleury ME, Farner AM, Unger JM. Association of the COVID-19 Outbreak With Patient Willingness to Enroll in Cancer Clinical Trials. JAMA Oncol. 2021;7(1):131-2.
389. Morse J. The Changing Face of Qualitative Inquiry. International Journal of Qualitative Methods. 2020;19:1609406920909938.
390. Reñosa MDC, Mwamba C, Meghani A, West NS, Hariyani S, Ddaaki W, et al. Selfie consents, remote rapport, and Zoom debriefings: collecting qualitative data amid a pandemic in four resource-constrained settings. BMJ Global Health. 2021;6(1):e004193.
391. Tremblay S, Castiglione S, Audet L-A, Desmarais M, Horace M, Peláez S. Conducting Qualitative Research to Respond to COVID-19 Challenges: Reflections for the Present and Beyond. International Journal of Qualitative Methods. 2021;20:16094069211009679.
392. Vindrola-Padros C, Chisnall G, Cooper S, Dowrick A, Djellouli N, Symmons SM, et al. Carrying Out Rapid Qualitative Research During a Pandemic: Emerging Lessons From COVID-19. Qualitative health research. 2020;30(14):2192-204.
393. Rhodes SD, Mann-Jackson L, Alonzo J, Garcia M, Tanner AE, Smart BD, et al. A rapid qualitative assessment of the impact of the COVID-19 pandemic on a racially/ethnically diverse sample of gay, bisexual, and other men who have sex with men living with HIV in the US South. Res Sq. 2020:rs.3.rs-57507.
394. QUESTS DCV-P. Rapid qualitative research: Current challenges and implications for qualitative research in clinical trials [Available from: https://quests.ie/rapid-qualitative-research-current-challenges-implications-qualitative-research-clinical-trials/.
395. Lewinski AA, Crowley MJ, Miller C, Bosworth HB, Jackson GL, Steinhauser K, et al. Applied Rapid Qualitative Analysis to Develop a Contextually Appropriate Intervention and Increase the Likelihood of Uptake. Medical care. 2021;59.
396. Vindrola-Padros C, Johnson GA. Rapid Techniques in Qualitative Research: A Critical Review of the Literature. Qualitative health research. 2020;30(10):1596-604.

Appendices

Appendix I Publications

Clement et al. Trials (2018) 19:589
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Trials

RESEARCH Open Access

Exploring qualitative methods reported in registered trials and their yields (EQUITY): systematic review

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Abstract

Background: The value of qualitative methods within trials is widely recognised, but their full potential is not being realised. There are also issues with the visibility, recognition and reporting of qualitative methods in trials. To identify potential improvements in qualitative research within trials, we need to study trials that have included qualitative methods. We aimed to explore the frequency of reporting qualitative methods in registered trials, the types of trials using qualitative methods and where in the world these trials were conducted.

Methods: We included registries if they were searchable using keywords and held summaries of trials rather than listing reports or publications. We searched the included registries from the first available record in 1999 to the end of 2016 for the term 'qualitative'. We included trials only if we could confirm that they used qualitative methods through documented use of qualitative data collection and analysis in the registry summary. We analysed registered trials reporting the use of qualitative methods by: year registered, the country responsible for overseeing governance of the trial and the type of trial intervention (categorised as surgical, medical device, behavioural, drug or other).

Results: We included three registries: ClinicalTrials.gov, the International Standard Randomised Controlled Trial Number Registry (ISRCTN) and the World Health Organisation International Clinical Trials Registry Platform (WHO ICTRP). A total of 615,311 trials appear in these three registries from 1999 until the end of 2016. Numbers differed across registries with the WHO ICTRP the largest (366,753 trials), ClinicalTrials.gov the second largest (233,277) and ISRCTN the smallest (15,301). Of these registered trials, we confirmed that 1492 (0.24%) reported using qualitative methods. The ISRCTN contributed the highest percentage of trials reported as using qualitative methods (3.4%); in contrast, ClinicalTrials.gov reported 0.3% and WHO ICTRP reported 0.03%. The number and percentage of trials reported to use qualitative methods increased over time from 0 (0.0%) in 1999 to 285 (0.38%) in 2016. Trials reported as using qualitative methods originated from 52 countries across the world. Most were in Western higher-income countries: 38% in the United Kingdom and 28% in the United States. Most registered trials reported as using qualitative methods evaluated behavioural (39%) or other interventions with many fewer trials evaluating drugs (5%), medical devices (5%) or surgical interventions (4%).

Conclusion: The reported use of qualitative methods in registered trials has increased over time and worldwide. They are reportedly more frequent in high-income countries and in trials of behavioural and other interventions. Trialists and other stakeholders need to recognise the benefits of using qualitative methods in surgical, device and drug trials, and trials conducted in poorer countries. Moreover, they should seriously consider using qualitative methods in these trials.

Keywords: Qualitative research, Randomised controlled trial, Research design, Registries, Income, Humans, Research support

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Background

The added value of using qualitative research methods within trials is widely recognised [1–6]. O'Cathain et al. [1] identified 22 ways in which qualitative research could benefit trials including: identifying and addressing recruitment and retention issues [4], ensuring trial designs are appropriate to the population and condition they are addressing [7] and facilitating the interpretation and implementation of trial findings through understanding trial context [8]. Qualitative methods can also assess whether trial processes are appropriate [9]. These methods have informed trial design and conduct, for example, by assessing fidelity and uptake of interventions and how and why they work or not [10, 11]. Randomised trials are the most appropriate design for robust evaluations of complex health interventions [12, 13]. However, they are not without criticism. There are concerns that they neglect patient and professional input [14] and are insensitive to the health-care context [15]. Critics see them as artificial constructs that depart from the real world [16] and therefore, cannot model health-care on the ground [17].

Hence, trialists have turned to complementary methods to address these concerns. Methodological guidance [18, 19] and mounting evidence of the added value conferred by qualitative methods in trials [1, 3, 20, 21] have led trialists increasingly to adopt a multi-method approach, integrating quantitative and qualitative components. While qualitative methods are increasingly used within trials, their full potential is often not realised [22]. They have not always been well integrated into trial designs, which reduces methodological rigour and transparency [3]. For example, excluding qualitative methodologists from the design phase, especially from the formulation of trial aims and objectives, may create conflict between qualitative and quantitative components. Poor integration at the design stage often leads to poor reporting that obscures qualitative methods and findings [22, 23]. To identify how to improve qualitative methods within trials, it is important to analyse how trials report the use of qualitative methods and whether these have changed over time.

Previous reviews have reported when, where and how qualitative methods are used within trials [3, 20]. Though the reported numbers of trials employing qualitative methods differ across reviews, they are consistently low compared with the total number conducted and published. The proportion of trials that have reported qualitative methods varies from 1% in palliative care trials [20] to 30% in trials of complex interventions [3]. The reviews also reveal that, though trials including qualitative methods are conducted worldwide with multi-national authorships, they are mainly within rich countries [3, 22]. However, these reviews are essentially cross-sectional, encompassing a couple of years, for example 2008–2010 [1]. Moreover, searches cover only single registries or published trials. Furthermore, these reviews have focused mainly on trials of complex interventions that evaluated behavioural interventions aimed at changing participants' behaviour at the individual or community level [20, 24]. More recently the term 'complex intervention' has evolved to cover a wider range of interventions, including surgical procedures, medical devices and drugs. This reflects the increasing complexity of clinical interventions [7, 19, 25]. It is, therefore, important to subdivide these complex interventions from previous reviews to characterise the trials that report qualitative methods.

Depending on the country of the sponsor, clinical trials are either required or encouraged to register prospectively with a trials registry. These registries have been established across the world to address concerns about access to trials, publication bias and more recently, trial results. In the United States, the Food and Drug Administration Modernization Act of 1997 and subsequent amendments mandated the development of a registry and registration of both federally funded and privately funded trials, with penalties for non-compliance [26]. In 2004, the members of the International Committee of Medical Journal Editors published an editorial promoting the prospective registration of all clinical trials, leading to the establishment of a trial registry within the United Kingdom [27]. This was later supported by the World Health Organisation (WHO), which promoted registration further afield [28]. Registries aim to provide increased access to information and transparency about trials for researchers, clinicians, patients and members of the public. These registries give access to information about each trial provided by the trial team, including: lead researcher's name and organisation, study design including type of trial and methods, and the organisation responsible for overseeing governance. In principle, they also report the extent of qualitative methods within the trial.

This review is part of a larger project to characterise best practice in conducting qualitative research within trials. The objectives of this project are:

1. To describe the characteristics of trials reporting the use of qualitative methods
2. To explore good practice in planning and running clinical trials using qualitative methods
3. To explore the roles that participants play in clinical trials using qualitative methods
4. To explore and identify potential facilitators of and barriers to qualitative research within trials
5. To make recommendations for best practice for using qualitative methods within trials.

This review builds on previous reviews by estimating the frequency of the reported use of qualitative methods in trials over 16 years, longer than previous reviews, and

analysing trials that report using qualitative methods, specifically the types of intervention evaluated and their locations.

Methods

To assess the use of qualitative methods in trials, we reviewed existing clinical trial registries and identified trials that reported using qualitative methods, in four main steps:

Step 1: We used internet search engines to identify existing clinical trial registries. We included registries if: they could be searched for keywords; they held records of individual trials, not merely reports or publications; and they held records in English. We searched all included registries from the first available record, which varied across registries, until 31 December 2016.

Step 2: We searched these registries for the keyword 'qualitative'. The lead researcher (CC) reviewed all identified trials and extracted the following data into an Excel spreadsheet: registry name (to allow comparison across registries), registry record number (as a unique identifier), trial title, year of first registration with registry, country responsible for overseeing governance of the trial (as many trials recorded multiple recruiting countries, we chose the most likely source of decisions about trial design) and type of trial intervention (categorised as surgical, medical device, drug, behavioural – which aimed to modify the behaviour of individuals or communities – or other). We derived these types from descriptions used by the registries, existing literature and previous reports [22, 29, 30].

Step 3: We checked the registry records for documented use of qualitative methods. We defined these as qualitative data collection (such as observation, interviews, focus groups, documents or visual data), qualitative data analysis (such as textual or visual) or both [31, 32].

Step 4: We analysed these data using the filter and count features within Excel. We counted frequencies for: number of registered trials reporting the use of qualitative methods, year of first registration with registry, country responsible for overseeing governance of the trial and type of trial intervention as defined in Step 2. We presented our findings as frequencies and percentages.

Results

Trial registries

Our search identified five main clinical trial registries: ClinicalTrials.gov, WHO's International Clinical Trial Registry Platform (WHO ICTRP), the International Standard Randomised Controlled Trial Number (ISRCTN) Registry, the Cochrane Central Register of Controlled Trials (Cochrane CENTRAL) and the European Union Clinical Trials Register. However, we excluded the last of these, as it forms part of the WHO ICTRP, and Cochrane, as it is a database of trial reports rather than a registry of trials.

Included registries

ClinicalTrials.gov

This registry was created in response to patient pressure for access to information on clinical trials. It is run by the United States National Library of Medicine within the National Institutes of Health and claims to be the largest clinical trials database in the world, registering trials from 200 countries [30]. It records information on federally, commercially and privately funded clinical trials, including information on participant eligibility, locations of trial activity, point of contact and, more recently, basic results. US law enforces penalties for non-compliance with this registry. Approximately 38% of the trials registered within ClinicalTrials.gov are based only inside the US, 56% are based only outside the US and 5% are based in both [30].

International Standard Randomised Controlled Trial Number Registry

The ISRCTN registry contains basic data on all clinical trials which have been assigned an ISRCTN number. The registry is a not-for-profit organisation sponsored by the Canadian Institute of Health Research, the Italian Instituto di Ricerche Farnacologiche 'Mario Negri', the Netherlands Organisation for Health Research and Development, the UK Department of Health, and the UK Medical Research Council. However, most of the registered trials are based in the UK [33]. The ISRCTN is a simple numeric system that facilitates the identification and tracking of trials throughout their life cycle. The registry uses the WHO 20-item Trial Registration Data Set covering: study hypothesis, study design, countries of recruitment, selection criteria, disease or condition, intervention, sponsor and contact information [33].

World Health Organisation International Clinical Trials Registry Platform

This registry also uses the WHO Trial Registration Data Set. The portal provides access to 16 separate registries from across the world [34], including ClinicalTrials.gov and ISRCTN. Thus, we took care not to duplicate trials from those registries.

Trials with confirmed use of qualitative methods

The three included registries recorded a total of 615,311 trials from their first record (occurring in 1999 for ClinicalTrials.gov, 2004 for ISRCTN and 2006 for WHO ICTRP) until 31 December 2016. The WHO ICTRP registry was the largest with 366,753 trials registered, ClinicalTrials.gov the second largest with 233,277 trials and ISRCTN the smallest with 15,301 trials. Of these, 2477 records included the keyword 'qualitative': 144 (0.03%) from WHO ICTRP, 1668 (0.7%) from ClinicalTrials.gov and 665 (4.6%) from ISRCTN. Of these 2477 records, we confirmed that 1492

(60.2%) trials had used qualitative methods. The main reasons for excluding 985 records were: use of the term 'qualitative' to describe quality of life measures, to refer to medical tests like 'qualitative urine test or MRI imaging' or to cite statistical tests as 'qualitative Fishers Exact Test'. None of these fitted our criteria for qualitative methods.

Table 1 shows that ISRCTN contributed by far the highest percentage of registered trials subsequently confirmed as using qualitative methods (3.4%). In contrast, ClinicalTrials.gov had only 0.3%, and WHO ICTRP had the smallest proportion at 0.03%.

Trials confirmed as using qualitative methods by year registered

The number of registered trials increased over time from 1999, when first reported in ClinicalTrials.gov, to the end of 2016. The number and percentage of these trials reported as having used qualitative methods also increased steadily over time across all registries (Figs. 1 and 2). The year in which the first trial reported to use qualitative methods was identified differed across the registries: 2000 in ISRCTN, 2001 in ClinicalTrials.gov and 2006 in WHO ICTRP. As all registries held records of trials reported as using qualitative methods from 2004, we compared the number across time within each registry between 2004 and 2016. This revealed substantial increases across time in all three registries: from 1.2% to 8.4% in ISRCTN, from 0.03% to 0.59% in ClinicalTrials.gov and from 0% to 0.06% in WHO ICTRP.

Types of registered trials confirmed as using qualitative methods

Of the 1492 registered trials confirmed as reporting the use of qualitative methods, most were evaluating a behavioural intervention (39%) or an other intervention that did not fit the defined categories, mainly vaccines, nutritional supplements and diagnostic testing (47%). In contrast, clinically orientated trials evaluating drugs (5%), medical devices (5%) or surgical interventions (4%) were much less likely to report the use of qualitative methods. This was broadly consistent across the three trial registries (Table 2).

Registered trials confirmed as using qualitative methods by country

Trials with confirmed use of qualitative methods were registered from 52 countries across the world. The highest number were registered in the UK (570 trials, 38.2%), followed by the US (425 trials, 28.5%), Canada (71 trials, 4.6%), France (67 trials, 4.5%), Australia (43 trials, 2.9%), Germany (37 trials, 2.5%) and Denmark (34 trials, 2.3%). None of the remaining 45 countries accounted for more than 2% of all confirmed qualitative trials.

We examined each registry for the country overseeing most of the registered trials reported to use qualitative methods. Most of the trials registered within ISRCTN were conducted in the UK (444, 77.9%); 124 UK trials (21.8%) were registered in ClinicalTrials.gov and two UK trials in WHO ICTRP. Most of the trials within Clinical Trials.gov were conducted in the US (419, 98.6%), with six US trials (1.4%) in ISRCTN but no US trials (0%) in WHO ICTRP. Most of the trials within WHO ICTRP were conducted in Australia (36, 15.5%), with four Australian trials (9.3%) in ClinicalTrials.gov and three Australian trials (6.8%) in ISRCTN.

We classified countries by gross national income (GNI), which was formerly known as gross domestic product (GDP), as estimated by the World Bank Group using the World Bank Atlas Method [35]. Most registered trials reported to use qualitative methods were conducted in high-income countries like the UK (570 trials, 38.2%) and the US (425 trials, 28.5%). Low- and low-middle-income countries had very few trials reported as using qualitative methods, for example Uganda (four trials, 0.26%) and Ethiopia (two trials, 0.13%) (Table 3). In all registries, most of the trials that reported using qualitative methods were in the high-income category. However, the distributions for each category differ across registries: most of the trials that reported using qualitative methods within low-income or low-middle-income countries were registered with ClinicalTrials.gov.

Discussion

Summary

This review has characterised trials registered on trial registries and confirmed as using qualitative methods, both across time (between 1999 and 2016) and across

Table 1 Registered trials using qualitative methods by registry

	WHO ICTRP	ClincalTrials.gov	ISRCTN	Overall
Total trials in registry from 1999 to 2016	366,753	233,277	15,301	615,311
Total identified with qualitative keyword	144	1668	665	2477
Total records excluded	46	790	149	985
Total confirmed with qualitative methods	98	878	516	1492
Percentage confirmed with qualitative methods	0.04%	0.4%	3.4%	0.2%

ICTRP International Clinical Trials Registry Platform, *ISRCTN* International Standard Randomised Controlled Trial Number Registry, *WHO* World Health Organisation

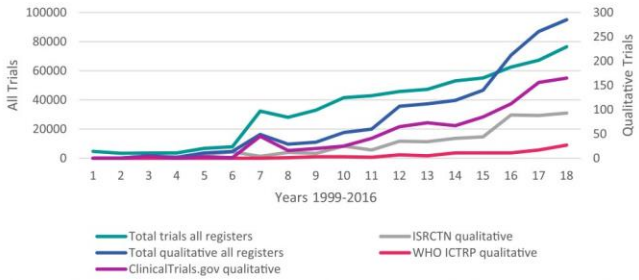

Fig. 1 Number of registered trials confirmed as using qualitative methods by registry by year. ICTRP International Clinical Trials Registry Platform, ISRCTN International Standard Randomised Controlled Trial Number Registry, WHO World Health Organisation

countries. Only 1492 (0.24%) of the 615,311 registered trials identified across the three included trial registries, either completed or in progress, reported the use of qualitative methods. Most of these were based in the US or UK, rich Western counties where the number of trials reported to use qualitative methods has increased steadily over time. Most trials reporting the use of qualitative methods investigated behavioural or other interventions, while trials evaluating drugs, medical device or surgical procedures each contributed fewer than 5% of registered trials reported to use qualitative methods.

Interpretation

Our finding that reported use of qualitative methods is rare amongst clinical registered trials is consistent with O'Cathain et al. [22], who found that few published drug or medical device trials employed qualitative methods. Surgical trials are reputedly difficult to design and conduct, so until recently, surgeons resisted the use of randomised trials [25]. Although the number of surgical trials being conducted is increasing [25, 36], they face challenges; in particular the beliefs and preferences of participating surgeons threaten their equipoise, that is whether they are genuinely uncertain about the effectiveness of a clinical intervention [37]. Many surgeons prefer not to standardise interventions, which contributes to good trial design [38]. However, qualitative methods can describe experiences and beliefs and help in the understanding of complex phenomena. They can explore factors affecting equipoise and how to overcome these, and help to establish core outcomes and minimum standards for interventions [7]. Hence, qualitative

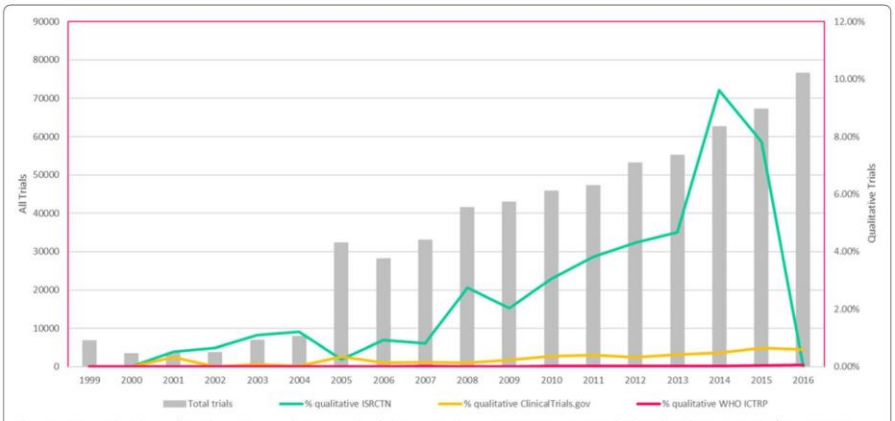

Fig. 2 Registered trials confirmed as using qualitative methods by registry by year. ICTRP International Clinical Trials Registry Platform, ISRCTN International Standard Randomised Controlled Trial Number Registry, WHO World Health Organisation

current practice, and the need to adapt trials to local context and culture. These issues make qualitative methods even more challenging [48, 49]. Nevertheless, Vischer and colleagues [48] have shown how qualitative methods can address these issues in low-income countries. They interviewed key informants in Burkina Faso, Ghana, Kenya and Senegal to investigate factors slowing clinical trials. Trial staff described factors apparently hindering trials, including lack of planning and poor understanding of trial processes. This generated recommendations for explicit trial planning and site organisation [48]. Thus, qualitative methods can improve the conduct of trials in poorer countries, such as by consulting stakeholders, not least about cultural acceptability, for example of trial outcome measures. It is important, therefore, to test whether applying this approach more widely can both increase the number of trials and the proportion that use qualitative methods. It is also important to disseminate such work through publication in international journals and rigorous training.

Strengths, limitations and future directions

This review is limited to trials reported by researchers in trial registries as using qualitative methods and confirmed by inspecting their registry summaries. However, there may be registered trials that use qualitative methods without reporting this to the registry. Indeed, searching the three registries for trials using the terms 'interviews,' 'focus groups' or 'mixed methods' identified 8267 registered trials. We checked a random 177 of these and found that 50 of their registry summaries reported the use of qualitative methods. Hence, the true number of clinical trials in these registries using qualitative methods is closer to 3800 (0.62%). This highlights two issues: Why did registries not check trials a little more thoroughly for use of qualitative components? How should registries identify trials with qualitative methods in future? We recommend that, as more trials use qualitative methods, trial registries should ask about qualitative methods within their application forms.

We did not address whether registries reported findings or whether qualitative methods influenced trial processes, outcomes or plans for implementation. With increasing pressure on trials to report findings within registries, now mandated within the US, it will soon be possible to see whether trials report qualitative findings and, in particular, whether they use qualitative methods to interpret findings or alter trial design. It will also become important to examine how registries apply those methods. Although they collect similar data, they differ in how they register trials and manage data, and above all in the proportion of trials that report the use of qualitative methods.

This review reports on important characteristics of registered trials that reported using qualitative methods, namely: when they registered, where they were conducted and the type of intervention they evaluated. Unfortunately, information was limited and inconsistent about other trial features, notably the design of the registered trials, their use of qualitative methods, their phase, sample sizes for both trials and their qualitative studies, trial outcome measures (for example, the balance between clinical and patient-reported), qualitative methods used, and how these methods related to trial objectives. While much of this information is available in the corresponding peer-reviewed publications, extracting it is a major task, as is analysing the relationship between these characteristics and trials' use of qualitative methods.

A strength of this review is the inclusion of all trials registered between the start of 1999 and the end of 2016. This has shown a clearly increasing trajectory of trials using qualitative methods. Previous reviews covered shorter periods of time and could not analyse changes over time [1, 3]. Including the three main international registries has improved our understanding of when and where trials are using qualitative methods.

Conclusion

This review has highlighted the increasingly reported use of qualitative methods in registered trials over time and across countries. However, these methods are more prevalent in rich Western countries and in less clinically orientated trials. Trialists and other stakeholders need to recognise the benefits of using qualitative methods in surgical, device and drug trials, and trials conducted in poorer countries, and should seriously consider the use of qualitative methods in these trials.

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Authors' contributions
All authors contributed to conception and design. CC was responsible for the acquisition and analysis of the data. All authors contributed to drafting the manuscript or revising it critically for important intellectual content. All authors ensured that questions related to the accuracy or integrity of the work were appropriately investigated and resolved, and they approved the version to be published.

Ethics approval and consent to participate
Not needed for a systematic review.

Consent for publication
Not needed for a systematic review.

Competing interests
The authors declare that they have no competing interests.

Publisher's Note

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References

1. O'Cathain A, et al. What can qualitative research do for randomised controlled trials? A systematic mapping review. BMJ Open. 2013;3(6).
2. O'Cathain A, et al. Maximising the impact of qualitative research in feasibility studies for randomised controlled trials: guidance for researchers. Pilot Feasib Stud. 2015;1(1):32.
3. Lewin S, Glenton C, Oxman AD. Use of qualitative methods alongside randomised controlled trials of complex healthcare interventions: methodological study. BMJ. 2009;339.
4. Donovan JL, et al. Optimising recruitment and informed consent in randomised controlled trials: the development and implementation of the Quintet Recruitment Intervention (QRI). Trials. 2016;17(1):283.
5. Elliott D, et al. Understanding and Improving Recruitment to Randomised Controlled Trials: Qualitative Research Approaches. Eur Urol. 2017;72(5):789–98.
6. Rapport F, et al. Qualitative research within trials: developing a standard operating procedure for a clinical trials unit. Trials. 2013;14(1):54.
7. Blencowe NS, et al. Novel ways to explore surgical interventions in randomised controlled trials: applying case study methodology in the operating theatre. Trials. 2015;16:589.
8. Clement C, et al. Healthcare professionals' views of the use and administration of two salvage therapy drugs for acute ulcerative colitis: a nested qualitative study within the CONSTRUCT trial. BMJ Open. 2017;7(2):e014512.
9. Moore GF, Audrey S, Barker M, Bond L, Bonell C, Hardeman W, et al. Process evaluation of complex interventions: Medical Research Council guidance. BMJ. 2015;350:h1258.
10. Sebire SJ, et al. Process evaluation of the Bristol girls dance project. BMC Public Health. 2016;16(1):349.
11. Mann C, Shaw A, Guthrie B, et al. Protocol for a process evaluation of a cluster randomised controlled trial to improve management of multimorbidity in general practice: the 3D study. BMJ Open. 2016;6:e011260. https://doi.org/10.1136/bmjopen-2016-011260.
12. Cochrane AL. Effectiveness and efficiency: random reflections on health services. London: Nuffield Provincial Hospitals Trust; 1972.
13. Sackett DL, et al. Evidence based medicine: what it is and what it isn't. BMJ. 1996;312(7023):71.
14. Ingersoll GL. Evidence-based nursing: What it is and what it isn't. Nurs Outlook. 2000;48(4):151–2.
15. Pope C, Mays N. Qualitative Research: Reaching the parts other methods cannot reach: an introduction to qualitative methods in health and health services research. BMJ. 1995;311(6996):42.
16. Stephenson J, Imrie J. Why do we need randomised controlled trials to assess behavioural interventions? BMJ. 1998;316(7131):611–3.
17. Timmermans S, Mauck A. The Promises And Pitfalls Of Evidence-Based Medicine. Health Aff. 2005;24(1):18–28.
18. Hawe P, et al. Methods for exploring implementation variation and local context within a cluster randomised community intervention trial. J Epidemiol Community Health. 2004;58(9):788–93.
19. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M, et al. Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ. 2008;337:a1655.
20. Flemming K, Adamson J, Atkin K. Improving the effectiveness of interventions in palliative care: the potential role of qualitative research in enhancing evidence from randomized controlled trials. Palliat Med. 2008; 22(2):123–31.
21. Oakley A, et al. Process evaluation in randomised controlled trials of complex interventions. BMJ. 2006;332(7538):413–6.
22. O'Cathain A, et al. Maximising the value of combining qualitative research and randomised controlled trials in health research: the QUAlitative Research in Trials (QUART) study – a mixed methods study. Health Technol Assess. 2014;18(38):1–197. https://doi.org/10.3310/hta18380.
23. Glenton C, Lewin S, Scheel IB. Still too little qualitative research to shed light on results from reviews of effectiveness trials: A case study of a Cochrane review on the use of lay health workers. Implement Sci. 2011;6(1):53.
24. National Research Council Panel on Race, E. and L. Health in Later. The National Academies Collection: Reports funded by National Institutes of Health. In: Anderson NB, Bulatao RA, Cohen B, editors. Critical Perspectives on Racial and Ethnic Differences in Health in Late Life. Washington (DC): National Academies Press (US) National Academy of Sciences; 2004.
25. Cook JA. The challenges faced in the design, conduct and analysis of surgical randomised controlled trials. Trials. 2009;10(1):9.
26. US Food and Drug Administration. Food and Drug Administration Moderization Act of 1997. p. 1997.
27. Dyer O. GlaxoSmithKline faces US lawsuit over concealment of trial results. BMJ. 2004;328(7453):1395.
28. Organisation, W.H., Ministerial Summit on Health Research. 2004.
29. Smith PG, Ross DA, Morrow RH. Field Trials of Health Interventions: A Toolbox. Oxford: Oxford University Press; 2015.
30. Health, N.I.f, ClinicalTrials.gov Background. 2018.
31. Silverman D. Doing Qualitative Research: A Practical Handbook. London: SAGE Publications; 2013.
32. Denzin NK, Lincoln YS. The SAGE Handbook of Qualitative Research, vol. 2017. London: SAGE Publications.
33. Ltd, B.C., ISRCTN About. 2018.
34. World Health Organisation, International Clinical Trials Registry Platform (ICTRP). 2018.
35. World Bank Group, World Bank Countries and Income. 2018; Available from: http://data.worldbank.org/country
36. McCall B. UK implements national programme for surgical trials. Lancet. 2013;382(9898):1083–4.
37. Freedman B. Equipoise and the ethics of clinical research. N Engl J Med. 1987;317(3):141–5.
38. Potter S, et al. Time to be BRAVE: is educating surgeons the key to unlocking the potential of randomised clinical trials in surgery? A qualitative study. Trials. 2014;15(1):80.
39. Paramasivan S, et al. Enabling recruitment success in bariatric surgical trials: pilot phase of the By-Band-Sleeve study. Int J Obes (2005). 2017;41(11):1654–61.
40. Gagliardi, A.R., et al., Factors influencing the reporting of adverse medical device events: qualitative interviews with physicians about higher risk implantable devices. BMJ Qual Saf. 2017;0:1–9. https://doi.org/10.1136/bmjqs-2017-006481.
41. Neugebauer EAM, et al. Specific barriers to the conduct of randomised clinical trials on medical devices. Trials. 2017;18(1):427.
42. Gargon E, Williamson PR, Young B. Improving core outcome set development: qualitative interviews with developers provided pointers to inform guidance. J Clin Epidemiol. 2017;86:140–52.
43. Ritchie J, et al. Qualitative Research Practice: A Guide for Social Science Students and Researchers. London: SAGE Publications; 2013.
44. Drabble SJ, et al. Describing qualitative research undertaken with randomised controlled trials in grant proposals: a documentary analysis. BMC Med Res Methodol. 2014;14(1):24.
45. O'Cathain A, et al. Getting added value from using qualitative research with randomized controlled trials: a qualitative interview study. Trials. 2014;15(1):215.
46. Jansen YJFM, et al. Coping with methodological dilemmas; about establishing the effectiveness of interventions in routine medical practice. BMC Health Serv Res. 2006;6(1):160.
47. Williams JG, et al. Comparison Of iNfliximab and ciclosporin in Steroid Resistant UlCerative Colitis: pragmatic randomised Trial and economic evaluation (CONSTRUCT). Health Technol Assess. 2016;20(44):1–320. https://doi.org/10.3310/hta20440.
48. Vischer N, et al. "You can save time if…"—A qualitative study on internal factors slowing down clinical trials in Sub-Saharan Africa. PLoS One. 2017;12(3):e0173796.
49. Franzen SRP, Chandler C, Enquselassie F, et al. Understanding the investigators: a qualitative study investigating the barriers and enablers to the implementation of local investigator-initiated clinical trials in Ethiopia. BMJ Open. 2013;3:e003616. https://doi.org/10.1136/bmjopen-2013-003616.

Appendix II Critical review search strategy

Search strategy used to identify literature in electronic databases for the critical review.

Search strand number	Search terms
S1	MP qualitative research OR qualitative research/
S2	MP (qualitative N3 method*)
S3	MP ((qualitative N3 study) OR (qualitative N3 studies))
S4	MP (focus group* OR focus-group*)
S5	MP narrative analysis
S6	MP grounded theory
S7	MP process evaluation
S8	MP (mixed method* OR mixed-method*)
S9	MP (in-depth N4 interview*)
S10	MP (((((semi structured N5 interview*) OR semistructured) N5 interview OR semi-structured) N5 interview*
S11	MP qualitative interview*
S12	MP (interview* AND theme*)
S13	MP interview* AND (audio recorder OR audio-recorded)))
S14	MP (qualitative case study OR descriptive case studies OR descriptive case-study OR qualitative case-studies)
S15	MP qualitative exploration
S16	MP (qualitative analysis OR qualitative analyses OR qualitatively analy?ed)
S17	MP (qualitative N3 data)
S18	MP qualitative evaluation
S19	MP qualitative intervention
S20	MP qualitative approach
S21	MP qualitative inquiry
S22	MP discourse analysis
S23	MP discursive
S24	MP Phenomenological
S25	MP thematic analysis
S26	MP ethnograph*
S27	MP action research

S28	MP (ethno methodology OR ethnomethodology)
S29	MP social construction* OR (S1-28)
S30	MP clinical trial* OR clinical trial*
S31	MP randomise control* trial*
S32	MP pragmatic trial
S33	MP complex intervention
S34	MP controlled trial* OR controlled-trial*
S35	(MP controlled trial* OR controlled-trial*) OR (S30-S34)
S36	S35 AND S29

Appendix III Critical review results tables in full

Extended results tables for the critical review in chapter 4.

Table 9 Health areas and conditions in which trials using qualitative research were conducted

	Number	Percentage
Mixed (2 or more health conditions)	347	14.8%
Mental health	322	13.7%
Oncology	231	9.9%
Infectious diseases	194	8.3%
Diabetes	114	4.9%
Maternity and natal	107	4.6%
Obesity	104	4.4%
Cardiovascular	99	4.2%
Gerontology	85	3.6%
Orthopaedic	83	3.5%
Respiratory	68	2.9%
Neurology	64	2.7%
Healthy participants	59	2.5%
Dementia	51	2.2%
Alcohol and substance use	32	1.4%
Musculoskeletal	30	1.3%
Smoking	29	1.2%
Palliative care	26	1.1%
Gastroenterology	19	0.8%
Sexual health	18	0.8%
Social care	17	0.7%
Urology	16	0.7%
Dentistry	15	0.6%
Renal	15	0.6%
Rheumatology	15	0.6%
Spectrum disorders	15	0.6%
Stroke	60	0.6%
Domestic violence	11	0.5%
Ear, Nose and Throat (ENT)	11	0.5%
Nutrition	10	0.4%
Haematology	9	0.4%
Dermatology	8	0.3%
Epilepsy	8	0.3%
Chronic Fatigue Syndrome (CFS)	7	0.3%
Optometry	7	0.3%
Trauma	6	0.3%
Intellectual Disabilities	5	0.2%
Child growth stunting	2	0.2%

Cerebral Palsy	4	0.2%
Injury	4	0.2%
Delirium	2	0.1%
Infection	2	0.1%
Sleep disorder	2	0.1%
Speech and language	2	0.1%
Pressure ulcers	2	0.1%
Allergy	1	0.0%
Burns	1	0.0%
Down's syndrome	1	0.0%
Male circumcision	1	0.0%
Medically Unexplained Symptoms	1	0.0%
Polio	1	0.0%
Total	**2343**	

Table 11. Qualitative analysis approaches used in trials (full version)

	Number	Percentage
Not described	794	33.8%
Thematic analysis	764	32.6%
Content analysis	247	10.5%
Framework analysis	181	7.7%
Grounded theory	153	7.7%
Constant comparative	90	3.8%
Interpretive Phenomenological Analysis (IPA)	21	0.9%
Mixed analysis (2 or more analysis approaches)	13	0.6%
Systematic text condensation	11	0.5%
Discourse analysis	9	0.4%
Narrative analysis	7	0.3%
Conversation analysis	5	0.2%
Immersion Crystallization Approach	5	0.2%
Template analysis	5	0.2%
Interpretive analysis	4	0.2%
Matrix analysis	3	0.1%
Critical analysis	2	0.1%
Descriptive analysis	2	0.1%
Dimensional analysis	2	0.1%
Editing analysis	2	0.1%
Interaction analysis	2	0.1%
Schema analysis	2	0.1%
Analytic hierarchy	1	>0.1%
Analytic induction	1	>0.1%
Cognitive debriefing	1	>0.1%
Context template	1	>0.1%
Cross case analysis	1	>0.1%

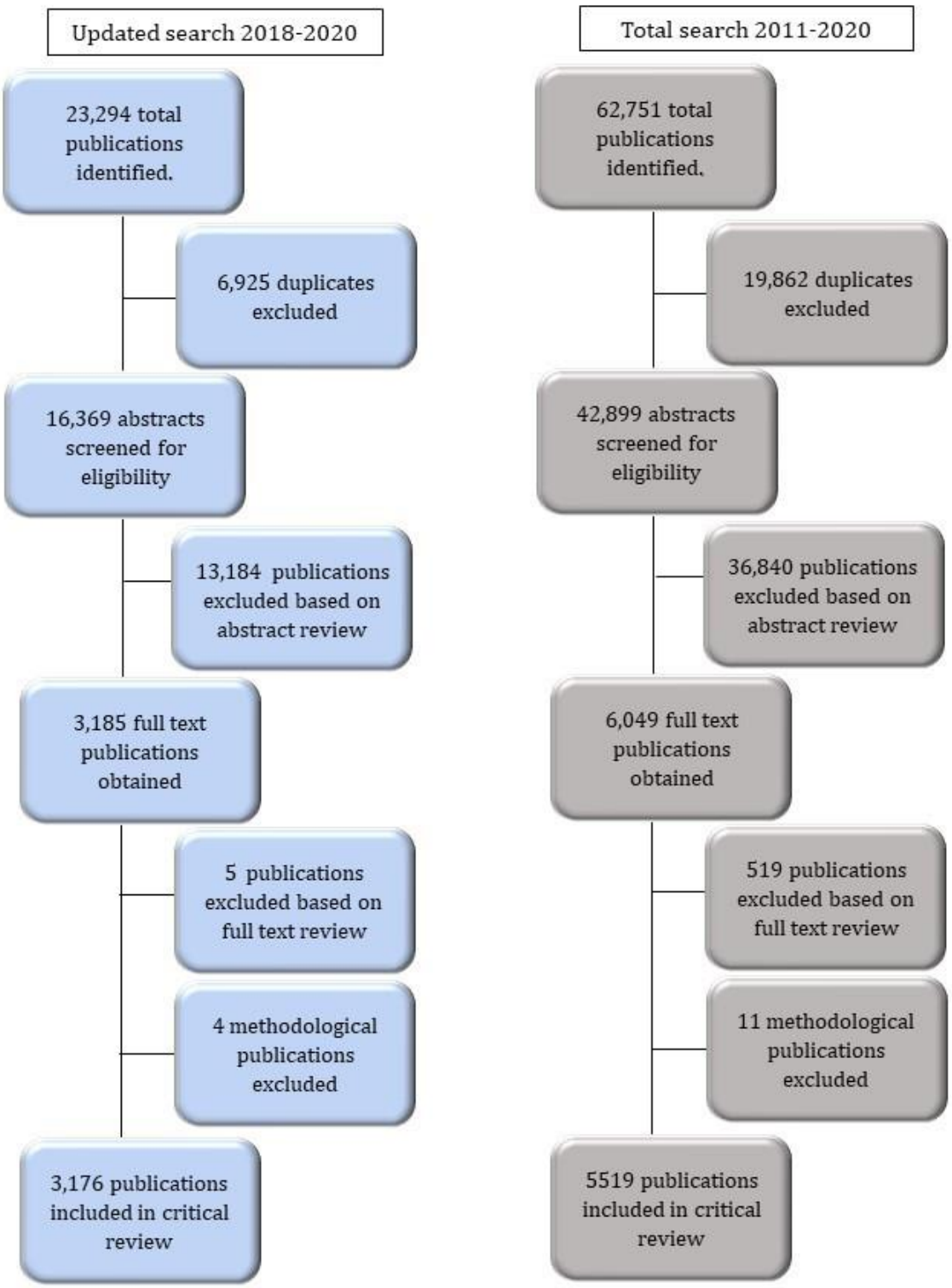
Domain analysis	1	>0.1%
Ethical analysis	1	>0.1%
Exploratory correlation analysis	1	>0.1%
Framing matrix	1	>0.1%
Inductive data reduction	1	>0.1%
Macrocognition coding	1	>0.1%
Magnitude coding	1	>0.1%
Mediation analysis	1	>0.1%
Q-QAT	1	>0.1%
Rapid analysis approach	1	>0.1%
Reciprocal translational analysis	1	>0.1%
Reconstructive interviews analysis	1	>0.1%
Social analysis	1	>0.1%
Spiral approach	1	>0.1%
Total	**2343**	

Table 12. Theoretical frameworks used with QRT (full version)

	Number	Percentage
Normalisation Process Theory (NPT)	26	25.0%
RE-AIM	9	8.7%
Theoretical domains framework	7	7.7%
Consolidation Framework for Implementation Theory (CFIT)	6	5.8%
Social Ecological Framework	6	5.8%
Theory of Planned Behaviour	4	3.8%
Health Belief Model	3	2.9%
Self Determination Theory	3	2.9%
Social Cognitive Theory	3	2.9%
Study specific conceptual framework	3	2.9%
Programme theory	2	2.2%
Adult Learning Theory	1	1.0%
Authoritative Knowledge (AK) framework	1	1.0%
Behaviour Change Framework	1	1.0%
Cabanna et al. Framework	1	1.0%
Cognitive Interaction and Intimacy Model	1	1.0%
Cognitive Social Learning Theory	1	1.0%
Communication Accommodation (AK) theory	1	1.0%
Communication theory of Identity (CTI)	1	1.0%
Damschrod et al. Consolidated framework	1	1.0%
Diffusion of Innovation	1	1.0%
Duel Process Model	1	1.0%
Elaboration Liklihood Model (ELM)	1	1.0%
Engel's Biopsychosocial model	1	1.0%
Feminist theory	1	1.0%

Fiedman's Framework	1	1.0%
Fleuren et al. Framework	1	1.0%
Framework for dissemination	1	1.0%
Harm Reduction	1	1.0%
Health Literacy Framework	1	1.0%
Hulscher's implementation for change	1	1.0%
Implementation Model	1	1.0%
Macro cognition theory	1	1.0%
Models of Hoping	1	1.0%
Organisational Change Model	1	1.0%
Organizational Innovation Adoption	1	1.0%
Ottawa Decision support framework	1	1.0%
PARiHS framework	1	1.0%
PRECEED-PROCEED theory of behaviour change	1	1.0%
Program planning framework (Chen's)	1	1.0%
Reflexive Modernisation	1	1.0%
Social Network Theory	1	1.0%
System's Theory	1	1.0%
Total	**104**	

Appendix IV Flow diagram for critical review updated search outcomes (2018-2020)



Appendix V List of analysis codes

List of codes from the early stages of the reflexive thematic analysis for the narrative synthesis

Barriers to QRT	**Facilitators to QRT**
Feasibility of qualitative methods	Appropriate time and resources
Serendipity and flexibility	Expertise
Journal or reporting conventions	Training and guidance
Poor, separate or lack of reporting of QRT	Implications
Timing of reporting	Reporting
Lack of engagement from trial and site teams	Use of frameworks
Lack of guidance	Integration of approaches
Lack of or issues with integration	Maintaining rigour
Lack of or poor planning	Timing and purpose of meetings
Limitations on range and depth of methods and analysis	Trial oversight
Loss of qualitative integrity or quality	Multidisciplinary teams
Pragmatic stance to mixed methods	Methodological bilinguilism
Timing of qualitative research in relation to the trial limiting value	Patient and Public Involvement (PPI)
Use of quantitative paradigm on qualitative research	Qualitative researcher integrated into CTU
Weight and connection	Recognition of value
Blinding issues	Research community support
Contamination of trial arms	Roles and responsibilities
Increased patient burden	Adaptability and flexibility
Recognising difference between Patient and Public Involvement (PPI) and qualitative	Adaptability of approach and methods
Skills and experience	Clarity in planning including funding sourcing
Lack of guidance	Consideration of appropriate methods and sampling
Attitudes to qualitative research and perceived value	Consideration of depth of qual research required
Team composition and fragmentation	Documenting procedures e.g., protocol

Qualitative research undervalued or underutilised	'Fit' with trial
Funding issues	Timing
Poor planning	Prior experience or perceived value of QRT led to use
	Roles of institutions
	Journals
	Stakeholders TMG TSC
	Reporting to trial management and oversight
	Stages of integration or embedding
	Weighting and connection of trial and quali
	What does success look like

Appendix VI Case study interview topic guide

Interview Topic Guide V1.0 14.2.16

- **Preliminaries**: Remind participant of study background and interview process; re-confirm consent verbally.
    - **Verbal Consent – if agree start audio recorder**
        - You agree to our conversation being audio recorded?
        - You know you are free to stop the interview at any point and you may skip questions you would prefer not to answer?
        - You understand that quotations from the interview may be used to illustrate our findings, but it will not be possible to trace who said them?

- **Participant background:** Clinical/research/methodological background, experience of working on trials/qualitative research and mixed method RCTs, current role.
- **Case study trial:** Describe trial, trial design, intervention type (considered complex intervention?), disease area, outcomes. Funding body?
- **Qualitative research(s)**: Purpose, aims and objectives, design, methods, analysis. Linked with trial aims and objectives? Funding and resources. How funded – grant or good will? Adequate funding and resources? Funding requested and how funding used (data collection, meetings, reporting? Role of funders, application? Order of design, conduct.
- **Trial team**: who involved? Roles? Backgrounds – experience, clinical/research/methodology, PPI? Worked together before – how long? In what capacity?
- **Interviewees role in trial**. Role in overall trial? How involved in qualitative? Design, conduct reporting? Qualitative knowledge and experience – how prepared for trial? Training, literature?
- **Integration of qualitative members within whole team:** communication, meetings (together whole team, separate), how much involvement with other members of team. Weighting of team members in discussions and decisions, recognition of qualitative member's contribution to trial. Disagreements – types of disagreement (practical, epistemological), how managed – outcomes. Was there clear roles and expectations who was responsible for what?
- **Trial oversight**: TMG, DMEC, TSC – funding bodies? How qualitative viewed by committees, valued? Oversight of qualitative aspects? Conduct, data quality, safety, ethics. Qualitative researcher attendance at these meetings? How progress, issues etc. reported, by whom? Issues, worked well?
- **Ethics and governance:** how obtained, integrated or separate, issues, what went well? Amendments? Who responsible? How ethical issues dealt with?
- **Conduct of qualitative research:**
    - Sampling and recruitment. Who involved, how sampled, how participants recruited and consented (verbal/written)? Separate or integrated with trial?

Issues? Good practice?
    - Data collection: re-cap methods. Type of data collection – face to face, telephone, observations, documents? How collected, how data managed? Who involved?
    - Who collaborated with – issues, went well? Set up and conduct. Transfer of information?
    - Analysis: Re-cap approach and how conducted? Who involved? Iterative or deductive (both). Timing within trial – fed back to trial team?
    - Systems/software used – how and why used? Who had access?
    - Timing with trial: specific timing or alongside? Why? Issues, went well?
    - Theoretical framework? Any used? How – outcomes, benefits? Issues. Should such frameworks, underpinnings be used in trials? Why?
    - Were there clear expectations of what would happen, when and who would be responsible? How did know what to do? Protocol, analysis plans, SOPs?
    - Time taken to conduct qualitative: How long? Expected? Issues, went well? Any flexibility?
- **Integration of qualitative and quantitative data (collection, type) and analysis, reporting:** Was there integration? If not, why? Issues, barriers? If yes, how integrated? Facilitators, barriers? Who involved? Who took lead?
- **Reporting:** How reported – to funder, publications, dissemination? Integrated reporting? Why? Issues, went well? Rigor in reporting of qualitative/integrated?
- **Final reflections:** Is there anything interviewee would do differently? Future trials with qualitative – recommendations to others? What would help you in your role to design, conduct and report qualitative research in future trials?

End of topic guide.

Appendix VII Case Study interview participant information leaflet

Participant Information Leaflet
Interviews
(Version 1.2 03/02/2017)

EQUITY

Swansea University
Prifysgol Abertawe

Evaluating Qualitative research In Trials and their Yields (EQUITY)

We invite you to take part in a research study.

- Before you decide whether to take part it is important for you to understand why the research is being done and what it will involve.
- Please take time to read the following information carefully. Discuss it with someone if you wish.
- You are free to decide whether to take part in this study. If you choose to take part, you are free to withdraw at any point.
- Please feel free to ask the study researcher, Clare Clement (details below), if there is anything that is not clear or if you would like more information.

Important things that you need to know.

- We want to find the best way to include qualitative research within and alongside trials.
- We will be carrying out interviews to explore views and experiences of people involved in trials that include qualitative methods.
- Taking part in this study will not affect any other aspects of your current trials work.
- You can withdraw from the study at any time without explanation.
- This study is being carried out as part of a PhD study within the College of Medicine at Swansea University.

Contents

How to contact us?

If you have any questions about this study, please contact:

Lead Researcher (PhD student),
Xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

Or one of the supervisors:

xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

Why are we doing this study?

Qualitative research provides an in-depth understanding of behavior, action and interaction and the underlying reasons, opinions and motivations for these. There are many benefits to including this type of research within and alongside trials that have been documented. However, there are problems of consistency and transparency with the way these methods are planned, used and reported. Also, little is known about how the people and organisations involved influence the way this research is carried out. We would like to learn more about the role of qualitative methods in trials including the best way of carrying out this type of research, and how the people involved can influence this.

This study is being carried out as part of a PhD study being undertaken by Clare Clement in the Swansea University Medical School. The PhD is being supervised by xxxxxxxxxxxxx and xxxxxxxxxxxxxx also based at the Swansea University College of Medicine.

What is involved in this study?

This study will be carrying out an in-depth examination of three trials which have involved qualitative methods. These will be trials you have been involved in. We will be looking at:

- What is involved in planning and setting up trials with qualitative methods?
- How trials using qualitative methods are carried out throughout the whole process?
- What is involved when reporting trials that include qualitative methods?
- How people and organisations are involved in trials that include qualitative methods and what their influences might be?

As part of this study we will be interviewing researchers and health professionals who have been involved in these trials. A total of 15 people will be interviewed.

What would taking part involve?

Taking part would involve agreeing to participate in an interview with the PhD student and completing a consent form which you will need to sign ahead of being interviewed. This interview will last no longer than 45 minutes. The interview will take place either face-to–face or over the telephone, at your convenience. If face-to-face, they will be conducted either at Swansea University or at your NHS or work site. The interview will involve answering questions about your views and experiences of the qualitative methods in the trials you have worked on. It is entirely up to you which questions you answer and how much or how little you say. With your permission, the interview will be recorded and then transcribed for analysis purposes. The transcript will be anonymised. At the point of transcription all identifying information will be replaced with pseudonyms. You will be paid any 'out of pocket' expenses incurred.

What are the possible benefits of taking part?

By taking part you will be helping us to understand more about how best to develop, conduct and report on trials which involve qualitative research. You will be helping to develop guidelines which will ensure that the benefits of using qualitative research in trials are maximised and their full potential achieved. You will be able to voice your views on any matters arising and your views may have an impact on the way research is carried out in the future.

What are the possible disadvantages or risks of taking part?

We are aware you are a busy person and by taking part in this study you will be giving 45 minutes of your time. It is possible that during the interviews practices which may have put patients at risk may be identified. If this is the case, confidentiality may be breached to alert the trial oversight group to this risk. This will be with your permission. No other unforeseen risks have been identified.

Is there any further information?

What if I want to leave the study?

You can leave the study at any time. If you do want to leave the study you should contact the lead researcher, xxxxxxxx on xxxxxxxxxx or xxxxxxxxxxxxxxx . If you want to leave the study you will be asked whether you are happy for any data collected to continue to be used.

How will my information be kept confidential?

All information will be kept securely at Swansea University's Medical School on password protected computers and all files and folders will be also be password protected. All hard copy information will be kept secured in locked filing cabinets within Swansea University. All your contact details will be kept separately to any information you provide during the interviews. Only the lead researcher, xxxxxxxxxxx and one of the supervisors, xxxxxxxxx will have access to any information that can be directly linked back to you. xxxxxxxxxx does not have any direct involvement with any trials being looked at. At the point of transcription all names including your own and places will be replaced with false ones.

Who has approved this study?

This study has been reviewed and approved by Swansea University, the Research Ethics Committee and by Research and Development offices for the locality you are in.

How is this study funded?

Teaching fees for this PhD study have been provided by Swansea University. All other activity is self-funded by the Lead Researcher.

What will happen to the results of the study?

Results of the study will be submitted as part of a thesis for the lead researcher's PhD qualification. This thesis will be available within Swansea University's library through a controlled process. A summary of the research and its findings will be available online on the lead researcher's website. Once this is available you will be informed and sent a link to view this information. Articles from the study will also be submitted for publication in peer reviewed scientific journals. No information, which can be directly traced back to you, will be published in either the thesis, on-line summary, or published articles.

Can I speak to anyone who is not part of the study to discuss taking part?

Yes, you can contact xxxxxxxxxx who is aware of the study and understands what is involved but does not have any direct involvement or influence and is therefore impartial.

What do I do if I wish to make a complaint?

If you are unhappy about anything relating to this study, you can contact:

- The lead researcher, xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
- Supervisors, xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxx

Or if you would like to speak to someone outside of the study you can contact.

xxxxxxxxxxxxxxxxxxxxx

I would like to take part in the study, what do I need to do now?

You now need to let the researcher know you are happy to take part and complete the consent form which accompanies this information sheet.

Appendix VIII Case study interview consent form

Participant Consent Form
Interviews
(Version 1.2/3.2.17)

Swansea University
Prifysgol Abertawe

Evaluating Qualitative research In Trials and their Yields (EQUITY)

Participant ID: **Date:**

Please initial the box if you agree to the following statements. Please only initial those to which you agree:

1. I confirm that I have read and understand the **Information Sheet (version 1.2 3/2/2017)** for the above project and have had the opportunity to ask questions and have had these answered satisfactorily. ☐
2. I confirm that I have had sufficient time to consider whether or not I want to participate in the project. ☐
3. I agree to participate in an interview to discuss my views and experiences of the qualitative methods in the trials I have worked on. ☐
4. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without my legal rights being affected. ☐
5. I agree that the information provided can be used for educational and research purposes including publications and presentations. ☐
6. I have been assured that confidentiality of my information will be protected as specified by the information sheet and my data will be stored carefully. ☐
7. I agree to the interview being recorded and transcribed. ☐
8. I understand that data will remain anonymous and agree to the use of anonymised quotations being used in any study outputs. ☐
9. I understand that if a risk to patient safety is identified within the interview, confidentiality may be breached to address this. ☐
10. I agree to take part in the above project. ☐

Name of participant (printed)	Date	Signature

Name of person taking consent (printed)	Date	Signature

If you have any questions or concerns, contact
xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

Appendix IX Safety protocol information for case study interviews

There is the possibility that during an interview with participants issues of inappropriate trial conduct which may have put patients at risk may come to light, which require reporting to the clinical trials unit (CTU) involved (for example, serious breaches). To ensure the lead researcher (PhD student) is aware of what this may constitute she will undertake training in the [CTU] SOP 32: Standard Operating Procedure for Detecting & Managing Misconduct, Serious Breaches and Deviations of GCP/Protocol - with the [CTU] Unit Manager. If such an issue is identified the lead researcher (PhD student) will firstly discuss with supervisors, whether this does constitute a breach and if so, report it to the CTU who will then investigate as appropriate. This will be noted in the participant interview information sheet and consent form with option to agree to confidentiality being breached if a risk to patients to be added to the consent form. The lead researcher (PhD student) should also attend Good Clinical Practice training.

To ensure researcher safety, interviews will either be conducted at Swansea University or at National Health Service (NHS) premises where participants are located.

Appendix X Coding categories guiding pattern matching analysis

P1. The use of QRT depends on people understanding its value and having positive views and experiences of QRT.

Categories

- People's views and experiences of QRT (linked to use)
- Perceived value (or not) of QRT (linked to use)
- Understanding of QRT (linked to use)

P2. Tensions arising from methodological differences between qualitative and quantitative approaches (perceived or actual) and prioritisation of one set of methodological aims and outputs over the other will be ameliorated if the means to integrate processes and findings are negotiated and established a priori.

Categories

- Tensions arising from methodological differences between qualitative and quantitative approaches (perceived or actual)
- Prioritisation of one set of methodological aims and outputs over the other
- Integration of processes and findings

P3. Having researchers with qualitative expertise work collaboratively within multidisciplinary trial teams will lead to qualitative research being designed, planned and implemented well.

Categories

- Qualitative expertise in trial teams (evidence of and outcomes)
- Working collaboratively within trial teams (evidence of and outcomes)
- Relationships and tensions within the team
- Communication, meetings, and activities

P4. Reporting conventions which favour quantitative research and limited words and space for research articles will lead to a lack of or poor reporting of QRT.

Categories

- Reporting practices for QRT
- Potential influence of limited word counts/space

Appendix XI Example of question synthesis for quality checklist development

The following table outlines the questions or items from the existing appraisal tools that were used to develop the question for Section A of the EQUITY checklist. Common aspects of the questions/items were extracted, synthesised and used to develop the checklist questions.

EQUITY checklist question	**Questions/items included in existing appraisal tools from which the EQUITY question was developed**
Section A – Is the qualitative question, clear, relevant and linked to the trial?	CASP – Was there a **clear statement** of the aims of the research?
	RATS – **Research question explicitly stated** and Is **research question relevant** to clinical practice, public health, or policy?
	MMAT – Are **there clear research questions**?

Appendix XII Quality checklist for appraisal of publications reporting the use of qualitative research in trials: EQUITY checklist

Questions to ask of the publication about the qualitative research	Item number	Information to be included in the publication	Present Y/N (If it is unclear whether the information is included then select N)
A. Research question(s)			
Is the research question clear, relevant and linked to the trial?	1	Clearly stated research question.	
	2	Research question to be justified including stated relevance. Research question should be linked to existing knowledge base (this may be research, practice guidelines, theory, or policy)	
	3	Is the research question linked to the trial?	
B. Methodological approach			
Is a qualitative approach appropriate?	4	Clearly described study design and justification for why qualitative research was used.	
C. Appropriateness and transparency of data collection			
Is enough information about the study/trial context provided?	5	Description of study context including information about the trial. Reference to the trial should be made explicit.	
Are the participants selected appropriate to provide data relevant to study questions?	6	Description of how participants were selected and why.	
Was recruitment conducted using appropriate methods?	7	Description of how the participants were approached.	
	8	Description of how many participants took part and didn't take part.	
	9	Description of sample characteristics.	
	10	Clarify links between qualitative sample and trial participants.	
Was data collection appropriate and clearly reported?	11	Clearly stated data collection method.	
	12	Details of data collection materials and outline of content. E.g., interview, focus group, observation topic guides, questions.	

	13	Description of how data is captured. E.g., audio or visual recordings, field notes.	
	14	Description of the number and duration of data sets. E.g., number and duration of interviews, focus groups, observations.	
	15	Description of when and why data collection was stopped. E.g., was data saturation or other approach discussed.	
	16	Description of when data collection was conducted in relation to the trial and outcome measures. E.g., before, after trial, baseline trial outcomes, final trial outcomes.	
Have ethical issues been taken into consideration?	17	Clearly described informed consent processes.	
	18	Discussion of how confidentiality and anonymity have been considered.	
	19	Details of ethical approval.	
D. Appropriateness and transparency of analysis and reported findings			
Was the analysis approach appropriate and justified?	20	Clearly stated analysis approach.	
Are findings clearly reported and supported with appropriate evidence?	21	Description of how themes were derived from the data. E.g., deductive or pre-determined, inductive.	
	22	Adequate evidence to support reported findings.	
	23	Description of when the analysis was undertaken in relation to data collection.	
	24	Description of when the analysis was undertaken in relation to the trial e.g., was the data analyses before or after trial results were known?	
	25	Description of how data and analysis were managed. E.g., use of software.	
Has reliability and rigour of analysis and interpretations been addressed?	26	Discussion of whether and how analysis has been evaluated for reliability and rigour. E.g., member checking, double coding, how disagreements were resolved?	
Is there evidence of consideration for both qualitative and other trial data sets together?	27	Is there evidence of integration of qualitative and other data sets during analysis? E.g., use of triangulation protocol, joint displays, matrix approach	
	28	Discussion of the qualitative data set in relation to other data sets (quantitative etc.). This may be within the findings or discussion sections. e.g., qualitative findings are used to interpret/explain trial findings (or vice versa).	
E. Researcher(s) roles and reflexivity			
What are the characteristics of the researcher(s)?	29	Details of which author(s) conducted the study procedures. E.g., recruitment, data collection, analysis.	

	30	Details of the researcher(s) experience or training.	
	31	Details of potential influences of the researcher(s) on the study. E.g., bias, assumptions, interest in the study.	
What is the researcher's relationship with participants?	32	Description of any relationship established with participants prior to data collection.	
F. Discussion and implications			
Have findings been considered within the existing evidence base?	33	Is there adequate discussion about the existing evidence base and how the findings contribute?	
Has the trustworthiness and validity of the study been considered?	34	Discuss the limitations and strengths of the study.	
Has the potential influence of the trial on the interpretation of qualitative findings been discussed?	35	Discussion of the potential influence of the trial on qualitative findings. E.g., are there any limitations resulting from conducting the qualitative research within the trial context? This may be timing, sampling of trial participants, participant burden.	
Are study implications considered and made clear?	36	Clearly state the implications for different stakeholders. E.g., researcher inc. trialists, intervention developers, service providers, patients.	

Appendix XIII Quality checklist for appraisal of published protocols reporting the use qualitative research in trials: EQUITY-P checklist

Questions to ask of the publication about the qualitative research	Item number	Information to be included in the publication	Present Y/N (If it is unclear whether the information is included then select N)
A. Research question(s)			
Is the research question clear and relevant?	1	Clearly stated research question.	
	2	Research question to be justified including stated relevance. Research question should be linked to existing knowledge base (this may be research, practice guidelines, theory, or policy).	
	3	The research question is to be linked to the trial.	
B. Methodological approach			
Is a qualitative approach appropriate?	4	Clearly described study design and justification for why qualitative research was used.	
C. Appropriateness and transparency of data collection			
Is enough information about the study/trial setting provided?	5	Description of study context including information about the trial. Reference to the trial should be made explicit.	
Will the participants selected be appropriate to provide data relevant to study questions?	6	Description of how participants will be selected and why.	
Will recruitment be conducted using appropriate methods?	7	Description of how the participants will be approached.	
	8	Clarify links between qualitative sample and trial participants.	
Is planned data collection appropriate and clearly reported?	9	Clearly stated planned data collection method.	
	10	Details of planned data collection materials and outline of content. E.g., interview, focus group, observation topic guides, questions	
	11	Description of how data will be captured. E.g., audio or visual recordings, field notes.	
	12	Description of the intended number and duration of data sets. E.g., number and	

		duration of interviews, focus groups, observations.	
	13	Description of when data collection is planned to take place in relation to the trial and outcome measures. E.g., before, after trial, baseline trial outcomes, final trial outcomes.	
Have ethical issues been taken into consideration?	14	Clearly described informed consent processes.	
	15	Discussion of how confidentiality and anonymity will be considered.	
D. Appropriateness and transparency of analysis and findings			
Is the planned analysis approach appropriate and justified?	16	Clearly stated analysis approach.	
	17	Description of when the analysis is planned to be conducted in relation to data collection.	
	18	Description of when the analysis is planned to take place in relation to the trial E.g., will the data analyses be conducted before or after trial results are known?	
	19	Description of how data and analysis will be managed. E.g., use of software.	
Has reliability and rigour of analysis and interpretations been addressed?	20	Discussion of whether and how analysis will be evaluated for reliability and rigour. E.g., member checking, double coding, how disagreements will be resolved.	
Is there evidence of consideration for both qualitative and other trial data sets together?	21	Discussion of how the qualitative data set may be considered in relation to other trial data sets (quantitative etc.).	