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Using qualitative methods in pilot and feasibility trials to inform recruitment and retention processes in full-scale randomised trials: a qualitative evidence synthesis

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Abstract

Objectives To systematically review published pre-trial qualitative research studies and explore how their findings were used to inform recruitment and retention processes in full-scale randomised trials.

Design Qualitative evidence synthesis using thematic analysis.

Data sources and eligibility criteria We conducted a comprehensive search of databases; Dissertation Abstracts International, CINAHL, Embase, MEDLINE, Sociological Abstracts and Psycinfo. We included all reports of pre-trial qualitative data on recruitment and retention in clinical trials up to March, 2018.

Data extraction and synthesis Two authors independently extracted data using a predefined data extraction form that captured study aims, design, methodological approach adopted and main findings, including barriers and facilitators to recruitment and or retention. The synthesis was undertaken using Thomas and Harden's three stage thematic synthesis method and reported following the ENTREQ guidelines. Confidence was assessed using GRADE-CERQual approach.

Results Thirty-five papers (connected to 31 feasibility studies) from three different countries, published between 2010 and 2017 were included. All studies were embedded in pilot or feasibility studies to inform design aspects in preparation for a subsequent full-scale trial. Twelve themes were identified as recruitment barriers and three as recruitment facilitators. Two themes were identified as barriers for retention and none as retention facilitators. The findings from qualitative research in feasibility or pilot trials are often not explicitly linked to proposed changes to the recruitment and retention strategies to be used in the future or planned full-scale trial.

Conclusions Many trial teams do pre-trial qualitative work with the aim of improving, among other things, recruitment and retention in future full-scale trials. Just over half of all reports of

such work do not clearly show how their findings will change the recruitment and retention strategy of the future trial. The scope of pre-trial work needs to expand beyond looking for problems and also look for what might help and spend more time on retention.

Strengths and limitations of this study

- Our comprehensive search strategy optimises the likelihood that we have identified relevant studies published in the time period in principal journals.
- Although we did not apply a quality assessment checklist to individual included studies to consider the relationship between quality and maximising the value of pre-trial qualitative research, the systematic methodology and the use of GRADE-CERQual assessment of confidence in the findings is a strength of the review.
- The review was based on what was written in published research and this may not reflect the breadth of qualitative research that is undertaken in practice.
- Most of the included studies were UK-based, that means it is uncertain whether and to what extent the findings apply to the trial environment outside the UK.

Introduction:

Recruitment of participants to, and their retention in, randomised controlled trials (RCTs) is a key determinant of research efficiency, but both can be challenging (1). Reviews of clinical trials funded by the UK Medical Research Council (MRC) and the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme have shown that the proportion of trials achieving their original recruitment target was in the range of 31%–56%, and some suffered loss to follow up of up to 77% (2-4). Despite a substantial body of literature on strategies to improve recruitment and retention in clinical trials, the quality of this evidence is lacking (5-9). The Cochrane Review on strategies to improve recruitment to RCTs found only three interventions with a high Grading of Recommendations Assessment, Development and Evaluation (GRADE) rated evidence and the corresponding review on interventions to improve retention found no high certainty evidence (5,10).

Given the lack of certainty around effective strategies to improve recruitment and retention, trialists are increasingly integrating qualitative methods within randomised trials to unpack the complex processes involved (11,12). However, much of the qualitative work to date has been on intervention development and often done when the full trial is ongoing (13), which means it can sometimes be too late to prevent or rectify a problem that has already happened. In its framework for the evaluation of complex interventions the UK MRC strongly recommended that trialists use qualitative methods prior to running a full-scale trial to understand barriers to participation and to estimate response rates (14). Briel and colleagues suggested that 89% of obstacles leading to the discontinuation of RCTs could be avoided if issues were identified and addressed during the trial planning stages (15). Likewise, a recent thematic synthesis of 45 qualitative studies (16) exploring adult patients' experiences with RCT participation identified the diverse psychological, physical, and financial burdens experienced by patients across the whole process of the trial. The consideration of these modifiable factors at the pre-trial stage (i.e. research conducted or embedded with feasibility or pilot trials to inform trial design and conduct before recruitment to the full-scale trial starts)

, such as the volume, timing, complexity, or format of trial information or the organisation of patients' follow-up, could help to deliver more efficient RCTs and timely delivery of trial results (16,17).

Qualitative research conducted during the pre-trial stage could have a role in improving efficiency by identifying problems with recruitment or retention early and then suggesting solutions for the full-scale trial (18,19). O'Cathain and colleagues noted, however, that pre-trial qualitative research is underutilised, despite its potential to optimise trial design and recruitment (20). A recent meta-epidemiological study conducted to determine how often pilot studies planned to use qualitative data to inform the design and feasibility of a larger trial also highlighted that qualitative data collection was planned for in less than half of the protocols of pilot trials (92/227) in PubMed between 2013 and 2017 (21). A recent methodological review of 160 publications (123 protocols and 37 completed trials) on the reporting of progression criteria from external pilot trials to definitive RCTs reported that recruitment and retention were the most frequent indicators contributing to progression criteria (22). However, progression criteria were mostly reported as distinct thresholds (eg, achieving a specific target; 133/160, 83%) with less than a third of the planned and completed pilot trials that included qualitative research reported how these findings would contribute towards progression criteria (34/108, 31%).

The aim of this qualitative evidence synthesis (QES) was to explore how pre-trial qualitative research with trial participants, recruiters, clinicians, chief investigators and trial managers was used to inform recruitment and retention processes in full-scale randomised trials. Understanding how existing studies have employed qualitative methods at the pre-trial stage to inform recruitment and retention in future full-scale trials has the potential to identify how the value of pre-trial work could be maximised and highlight key aspects for others to focus on when considering this type of work.

Methods

This systematic evidence synthesis is reported in accordance with the Enhancing Transparency in Reporting the Synthesis of Qualitative Research (ENTREQ) statement (23) (See supplementary document 1). The protocol was developed but was considered outside of scope by PROSPERO as it does not address health outcomes. .

Search strategy

Searches were conducted on key electronic databases: Dissertation Abstracts International, CINAHL, Embase, MEDLINE, Sociological Abstracts, Psycinfo,SSCI (Social Science Citation Index), the Cochrane Library, Health Technology Assessment. The MEDLINE search strategy is included in supplementary document 2.

Different search strategies were used alongside electronic databases as using multiple search methods is more likely to locate relevant qualitative studies than relying solely on bibliographic databases (24). Methods applied included following up reference lists, hand searching and contacting experts or authors.

Inclusion/Exclusion criteria

Types of studies

We included all primary qualitative studies embedded in health-related feasibility or pilot studies. We also included studies using mixed methods if a clearly identifiable qualitative component was present. Qualitative studies that explored recruitment and/or retention issues in a feasibility or pilot study to inform a subsequent, fully powered, Phase III randomised trial were included. Pre-trial qualitative studies that indicated progress to a full-scale trial was not feasible due to poor recruitment were also included.

Participants

Stakeholders directly or indirectly involved in recruiting or retaining participants to RCTs (including chief investigators, trial managers, research nurses, participants, funders and research ethics committees).

Intervention/phenomena of interest

The body of research for which qualitative research was used to explore ways of optimising recruitment and or retention in RCTs at the pre-trial stage. All studies focusing on the perceptions and experiences of trial participants, recruiters, chief investigators and other trial stakeholders were included.

Evaluation

To identify perceived barriers and facilitators to recruitment and or retention and the changes made to inform the design of a definitive trial.

Study selection

Titles and abstracts were screened by two reviewers independently (AE reviewed all studies along with either ST or KG). The full-text of all studies appearing to meet the inclusion/exclusion criteria was obtained for further screening and assessment. These were then considered by two review authors to confirm inclusion with a third opinion being sought if necessary.

Data extraction

Two reviewers independently (AE extracted data from all the included studies along with either ST, KG or HB) extracted data from eligible full-text papers using a prespecified data extraction form that included study aims, design, methodological approach adopted and main findings, including barriers and facilitators to recruitment and or retention. This was piloted on

a subset of relevant studies and modified where necessary. All qualitative findings from the primary studies relevant to the research question were extracted. Findings were defined as any qualitative data describing a new concept, theme, sub-theme or finding statement, presented in forms including, but not limited to, text, tables, diagrams, supplementary files located anywhere in the paper.

Quality appraisal of included studies

The application of quality criteria to qualitative research is widely debated. In this QES we are not concerned with the methodological quality of the included qualitative work *per se* but its contribution to planning the future full-scale. We therefore defined quality as the contribution of the pre-trial qualitative research to the full-scale trial endeavour (recruitment and retention) and whether the findings were used explicitly (as reported in the publications) to inform the plan of action before moving onto a full-scale trial. The assessment of quality of the included studies against of a specific checklist was not applied.

Data synthesis

We followed the detailed methods for thematic synthesis outlined by Thomas and Harden (25). The thematic synthesis included three overlapping stages: line by line coding, developing descriptive themes, and generation of analytical themes. First, through a line-by-line coding process (AE) we developed 'free codes' (without hierarchical structure), this bank of codes grew as each paper was coded. We pre-specified and coded the results/findings and discussion sections covering the authors' interpretation of their data as well as any text reported as direct/verbatim participant quotes. Second, the open codes were organised into structured descriptive themes based on similarities and differences between codes. Third, three reviewers (AE, KG, KH) met to reach consensus on the codes and themes, with further interpretative discussion focused on the research question to generate analytical themes. Throughout the coding process, the review authors met regularly to cross-check newly

generated codes and themes against the data, discuss interpretation, and synthesise the analytical themes.

To assess the practical significance of pre-trial qualitative research, we looked at each paper to identify whether qualitative findings were linked to any proposed changes to the recruitment and retention plan of action for subsequent full-scale trials.

Assessment of the certainty in evidence

The Confidence in the Evidence from Reviews of Qualitative research (CERQual) approach was used to to assess our confidence in the review finding (26). The CERQual approach is based on four components which include: the methodological limitations of included studies, the coherence of the review findings, the adequacy of data contributing to the review findings and the relevance of the included studies to the review question.

Each review finding was assessed by two reviewers (AE, KG) and concerns regarding any of the four components were noted. Four levels were used to describe the overall assessment of confidence in a review finding- high, moderate, low or very low. All review findings started off by default as 'high confidence' and were then 'rated down' by one or more levels if there were concerns regarding any of the CERQual components.

CERQual assumes that qualitative research holds the potential to produce knowledge that can directly inform decision-making processes (27). Accordingly, and to fulfil the aim of this QES, it was important to assess how qualitative findings from each of the included studies were used to inform decision-making before the commencement of a full-scale trial. Simply put, we looked at the reported qualitative findings in each paper to identify whether each finding informed a particular change made to the recruitment or retention plan for the full-scale trial. Our judgement was one of "yes, no or unclear''.

For CERQuaL assessment, we had no concerns regarding methodological limitations and relevance for the body of data contributing to each review finding. Our goal was not to judge

whether some absolute standard of methodological quality had been achieved, but rather to indicate how and if findings from the qualitative research were transformed into an action plan to inform recruitment or retention processes for the full-scale trial. Considering that, a specific methodological quality checklist was deemed unnecessary as high or low scores would not affect our confidence in how and if qualitative findings informed the design of a subsequent full-scale trial. For the sake of brevity these two components were not included in the CERQual evidence profile.

Patient and public involvement statement

Patients and the public were not involved in the design, conduct, reporting or dissemination of our research.

Results

Thirty-five studies (connected to 31 feasibility studies) met the pre-specified inclusion criteria and were included in this QES. No additional papers were identified from reference searches, review papers or reports. Supplementary document 3 shows details of studies screened, excluded and included.

Characteristics of the included studies

All of the included studies were published in English between 2010 and 2017. All the included studies were conducted in three high-income countries: the UK (n=33), Canada (n=1) and Norway (n=1). Each study included between 10 and 69 participants, with findings from 917 people in total reported across the papers. Contributing to the sample were: trial participants (629, 69%), clinicians and recruiters (234, 26%), family carers (26, 3%) and members of the Trial Management Group (19, 2%). Supplementary document 4 details the characteristics of the studies included in the review.

The setting of the feasibility studies in which the qualitative research was embedded included a range of clinical contexts such as; cancer (n=11), mental health (n=5), obesity (n=3), sexual and reproductive health (n=3), chronic fatigue (n=2), musculoskeletal conditions (n=2), pain (n=2), incontinence (n=2), tooth decay (n=1), childhood intermittent exotropia (n=1), renal disease (n=1), non-adherence to medications (n=1) and appearance-related distress (n=1). As expected, the clinical context differed as did the interventions under investigation; two studies (28,29) were Clinical Trials of an Investigational Medicinal Product (CTIMP) and 29 were non-CTIMP studies .

All the included studies were embedded in pilot or feasibility trials to inform design aspects in preparation for a subsequent full-scale trial. The main data collection and analysis methods used were interviews (n = 31; 88%) and thematic analysis (n = 25; 71%). Audio recording of recruitment consultations and non-participant observations of consultations were used in six of the included studies (30-35).

Findings

Twelve themes were identified as recruitment barriers and three as recruitment facilitators, whereas only two themes were identified as barriers for retention and none as retention facilitators (Table 1). The findings from the included studies focused more on recruitment than retention and researchers tended to focus on problems (barriers) rather than what might help (facilitators). The link between pre-trial qualitative findings and proposed changes to the recruitment and retention strategies to be used in any future full-scale trial were not always clear (Table 2).

The findings that led to the identification of the barriers and facilitators highlighted in Table 1 and their link to the proposed changes for the full-scale trial summarised in Table 2 are presented below in more detail.

Table 1 Summary of findings for themes linked to recruitment and retention barriers and facilitators.

	Barriers	Facilitators
Recruitment	1- Lack of clarity or understanding of randomisation	1- Personal gain and making a difference
	2- Lack of clinical equipoise	2- Communicating study information
	3- Strong patient treatment preferences	3- Social networks and experience of research
	4- Issues related to the control group	
	5- Communicating study information and associated terminology	
	6- Issues around the eligibility criteria	
	7- Practical barriers	
	8- Commitment of staff and participants to the trial	
	9- Beliefs and expectations about trial participation	
	10- Mismatch between the trial protocol and clinical care pathways	
	11- Participation burden	
	12- Lack of confidence in approaching study participants	
Retention	1- Burden of follow-up questionnaires	None identified
	2- Practical barriers	

Table 2 The link between qualitative findings and changes proposed to recruitment and retention for the full-scale trial for each barrier and facilitator.

Barriers (number of studies contributing to the review finding and percentage relative to the total number of included studies)	Were there any changes planned for the full-scale trial based on pre-trial qualitative data? (Yes, Unclear, No, number of studies and percentage relative to the number of studies contributing to the review finding	Facilitators	Were there any changes planned for the full-scale trial based on pre-trial qualitative data? (Yes, Unclear, No)

Recruitment	1- Lack of clarity or understanding of randomisation (n=6/35[1] (17%))	Yes (3/6 (50%)) Unclear (n=2/6 (33%)) No (n=1/6 (17%))	1- Altruism and personal gain (n=5/35[1] (14%))	No changes reported	
	2- Lack of clinical equipoise (n=12/35 (34%))	Yes (n=5/12 (42%)) Unclear (n=4/12 (33%) No (n=3/12(25%))	2- Communicating study information (n=7/35 (20%))	Yes (n=1/7 (14%)) No (n=6/7 (86%))	
	3- Strong patient treatment preferences (n=9/35 (26%))	Yes (n=4/9 (44%) No (n=5/9(56%))	3- Social networks and experience of research (n=2/35(6%))	No changes reported	
	4- Issues related to the control group (n=4/35 (11%))	Yes (n=4/4 (100%))			

[1] There were 35 included studies in total.

5-	Communicating study information and associated terminology (n= 8/35(23%))	Yes (n=5/8 (62%)) Unclear (n=2/8 (25%)) No (n=1/8 (13%)
6-	Issues around the eligibility criteria (n=6/35 (17%))	Yes (n=4/6(66%)) No (n=2/6 (34%))
7-	Practical barriers (n=12/35 (34%))	Yes (n=5/12 (42%)) Unclear (n=4/12(33%)) No (n=3/12 (25%))
8-	Commitment of staff and participants to the trial (n= 2/35(6%))	Yes (n=1/2 (50%))

	No (n=1/2 (50%))
9- Beliefs and expectations (n= 10/35(28%))	Yes (n=6/10 (60%))
	Unclear (n=1/10(10%))
	No (n=3/10 (30%))
10- Mismatch between the trial protocol and clinical care pathways (n= 4/35(11%))	Yes (n=2/4 (50%))
	Unclear (n=2/4 (50%))
11- Participation burden (n= 4/35 (11%))	Unclear (n=3/4 (75%))
	No (n=1/4 (25%))
12- Lack of confidence in approaching study participants (n= 2/35(6%))	Yes (n=1/2 (50%))

		Unclear (n=1/2 (50%))	
Retention	1- Burden of follow-up questionnaires (n= 9/35[1](26%))	Yes (n=5/9 (56%))	None identified
		Unclear (n=2/9 (22%))	
		No (n=2/9(22%))	
	2- Practical barriers (n= 2/35(6%))	Unclear (n=1/2 (50%))	
		No (n=1/2 (50%))	

Barriers to recruitment

A total of 12 recruitment barriers were identified. Supplementary document 5 outlines the findings associated with each theme and their link to the proposed changes for the full-scale trial.

1. Lack of clarity or understanding of randomisation

Six studies (32,36-40) outlined the influence of randomisation as a major barrier to recruitment. The concept of randomisation was often not clear or perceived haphazardly and some participants struggled to understand the need for randomisation (19,37). Despite explaining random allocation, some participants were still uncertain whether they would be selected based on some personal or illness characteristics (19,40).

> *"How do they choose? Say, likes of five will go for the test and five will'nae, how do they actually choose?' (Male 64, Darnley)'* (36)

Link between randomisation findings and changes proposed for the full-scale trial

The changes planned before the full trial to deal with issues around clarity of the randomisation process were clearly linked to coded data in three of the six studies (32,38,41). To clarify the concept of randomisation, one study reported that randomisation will be explained to participants in the following way: ''To try and make sure both groups are the same, each person is put into a group at random. This is the fairest way of deciding who gets the test and means everyone will have a 50/50 chance of being put in either group'' (41). In other cases, randomisation period was simplified and clarified and recruiters were encouraged to elicit patients' lay views and explain that randomisation offered a way of resolving the dilemma of treatment choice (32,35).

Two studies reported changes that were not explicitly linked to the qualitative findings (37,40). In one study, authors suggested that the focus would be on training trialists who are involved in recruitment to complicated trials, both in terms of communication processes and on the assimilation of complex trial pathways (37). To resolve misunderstanding about the process of random allocation, one study reported that the study team needs to spend more time at participating practices training them in the recruitment process; patients should be supported to take the necessary time to ensure understanding of patient information sheets before signing consent (40).One study reported no changes to address lack of understanding of randomisation (39).

2. Lack of clinical equipoise

Twelve studies outlined the influence of lack of clinical equipoise as a major barrier to recruitment (32-34,37,38,42-48). Recruiters and clinical staff found it difficult to maintain equipoise as interviews revealed treatment preferences for certain subgroups of patients and this affected not only the number of individuals approached and invited but also the number of randomised participants (30,44,45,47,49). In many cases the explanation of the lack of evidence underlying the effectiveness and timing of intervention served to undermine the participant's confidence in the treating clinician, and by extension, the trial (43,46).

Audio recording of recruitment consultations revealed that the terminology used created unbalanced presentations of treatment options for which one treatment was presented at greater length and more favourably than the other and this was a strong indicator for the lack of trial equipoise (30,32,34,38,43,49).

> *''I share the concerns and doubts that many of the patients do, i.e. that it won't work and it's difficult to sell a treatment when you yourself don't really believe it's going to make any difference''. Principal investigator 4* (43)

Link between clinical equipoise findings and changes proposed for the full-scale trial

Changes planned before the full trial to maintain clinical equipoise were explicitly linked to qualitative data in six studies (30,32,33,44,46,48). Changes reported were: Feedback sessions to be used to make recruiters aware of instances where they inadvertently used loaded terminology (30), asking recruiters to gently challenge and acknowledge their own bias in device preference (44), highlighting the need for principal investigators and recruiters to think more critically about the concept of scientific equipoise and how that should underpin the RCT (33), separation of the role of the treating clinician from the main recruiter to the trial (46), changing the order in which the treatments were presented and to describe their respective advantages and disadvantages in equivalent detail (32), training and monitoring of trial personnel to ensure notions of equipoise are delivered and reinforced consistently (48).

Three studies suggested changes to maintain clinical equipoise but were not clearly linked to qualitative data (37,43,45). These changes involved providing frequent and comprehensive training to recruiters (37,43) and finding ways of enabling practitioners to engage with study procedures (45). In three studies, no specific changes were reported to maintain clinical equipoise (34,38,47).

3. Strong patient treatment preferences

Stated treatment preferences was a theme in nine studies (32,38,39,42,43,46-49). Recruitment was hampered by strong preferences with patients often wanting the intervention and then expressing disappointment at being allocated to the control group (30,39,43,46-48). Non-equivalence of the treatment processes was also a common perception among recruiters, and they were convinced that many patients opted for one treatment because it was perceived as more convenient (49). In two studies (32,33), patients came with media information that was

biased in favour of the intervention (radical treatment) and often expressed lay views that cancer should be removed.

> *"I still think to leave everyone, if you told in that group 'right half of you are going to go to physio [therapy] and half advice.' I think wouldn't you feel a little bit jipped, knowing 'wait a minute how come I'm not going to get anything'?" (patient A)* (48)

Link between treatment preferences findings and changes proposed for the full-scale trial

The changes proposed before the full trial to address patient treatment preferences were clearly linked to qualitative data in four studies (42,43,46,49). Changes reported were: recruiters were asked to move beyond initial probing questions in relation to patient preferences toward rectifying any erroneous views and to ask patients who appear to have a preference to 'keep an open mind' until they had heard all the relevant information (42), the need to gently challenge preferences that are based on inaccurate information and training recruiters to enable them to explain the need for randomisation and the rationale for the RCT to patients (49) and the incorporation of a preference arm in a future trial to account for parental preferences (46).

In five studies, no specific changes were reported to account for strong patient treatment preferences (32,38,39,47,48).

4. Issues related to the control group

Lack of understanding the rationale for having a control group was a dominant theme that was identified in four studies (32,36,40,48). Some participants struggled with understanding the need for a control group and said that allocation to the control arm of the study would put them off

from participating (36). The perceived inequity in the content of the control arm was a major barrier to recruitment as some patients felt that they would not receive the best treatment if they were allocated to standard care (40,48). In one study, the presentation of the control arm caused difficulties for both patients and recruiters with the potential for interpretation as 'no treatment' (32).

> *"Participant: Aye. If I was one of the 50% when they said, "Right, we're gonna take a sample from you and test it", then yeh, but if I was one of the 50% that didn't get picked (the control group), then no. I would rather not know, actually. No." (Patient 63)* (36)

Link between control group findings and changes proposed for the full-scale trial

The changes proposed before the full trial to address the issues related to the control group were clearly linked to qualitative data in all four studies (32,36,48). The changes reported were: modification of the Participant Information Leaflet (PIL) where the control group will be changed to non-test group, which is what participants were most comfortable with (36), giving participants the necessary time to ensure understanding of patient information sheets before signing consent, especially with regard to clinical equipoise and that they will not necessarily benefit from participation (40) and augmenting the content of the control arm so that the trial arms could be perceived as more equitable (48).

5. Communicating study information and associated terminology

Presentation of trial information was a major barrier to recruitment and this was evident in eight studies (32,34,37,43,50-53). In many cases, patients failed to understand the language of trial procedures or interpreted trial and clinical terminology quite differently than as intended by practitioners (for example, 'trial' was interpreted as 'try and see') (30,32,37). In other cases,

recruiters and investigators agreed that the trial was difficult to explain and indicated that they found the quantity and content of trial information problematic (30,51). There were also cases where study documentation were perceived as long, difficult to understand or repetitive in places and this affected decision making (34,50). In the study by Griffin (2016), graphic description of surgery was thought to have put patients off randomisation and surgeons tended to go beyond their protocol brief, to explain the trial rather than referring patients on to the trial recruiter for this information (43).

> *''There's always a risk from the traction that it may stretch the nerves down the leg, so that could leave you with some numbness. If you're very unlucky it could leave you with a little bit of weakness there''. Principal investigator 4* (43)

Link between communication findings and changes proposed for the full-scale trial

The changes proposed before the full trial to address the problems related to the communication of study information and associated terminology were explicitly linked to qualitative data in five studies (32,34,50,52,53). The changes reported were: changing the order in which the treatments were presented and describing their respective advantages and disadvantages in equivalent detail (32), construction of a simpler version of the study flowchart and drafting a new, shorter and clearer participant information sheets which removed the 'loaded' terminology (34,52).

Two studies suggested changes to improve trial presentation but were not clearly linked to qualitative data (37,43). These changes involved providing frequent and comprehensive training to recruiters on the assimilation of complex trial pathways (37,43). In one study, no specific changes were reported to address this barrier (51).

6. Issues around the eligibility criteria

Another recurring theme that hampered recruitment efforts was the complexity trial staff faced in applying the eligibility criteria, which appeared in six studies (35,46,47,49,53,54). In some cases, interpretation of the eligibility criteria differed between centres; there was less clarity over the minimum age for recruiting participants to the study and recruiters thought there was leeway for interpretation of the inclusion/exclusion criteria in partnership with the trial team (33,38,47,54). In other cases, highly restrictive eligibility criteria and the difficulty to confirm eligibility for the trial at the initial screening visits hindered recruitment efforts (46,53).

> *I personally don't have a problem (with applying the eligibility criteria), but that's because I deal with trials all the time (...), but I think with some of my colleagues, both juniors within oncology and colleagues in surgery are not as familiar with trials, maybe have a little more difficulty in interpretation (Oncologist, Recruiter).*(38)

Link between eligibility findings and changes proposed for the full-scale trial

The changes proposed before the full trial to address the problems related the complexity of applying the eligibility criteria were clearly linked to qualitative data in four studies (46,47,49,54). The changes reported were: running screening training exercises to ensure similar screening standards and practices and an 'assumed eligibility' approach in all centres (47), close examination and regular meetings to discuss and resolve evolving issues (49) and considering a limit on the upper age at which participants would be included (46). Two studies reported no changes to address this issue (35,53)

7. Practical barriers

Practical barriers to recruitment was a major recurring theme in twelve studies (29,43,45,46,50,51,53,55-59). Commonly cited barriers were: difficulty in implementing

procedures owing to the multi-centre nature of the pilot (43), barriers of the primary care environment (55,56) (time-limited consultations, high workload and competing studies), widespread reluctance in practice to forgo written consent procedures at the time of trial enrolment (60), staffing issues (staff attrition, insufficient time, sub-optimal use of skill-mix) (45,57-59) and delay in recruitment appointments (46).

> *'I then had a full caseload, so I wasn't taking on any new patients for quite a long time. […] We've had the consultants doing first visits and I would follow on afterwards because we've been so short staffed'. (N02cSE)* (59)

Link between practical barriers findings and changes proposed for the full-scale trial

The changes proposed before the full trial to address practical barriers were clearly linked to qualitative data in five studies (29,50,51,53,57). The proposed changes included allowing flexibility in terms of how and when the research was conducted (50), ensuring that future trial centres are allocated adequate time and personnel (57), advising practitioners that patients will require longer appointments than normal for involvement in the trial (51).

Four studies reported changes to address this barrier but these were not clearly linked to qualitative data (43,45,46,58). No changes were reported in three studies (55,56,59).

8. Commitment of staff and participants to the trial

Variable commitment by both participants and staff to the trial was a major barrier to recruitment in two studies (35,59). Recruiters believed that some trial members were very committed to the trial but others were less dedicated or even antagonistic to it, and this contributed to the development of strong patient treatment preferences to one arm or the other (35). In other

cases, recruitment of fewer than anticipated dyads affected nurses' commitment and the priority given to the trial (59).

> *''when we were doing the training it's just right there. And then it slips to tenth place. And if you haven't recruited, it's twentieth place because you're doing this, this and this'. (Nurse, recruiter)* (59).

Link between staff commitment findings and changes proposed for the full-scale trial

The changes proposed before the full trial to address variable commitment by both participants and staff were clearly linked to qualitative data in one study (35) where clinical centres were asked to identify two Lead Recruiters (LRs) per site whose responsibilities would be to act as the focus for trial recruitment activity. The remaining study reported no changes to account for this barrier (59).

9. Beliefs and expectations about trial participation

Pre-existing beliefs and expectations amongst recruiters and study participants hindered recruitment efforts in ten studies (33,36,37,40,44,53,55,57,59,61).

Participants' beliefs that undermined involvement in the trial process were: feelings of anxiety about a poor medical outcome and scepticism about being experimented on (40,61), negative image about the hospital 'a place to die'(49), social desirability perception that the trial was designed to encourage people to stop smoking (40,41), feelings of isolation and powerlessness (37) and a sense of denial (participants tended to deny their symptoms and therefore were ineligible) (53). In other cases, nurses believed they needed to protect patients from additional burden (which implicitly they believed the trial would cause) and this was cited as a main recruitment barrier (59).

'I felt quite uncomfortable [introducing the study] sometimes, because I knew it was going to add to the burden of everything else that they were doing'. (Nurse, recruiter) (59)

Link between beliefs and expectations findings and changes proposed for the full-scale trial

The changes proposed before the full trial to address pre-existing beliefs and expectations were clearly linked to qualitative data in six studies (36,40,44,55,57,61). The changes proposed included asking recruiters to gently challenge patients' preconceptions (44) and to wait until the patient's condition is more settled before providing appropriate written informed consent (61).

One study reported changes which were not explicitly linked to coded data (37). In three studies, no specific changes were planned to address these issues (33,53,59).

10. Mismatch between the trial protocol and clinical care pathways

Integrating the trial into clinical practice was considered a particular challenge hindering recruitment in five studies (42-44,48,52). In some cases, the trial was presented as an 'add-on' rather than an integral part of existing clinical services (30,43). In other cases, the pathway that potential participants had to follow from diagnosis to being recruited to the trial proved extremely complex (35).

''I think what we didn't appreciate was the number of the different pathways with which people actually come into that system, and the complexity (...) in terms of the treating centres and the randomising centres and all the different centres that are involved in an individual patient's care (Investigator)'' (35).

Link between integration findings and changes proposed for the full-scale trial.

The changes proposed before the full trial to account for poor trial integration into clinical care pathways were clearly linked to qualitative data in two studies (42,52). Clinicians were asked to mention the study in the opening statements of the surgical consultations and to express enthusiasm for the study (42).

Two studies proposed changes that were not explicitly linked to coded data (43,44). These involved providing frequent and comprehensive training to recruiters (43) and recruiting a trial Champion to encompass coordination and facilitation of appointments and communication (44). One study reported no changes to account for this barrier before the full trial (48).

11. Participation burden

The burden imposed by participation in the trial was a prominent theme in four studies (29,36,37,46). The experience of completing and signing a consent form at the time of enrolment was burdensome in one study (29). In two studies, limited appointment time for the initial screening and the need for flexible appointments presented a challenge for participants to fully consider participation in the trial (36,46). In the study by Moynihan (2012), patients commented on how poor administration and the need to 'work' their way around NHS waiting times prevented them from being fully included in the trial enterprise (37).

> *"Well, your appointments would have to be flexible, because people are still working. Not myself, I'm retired, but there are always people working who might not be able to get time off work." (patient 64,)* (36)

Link between participation burden findings and changes proposed for the full-scale trial

The changes proposed before the full trial to account for participation burden were not clearly linked to qualitative data in three studies (36,37,46). The changes proposed included facilitating

a context in which patients feel fully included in the trial enterprise (37), separation of the role of the treating clinician from the main recruiter to the trial (46) and providing a phone call to potential participants to discuss the study after anticipated receipt of the full PIL (19).

One study reported no specific changes to address this barrier (29).

12. Lack of confidence in approaching study participants

Lack of confidence in approaching study participants or the topic of interest hindered recruitment in two studies (43,55). In one study (43), time lag between recruitment clinics posed a challenge for research staff to preserve confidence and knowledge about the study. Research staff also showed their concerns about not being able to respond to patients' questions and ask for consent without a senior clinician or surgeon signing the form for them (55).

> *"The gaps can be quite big between the patients, so I go back to my notes and reread everything again just before I'm going to see them so it's fresh in my mind because otherwise you're likely to forget". (R3)* (43).

Link between 'lack of confidence in approaching participants' findings and changes proposed for the full-scale trial

The changes proposed before the full trial to account for the lack of confidence in approaching study participants were clearly linked to qualitative data in one study (55). The study highlighted the need for training primary care staff to broach the topic of a visible difference confidently (they appeared to lack confidence in raising the sensitive issue of appearance-altering conditions and adopted strategies to avoid mentioning the topic), both within and outside the research parameters.

For the remaining study reported changes were not clearly linked to qualitative data (43). The study proposed providing frequent and comprehensive training to recruiters and modifying the support to teams in other centres according to their research experience.

Facilitators of recruitment

A total of three recruitment facilitators were identified. Supplementary document 6 outlines the findings associated with each theme and their link to the proposed changes for the full-scale trial.

1. Personal gain and making a difference

Potential participants' sense of obligation and altruism was a major factor that impacted positively on their decisions to participate in five studies (47,54,55,61,62). Altruism was often cited as an important motivating factor, contributing to improved care for others in the future (47,54,61,62). In other cases, participants were motivated by having a personal interest in the topic and perceived that research may bring direct personal benefit (54,55,61).

> *'I know that's sort of a I´ thing to say, but it's true, I mean I'm not try'..., for sympathy, but I have had a terrible time, and I don't want other people to have it like, if you know, if I have children I wouldn't want them to have go through that I went through, and um, in generally I just, you know, want to take part in it for other people.'(M006)* (62)

Link between altruism findings and changes proposed for the full-scale trial

No changes were reported in the five studies to take advantage of the conditional altruism expressed by participants and its potential impact on recruitment before the full-scale trial starts.

2. Communicating study information

Providing clear and informative study information to potential participants was an important facilitator for recruitment in seven studies (31,34,47,50,61,62). In many cases, providing clear and informative study information and ensuring study participants had a thorough understanding of the study were important factors to facilitate a decision about taking part (34,47,50,61,62). In the study by Realpe, a logical sequence for information sharing (six step recruitment model) emerged after analysis of recruitment consultations and this seemed to facilitate recruitment (31).

> *''So everything was really well explained you know, so yeah I mean I can't fault it really, no I was well impressed with it all''. (Participant 25)* (47)

Link between information communication findings and changes proposed for the full-scale trial

The changes planned before the full-scale to take advantage of providing clear study information were reported in only one study (31). The study proposed a six-step recruitment model (specifying: explain the condition, reassure patients about receiving treatment, establish uncertainty, explain the study purpose, give a balanced view of treatments, and explain study procedures) to train and support recruiters in the large number of new centers in the full-scale trial.

3. Social networks and experience of research

Patients' social networks and positive experience of research helped to promote study participation in two studies (61,63).

> *'So, I think because a lot of them are friends here, so they talk, and, you know, if you're doing that, "What do you think about it?" So, they ask each other.…Cause a lot of things happen that way here, cause they listen to what other patients talk to nurses about, then they think, "Oh, okay, I'll try that, too"'. [participant?]* (63)

Link between networks and experiences findings and changes proposed for the full-scale trial

No changes were reported in the two studies that identified social networks as influential for recruitment before the full-scale trial starts.

Barriers to retention

Two retention barriers were identified. Supplementary document 7 outlines the findings associated with each theme and their link to the proposed changes for the full-scale trial.

1. Burden of follow-up questionnaires

Nine studies outlined that the burden of follow-up questionnaires was a major barrier to retention (34,39,40,47,53,56,64-66). Across a variety of contexts, questionnaire structure was perceived to be burdensome and this encompassed many forms: forced choice responses of questionnaires which did not capture the reality of patients' experiences (56), lack of clarity and difficulties with some of the wording in the questionnaires (40,64), repetitive and difficult-to-complete questionnaires (65,66). In two studies, the timing of questionnaires was perceived to be burdensome and irrelevant because it did not allow time for change when many patients had few, if any symptoms to report (34,47).

> *"I didn't understand a lot of the questions so she [researcher] was having to interpret them . . . and that probably it probably went longer than what it should have done. (Participant?)"* (56)

Link between questionnaire burden findings and changes proposed for the full-scale trial

The changes proposed before the full trial to address the burden of follow-up questionnaires were clearly linked to qualitative data in five studies (39,47,53,64,65). The changes reported involved modifying questionnaires to allow 'short-cutting' of irrelevant areas to reduce respondent burden (47), reducing the number of questionnaires in the subsequent trial (53) and training fieldworkers in assisting participants with questionnaire completion if required (64).

In two studies, changes reported were not clearly linked to coded data (34,66). These involved identifying measures to improve outcome data collection using a variety of strategies. Two studies reported no changes to address this barrier (40,56).

2. Practical barriers

Practical issues appeared to hinder participant retention in two studies (39,40). Some participants reported that making journeys required considerable effort (39,40). A small minority of patients found the process of getting a chest X-ray difficult. Some participants had to pay for the parking costs and using public transport seemed to be too problematic (40).

Link between practical barriers findings and changes proposed for the full-scale trial

One study reported changes to account for practical barriers but were not clearly linked to qualitative data (40). The study reported that patients should be reassured that participation in the trial should cause them the least amount of inconvenience. One study reported no changes to address practical barriers (39).

Facilitators for retention

There were no facilitators for retention reported in the included studies.

GRADE-CERQual assessment

The CERQual Evidence profile is presented in supplementary documents 8 and 9 which highlights each review finding along with its CERQual assessment.

Discussion

Embedded qualitative investigations to examine and address key uncertainties with respect to recruitment and retention prior to a full-scale trial have increased in the last decade. This systematic qualitative evidence synthesis was based on findings from 35 studies and its aim was to explore how the findings of qualitative research methods at the pre-trial stage were used to make changes to the recruitment and retention plan of the future full-scale trial.

Most of the included studies reported changes that would be made to the recruitment and retention plan for the full-scale trial based on pre-trial qualitative findings. However, in many cases, the link between the changes proposed for the full-scale trial and the pre-trial qualitative findings was not explicit. This was the case in nearly 50% of the included studies, meaning that capitalising on the value of pre-trial qualitative research when reporting these studies was not clear despite findings suggesting there was a problem that needed to be addressed. This might be because of limited article word count in papers reporting the results of the qualitative work alongside the pilot trial results, where very little space was allocated to the qualitative component and its impact was usually reported rather than demonstrated. It could also, of course, be because the proposed changes were not related to the pre-trial qualitative findings. It is impossible to tell from many published reports.

The review highlights the potential benefits of qualitative research at the early stages of the research continuum, not just in identifying barriers and facilitators to recruitment and retention during the feasibility work but also in informing the plan of action before the commencement of a full-scale trial. The changes reported to address recruitment barriers included changes to clarify the concept of randomisation to study participants, to maintain clinical equipoise, to address issues with patient treatment preferences and changes made to the study design to resolve issues related to the control group. Other changes were reported to ensure clarity around the eligibility criteria, to address practical barriers, to facilitate effective communication of study information and associated terminology and to promote assiduousness of recruiters. The changes reported to address retention barriers centered around identifying ways to ease the burden of follow-up questionnaires and to address practical barriers.

The systematic synthesis identified an assortment of recruitment barriers (n=12) but only two identified barriers to retention. There were only three facilitators for recruitment, and there were no facilitators for retention. The findings of included studies tended to focus more on the challenges to recruitment and retention rather than the facilitators. Perhaps researchers are instinctively more interested in what is not working well (the barriers) and trying to make changes to remove those barriers. However, it is also important for researchers to take advantage of what facilitated recruitment and retention at the pre-trial stage and to ensure 'what worked well' stays working well in the full-scale trial and that should be reflected in the reporting.

Of the three recruitment facilitators identified, only one study (53) explicitly reported how these facilitators would be used to improve the recruitment process in the subsequent full-scale trial. It is hard to believe that there are no facilitators for retention in the included studies; perhaps researchers were not looking for, or reporting, this. The focus on recruitment may have meant that retention was overlooked, something that is in line with findings from a qualitative interview

study with stakeholders from five trials (95). The study identified that extensive work on recruitment targets was deemed detrimental to retention activities and highlighted the need for efficient training and support for trial staff involved in retention practices and a wider recognition of the importance of retention from funding organisations (67).

Quality of the evidence and certainty of the findings

Since the main aim of this qualitative evidence synthesis was to explore the practical utility of using qualitative research methods at the pre-trial stage with the aim of maximising the chances of recruitment and retention success in a future full-scale trial, CERQual assessment of the overall confidence in the evidence was applied to assess whether qualitative findings were used to inform changes to the recruitment and retention plan. We considered a little less than half of the findings as of high certainty because the findings showed high levels of coherence and adequacy, while we assessed the remaining findings to be of moderate certainty because of concerns regarding both the coherence of the findings and the adequacy of data in the underlying studies. This means that for over half of the included studies, the contribution of pre-trial qualitative research to the decision-making process and how it informed recruitment and retention processes for any subsequent full-scale trial was not explicit.

Limitations and strengths of the review

This qualitative synthesis brings together the evidence-base of barriers and facilitators to recruitment and retention identified in pre-trial qualitative work together with an assessment of the practical utility of pre-trial qualitative research in informing the recruitment and retention plan before the commencement of a full-scale trial. The comprehensive search strategy optimises the likelihood that we have identified all relevant studies published in the time period. Although we did not apply a quality assessment checklist to individual included studies to consider the

relationship between quality and maximising the value of pre-trial qualitative research, the systematic methodology and the use of GRADE-CERQual assessment of confidence in the findings is a strength of the review (68).

There are however limitations. The review was based on what was written in published research and this may not reflect the breadth of qualitative research that is undertaken in practice. Every effort was made to contact corresponding authors to obtain a full account of qualitative data where information was lacking in the published report, or when researchers reported that a stand-alone article based on qualitative research will be published separately but was not yet available. However, not all authors provided these data, in which case it means the synthesis was limited to the findings and quotes published in the qualitative reports. Of the 35 included studies, 33 were UK based (the other two were conducted in Canada and Norway) and this resonates with the fact that both recruitment and retention are among the top three methodological research priorities in the UK (69). It does, however, mean it is uncertain whether and to what extent the findings apply to the trial environment outside the UK.

Suggestions for good practice and maximising value

While pre-trial qualitative research can be very illuminating in identifying barriers and facilitators to recruitment and retention, researchers need to clearly report how and if the findings from the qualitative research will be used to optimise their recruitment and retention approaches in the full-scale trial. This qualitative evidence synthesis highlights the inefficient use of pre-trial qualitative research; despite identifying an assortment of barriers to recruitment or retention, researchers failed, in most cases, to articulate how their qualitative findings would be put into a clear action plan to optimise the conduct of a future full-scale trial. The key issues identified by qualitative research need to be discussed with trial stakeholders and used in support of making

practical changes to the trial design, presentation, or amendments to the study protocol and that should be made explicit in the reporting. This could help make a stronger case when submitting funding applications for a planned full-scale trial and reassure funders that extensions will not be required.

This evidence synthesis provides some pointers for how researchers can improve their approach to pre-trial qualitative work. Below we have suggested two summary recommendations that may help to maximise the value of undertaking this type of work:

1. **Plan the qualitative research with the full-scale trial in mind**

   Researchers need to think about the recruitment and retention challenges their planned trial is likely to face and design the pre-trial qualitative research to specifically address these, while of course allowing for a degree of openness and flexibility to address possible emerging issues as the trial progresses. Researchers need to prioritise the practical importance of qualitative research and its potential to optimise the conduct of the full-scale trial.

2. **Be clear that changes were made to the recruitment or retention plan**

   In some cases, there was a clear link between qualitative findings and a particular change being made to the recruitment or retention plan for the full-scale trial. In others, there was no explicit link between findings and changes, or the lack of changes. For these the influence of pre-trial qualitative work on the recruitment or retention plans for the full-scale trial remained unclear, either because of poor reporting or because there was no link. Researchers should provide a clear statement of their findings and the linked changes, if any, to the recruitment and retention plan for the full-scale trial.

A good example of how barriers to recruitment and the corresponding changes were reported in a study is that by Paramasivan et al 2017 ‘‘Enabling recruitment success in bariatric surgical trials: pilot phase of the By-Band-Sleeve study’’ (30). This study was highlighted as a good example because qualitative findings were clearly reported, and the decision-making process was made explicit with regards to how the findings were transformed into actions to mitigate against recruitment problems before the commencement of a full-scale trial.

Conclusion

Many trial teams do pre-trial qualitative work with the aim of improving, among other things, recruitment, and retention in future full-scale trials. Just over half of all reports of such work do not clearly show how their findings will change the recruitment and retention strategy of the future trial. The scope of pre-trial work needs to expand beyond looking for problems and also look for what might help and spend more time on retention.

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S1 Table. Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ Checklist (Tong, *et al.*, 2012)

Item No.	Guide and Description	Report Location
1. Aim	State the research question the synthesis addresses	Introduction
2. Synthesis methodology	Identify the synthesis methodology or theoretical framework which underpins the synthesis, and describe the rationale for choice of methodology (e.g. meta-ethnography, thematic synthesis, critical interpretive synthesis, grounded theory synthesis, realist synthesis, meta-aggregation, meta-study, framework synthesis)	Methodology of synthesis
3. Approach to searching	Indicate whether the search was pre-planned (comprehensive search strategies to seek all available studies) or iterative (to seek all available concepts until they theoretical saturation is achieved)	Study search strategy
4. Inclusion criteria	Specify the inclusion/exclusion criteria (e.g. in terms of population, language, year limits, type of publication, study type)	Literature search and selection - *Inclusion criteria*
5. Data sources	Describe the information sources used (e.g. electronic databases (MEDLINE, EMBASE, CINAHL, psycINFO), grey literature databases (digital thesis, policy reports), relevant organisational websites, experts, information specialists, generic web searches (Google Scholar) hand searching, reference lists) and when the searches conducted; provide the rationale for using the data sources	Study search strategy and process – *Electronic searches & searching other resources*
6. Electronic Search strategy	Describe the literature search (e.g. provide electronic search strategies with population terms, clinical or health topic terms, experiential or social phenomena related terms, filters for qualitative research, and search limits)	S2 – *search strategy*
7. Study screening methods	Describe the process of study screening and sifting (e.g. title, abstract and full text review, number of independent reviewers who screened studies)	Study selection – S2-*Fig 1 PRISMA flow diagram*
8. Study characteristics	Present the characteristics of the included studies (e.g. year of publication, country, population, number of participants, data collection, methodology, analysis, research questions)	S4 - *Characteristics of included studies*
9. Study selection results	Identify the number of studies screened and provide reasons for study exclusion (e.g. for comprehensive searching, provide numbers of studies screened and reasons for exclusion indicated in a figure/flowchart; for iterative searching describe reasons for study exclusion and inclusion based on modifications to the research question and/or contribution to theory development)	S2-Fig 1 - PRISMA flow diagram
10. Rationale for appraisal	Describe the rationale and approach used to appraise the included studies or selected findings (e.g.	Appraisal of the methodological

	assessment of conduct (validity and robustness), assessment of reporting (transparency), assessment of content and utility of the findings)	limitations of included studies
11. Appraisal items	State the tools, frameworks and criteria used to appraise the studies or selected findings (e.g. Existing tools: CASP, QARI, COREQ, Mays and Pope [25]; reviewer developed tools; describe the domains assessed: research team, study design, data analysis and interpretations, reporting)	Appraisal of the methodological limitations of included studies - *CASP*
12. Appraisal process	Indicate whether the appraisal was conducted independently by more than one reviewer and if consensus was required	Appraisal of the methodological limitations of included studies
13. Appraisal results	Present results of the quality assessment and indicate which articles, if any, were weighted/excluded based on the assessment and give the rationale	S8,9- CERQual Evidence profiles
14. Data extraction	Indicate which sections of the primary studies were analysed and how were the data extracted from the primary studies? (e.g. all text under the headings "results /conclusions" were extracted electronically and entered into a computer software)	Methodology of synthesis – *"all relevant qualitative data"*
15. Software	State the computer software used, if any	None used
16. Number of reviewers	Identify who was involved in coding and analysis	Methodology of synthesis
17. Coding	Describe the process for coding of data (e.g. line by line coding to search for concepts)	Methodology of synthesis
18. Study comparison	Describe how were comparisons made within and across studies (e.g. subsequent studies were coded into pre-existing concepts, and new concepts were created when deemed necessary)	Findings mapped to *Theme Matrix* tables- S5,6,7
19. Derivation of themes	Explain whether the process of deriving the themes or constructs was inductive or deductive	Inductive process - *Theme Matrix* tables – S5,6,7
20. Quotations	Provide quotations from the primary studies to illustrate themes/constructs, and identify whether the quotations were participant quotations of the author's interpretation	Findings - *Quotations and all sources given*
21. Synthesis output	Present rich, compelling and useful results that go beyond a summary of the primary studies (e.g. new interpretation, models of evidence, conceptual models, analytical framework, development of a new theory or construct)	Findings and discussion

MEDLINE MULTI-FILE SEARCH STRATEGY

Database: Embase Classic+Embase <1947 to 2018 Week 9>, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>

OVID Multi-file Search URL: https://shibboleth.ovid.com/

Search Strategy:

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1 qualitative research/ (89507)

2 qualitative research.tw,kw. (33140)

3 (qualitative adj3 method$).tw. (52706)

4 (qualitative method? or qualitative methodology).kw. (2407)

5 (qualitative adj3 stud$).tw. (94525)

6 qualitative study.kw. (2277)

7 focus groups/ use ppez (25522)

8 focus group?.tw,kw. (80757)

9 grounded theory/ (5381)

10 grounded theory.tw,kw. (20998)

11 narrative analys?s.tw,kw. (2073)

12 process evaluation.tw,kw. (5813)

13 mixed method?.tw,kw. (27752)

14 mixed method$.mp. (28575)

15 mixed methodology.tw,kw. (675)

16 (in depth adj4 interview$).tw. (40998)

17 in depth interview?.kw. (159)

18 ((semi structured or semistructured) adj5 interview$).tw. (87381)

19 semi structured interview?.kw. (250)

20 qualitative interview$.tw. (17258)

21 qualitative interview?.kw. (396)

22 (interview$ and theme$).tw. (58848)

23 interview?.kw. (6522)

24 (interview$ and audio recorded).tw. (4755)
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26 descriptive case stud$.tw. (476)
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28 descriptive case study.kw. (0)
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30 qualitative evaluation.tw,kw. (6656)
31 qualitative intervention.tw,kw. (25)
32 qualitative approach.tw,kw. (7695)
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41 thematic analysis.tw,kw. (24656)
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43 ethnography.kw. (1721)
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45 ethno?methodology.tw,kw. (156)
46 social construction.tw,kw. (1763)
47 or/1-46 (426888)
48 Patient Dropout/ use ppez (8077)
49 Patient Dropouts/ use emcz (539)
50 Patient Recruitment/ use ppez (62890)
51 Research Subjects/ use emcz (5835)
52 Patient Selection/ (145510)

53 Informed Consent/ (125958)

54 patient recruitment.kw. (179)

55 attrition.kw. (1400)

56 patient retention.kw. (32)

57 ((recruit$ or participat$ or take part or dropout$ or drop$ out$ or withdr?wl$ or barrier$ or retention or response$ or respond$ or attrition) adj4 trial?).tw. (58536)

58 or/48-57 (333454)

59 47 and 58 (8081)

60 Feasibility Study/ use emcz (88085)

61 Feasibility Studies/ use ppez (63390)

62 Pilot Projects/ use ppez (113723)

63 Pilot Study/ use emcz (119757)

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65 pilot.tw. (320772)

66 pre trial$.tw. (1487)

67 ((early or develop$) adj3 phase).tw. (110286)

68 vanguard.tw. (1626)

69 ("proof of principle" or "proof of concept").tw. (62696)

70 or/60-69 (741610)

71 59 and 70 (983)

72 71 not abstract.pt. (799)

73 limit 72 to English language (832) MEDLINE 422 EMBASE 351

74 remove duplicates from 73 (504)

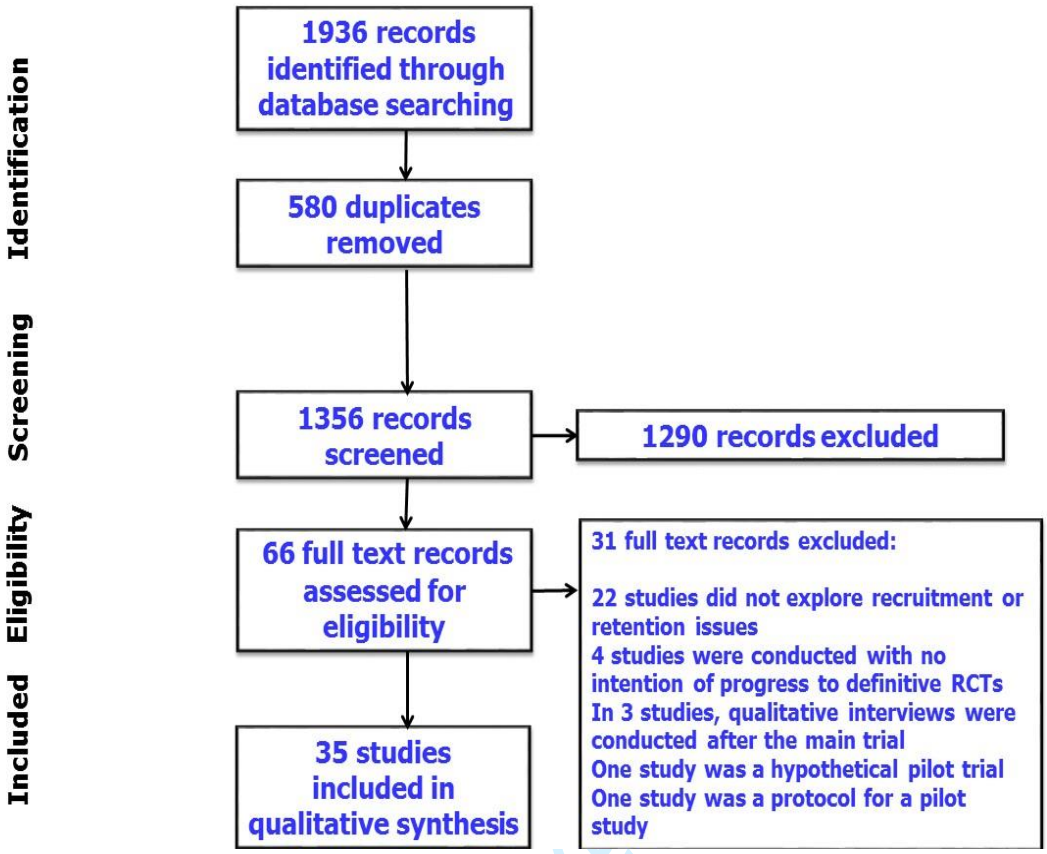

Figure 1 PRISMA flow diagram

S4: Characteristics of included studies.

Study ID	Country	Clinical area	Study aim/ objective	Participants	Method of data collection	Method of analysis
Michie 2016	UK	Sexual and reproductive health	To identify barriers and facilitators to providing interventions from pharmacies routinely.	12 women, four from each arm of the pilot study and the pharmacists involved	Semi-structured interviews	Thematic analysis
Palmer 2016	UK	Joint hypermobility syndrome	To explore Patients' and health professionals' perspectives on the intervention and the proposed trial	25 patients (three men and 22 women; aged 19–60 years) 16 health professionals (three men and 13 women; 0–30 years post qualification; 14 physiotherapists and two podiatrists)	Seven focus groups were conducted with patients and health professionals before the pilot trial Interviews with participants and health professionals and short telephone interviews with six patients who declined to take part in the trial.	Thematic analysis
Latter 2018	UK	Cancer	To evaluate participants' experiences of Cancer Carers Medicines Management and trial procedures.	12 nurses and 9 family carers	Face-to-face semi-structured qualitative interviews	Framework approach

Paramasivan 2017	UK	Severe and complex obesity	To improve information provision and recruitment organization	12 in-depth staff interviews, 84 audio recordings of patient consultations, 19 non-participant observations of consultations and patient screening data	Interviews, audio recording of recruitment consultations and non-participant observations of consultations	Thematic analysis using constant comparative methods
Griffin 2016	UK	Femoroacetabular impingement syndrome	To understand the recruitment process so that any difficulties related to design or conduct can be identified and changes put in place.	Ten interviews conducted with members of the TMG, Twenty-one interviews with clinicians and research associates	Face-to-face In-depth interviews	Constant comparison and case study approaches
Hamlet 2017	UK	Appearance-related distress, teasing or bullying	To explore GP and nurses' experiences of recruiting to the feasibility trial	Nine different GPs and two nurses	Focus groups, face-to-face or telephone interviews	Thematic analysis
Aventin 2016	UK	Sexual health	To determine the facilitators and barriers to recruitment and retention to a school-based sexual-health trial	Principals, vice-principals, teachers, pupils and parents recruited to the study	Semi-structured interviews and focus groups	Thematic analysis

Hilton 2015	UK	Stress urinary incontinence	To explore women's understandings and experiences of the consent process and their decision to participate in the pilot RCT	29 women who had participated in the pilot study.	Semi-structured interviews	Framework analysis
Van Den Berg 2017	UK	Cardiac chest pain	To explore patient attitudes and potential barriers to participation in a full-scale randomised trial.	10 participants	Semi-structured interviews (two interviews were undertaken face to face and eight by telephone).	Framework analysis
Gabbay 2017	UK	Depression and debt	To explore participants' experience of involvement in the trial, including the acceptability of trial processes and outcome measures To access narrative voices of those involved in the design and delivery of the trial, including the different roles played by each team member.	23 patients, 7 GPs and 4 CAB (Citizens Advice Bureau) advisors who participated in the trial	Semi-structured interviews	Thematic analysis

Lawton 2017	UK	Women who have a retained placenta	To explore women's and staff experiences of, and views about, the recruitment and consent procedures used during the pilot.	Interviews with staff (n = 27) and participating women (n = 22).	Semi-structured interviews	Thematic analysis
Trevelyan 2016	UK	Phantom limb pain	To inform the development of an appropriate and feasible protocol for use in a definitive multicentred RCT.	13 patients	Semi-structured interviews	Thematic analysis
Thompson 2016	Canada	End-stage renal disease	To better understand feasibility of a main study evaluating the efficacy of cycling and resistance exercise each performed during the haemodialysis treatment on QoL	25 patients and 11 staff were interviewed	Semi-structured interviews	Thematic analysis
Bhattacharya 2016	UK	Older people with unintentional non-adherence to medications	To gain opinions on each stage of the trial process to identify what worked well and less well with a view to optimising definitive study design	Two mixed focus groups of RCT participants (Eight) and a range of health-care professionals (Seven) involved in the delivery of the RCT.	Focus groups	Thematic analysis

Ritchie 2015	UK	Cancer	To provide in-depth, explanatory information to inform the main trial	Three patient focus groups (each comprising three patients) and 23 interviews with clinical staff were conducted.	Focus groups and semi-structured interviews	Thematic analysis
Blekken 2015	Norway	Fecal incontinence	To improve the quality of the planned trial	One focus group interview (n = 7) and 4 individual interviews.	Focus groups and semi-structured interviews	Thematic analysis
Notley 2015	UK	Mental health difficulties	To explore individual experiences of participating in the pilot randomised, controlled trial	13 participants	Face-to-face qualitative semi-structured interviews	Thematic analysis
Hamilton 2013	UK	Cancer	To investigate the factors contributing to poor recruitment to the EaStER trial ''Early Stage glottic cancer: Endoscopic excision or Radiotherapy'' feasibility study.	Surgeons and nurse recruiters	Semi-structured interviews, focus groups and audio-recordings of recruitment encounters	Thematic analysis
Realpe 2016	UK	Femoroacetabular impingement syndrome	To understand the recruitment process so that any difficulties related to design or conduct can be	12 consultations with 60 patients were recorded	Audio-recoding of recruitment consultations	Thematic analysis and focused conversation analysis.

			identified and changes put in place.			
Foster 2016	UK	Moderate to severe fatigue	To test the proof of concept and inform the design of an effectiveness trial.	19 participants	Semi-structured telephone interviews.	Content analysis
Pentecost 2015	UK	Depression	To inform the design of a full-scale trial	Nine psychological wellbeing practitioners and 15 participants	Semi-structured interviews	Thematic analysis
Clarke 2015	UK	Intermittent Exotropia X	To inform the design and conduct of a future full randomised controlled trial (RCT).	parents and treatment orthoptists	Semi-structured interviews	Thematic analysis
Crawley 2013	UK	Chronic fatigue syndrome	To explore the feasibility and acceptability of the recruitment, randomization and interventions.	13 mothers and 12 children on three occasions	In-depth interviews and audio-recordings of recruitment consultations	Thematic analysis
Gray 2013	UK	Obesity	To elicit men's experiences of participation in the pilot trial.	Four focus groups total of 26 men sampled purposively from a list of volunteers to include men of different ages and baseline BMIs	Focus groups	Framework approach

Nair 2014	UK	Lung Cancer	To explore the potential barriers and facilitators that would impact recruitment.	32 people who matched the inclusion/exclusion criteria for the trial took part in four focus groups	Focus groups	Thematic analysis
Moynihan 2012	UK	Transitional Cell Carcinoma (TCC) of the bladder	The aim was to illuminate problems in the context of randomization.	24 patients (accepters and decliners to randomization	Semi-structured interviews	Thematic analysis
Marshman 2012	UK	Tooth decay	To describe service providers' and users' perspectives on the pilot trial to identify improvements to the conduct and design of the FiCTION main trial.	Individual interviews were held with 4 dentists and a group interview was held with 17 dental team members. Face-to-face interviews were held with 4 parents and children and 5 telephone interviews were conducted with parents	Individual, group interviews face-to-face and telephone interviews	Framework approach
Audrey 2011	UK	Localized prostate cancer	The purpose of ASPECTS (Aspirin and Esomeprazole Chemoprevention in Barrett's metaplasia) was to explore patients' experiences of palliative	45 patients	In-depth interviews and audio-recording of recruitment consultations	Framework approach

			chemotherapy treatments as part of ASPECTS (Aspirin and Esomeprazole Chemoprevention in Barrett's metaplasia) trial.			
Paramasivan 2011	UK	Transitional cell carcinoma of the bladder	To explore reasons for low recruitment and attempt to improve recruitment rates to the SPARE (Selective bladder Preservation Against Radical Excision) trial by implementing changes suggested by qualitative findings.	9 recruiters and 9 non-recruiters were interviewed across four centers.	Audio recording of discussions between potential RCT participants and recruitment staff In-depth interviews with Trial Management Group	Simple counts, cross tabulations and content analysis
Forbes 2010	UK	Breast cancer	To explore women's views of the design of a large pragmatic randomised controlled trial of the policy of offering a health professional-delivered intervention to promote early presentation with	69 women participating in 7 focus groups and 17 in-depth interviews	Focus groups and in-depth interviews	Thematic analysis

			breast symptoms in older women			
McEachan 2016	UK	Childhood obesity	To inform progression to a definitive trial comparing Healthy and Active Parenting Programme for early Years intervention and usual care	14 parents (across intervention and control groups) 7 telephone interviews with women who were randomised to the intervention group but who did not attend any sessions	Semi-structured interviews and focus groups	Thematic analysis
Tsianakas 2016	UK	Recurrent or metastatic cancer	To explore the acceptability of CanWalk intervention, randomisation process and outcome measures.	10 participants (5 per group; 6 men and 4 women; 5 >65 years; 9 White British or Irish)	Semi-structured telephone interviews	Thematic analysis
Ellis 2016	UK	lung cancer	To elicit the views and perceptions of those who participated in a randomised controlled feasibility trial testing a non-pharmacological intervention, Respiratory Distress Symptom Intervention (RDSI)	11 lung cancer patients, 3 caregivers and 7 researchers involved in recruitment	Semi-structured interviews	Thematic analysis

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Kendrick 2017	UK	Depression	To determine key elements of the best design for a trial of patient-reported outcome measures (PROMs) for monitoring primary care patients with depression.	14 patients and 13 practice staff.	Semi-structured interviews	Thematic analysis
Myall 2015	UK	Cancer-related Fatigue	To assess feasibility and acceptability of RESTORE, an exploratory RCT of a web-based intervention to enhance self-efficacy to manage cancer-related fatigue (CRF) following primary cancer treatment	19 patients	Semi-structured telephone interviews	Framework approach

S5: Barriers to recruitment

Study ID (disease area)	Findings associated with code: issues with the randomisation process	Changes planned before the full trial	Were the proposed changes clearly linked to coded data?
Nair 2014 (Lung Cancer)	• Some participants struggled to understand the concept or need for randomisation. • Despite explaining random allocation, some participants were still uncertain whether they would be selected based on some personal or illness characteristics.	• Randomisation will be explained to participants in the following way: 'To try and make sure both groups are the same, each person is put into a group at random. This is the fairest way of deciding who gets the test and means everyone will have a 50/50 chance of being put in either group'.	Yes
Moynihan 2012 (Transitional Cell Carcinoma (TCC) of the bladder)	• Often randomisation was perceived haphazardly as patients strove to make sense of their involvement in the trial process while questioning scientific principles.	• Attention to be focused on training trialists who are involved in recruitment to complicated trials, both in terms of communication processes and on the assimilation of complex trial pathways.	Unclear
Audrey 2011 (Prostate cancer)	• Patients and recruiters had difficulty with randomization. Patients commonly expressed lay views that cancer should be removed, told stories of friends or relatives who had died of advanced disease, or brought media information that was often biased in favor of radical treatments.	• It was necessary to emphasize that recruiters must be genuinely uncertain about the best treatment, believe the patient to be suitable for all three treatments, and be confident in these beliefs. • Recruiters were encouraged to elicit patients' lay views and then discuss differences with ProtecT study information, explain that randomisation offered a way of resolving the dilemma of treatment choice.	• Yes

Paramasivan 2011 (Transitional cell carcinoma of the bladder)	• The complexity of the trial design led to confusion among some patients and recruiters about the timing of randomization.	• The randomization period was simplified and clarified so that patients could be randomized at any time before the three cycles of chemotherapy rather than during the second cycle.	• Yes
McEachan 2016 (Childhood obesity)	• Many women said they were unsure about why they had been approached to take part in the study and some said they did not realise the intervention was aimed at overweight/obese women. • Some control group women interviewed expressed disappointment at being allocated to the control group.	• No changes reported to address this barrier	• No

Kendrick 2017 (Depression)	• Many patients were confused as to the process of randomization with some believing that the process of being assigned to an arm of the trial was decided by the doctor in view of their past medical history or their smoking status. • It was apparent that several of the standard care patients had not adequately understood management allocation prior to agreeing to participate in the trial. • Some patients felt that they would not have the best treatment if they were randomized to standard care indicating a lack of understanding of trial equipoise.	• Practices should be cluster randomized to streamline recruitment and follow-up, so all patients in each are treated the same, by whichever GP or PN they see. • The study team needs to spend more time at participating practices training them in the recruitment process. • Patients should be supported to take the necessary time to ensure understanding of patient information sheets before signing consent, especially with regard to clinical equipoise and that they will not necessarily benefit from participation.	Unclear
Citation	**Findings associated with code: clinical equipoise**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**

Paramasivan 2017 (Complex obesity)	• Recruiters found it difficult to maintain equipoise. • Audio recordings revealed that the terminology used by recruiters in the appointments favoured bypass and they tended to present it more positively than band surgery)	• Feedback sessions used to make recruiters aware of instances where they inadvertently used loaded terminology.	Yes
Griffin 2016 (hip impingement)	• Lack of equipoise in research teams: five surgeons (36%) and two physiotherapists (10%) showed a lack of active clinical equipoise when faced with real-life case scenarios or discussing involvement with a pilot RCT. One surgeon has a fundamental disbelief in femoroacetabular impingement, so that a trial of its treatment lacks relevance for them. • Unbalanced presentations of treatment options for which surgery has been presented at greater length and more favourably than either choosing conservative care or participating in the RCT (surgeons tend to talk most about what they are most familiar with). • Some surgeons favoured surgery as the optimal treatment for FAI (n = 2), which is the case for the two	• Providing frequent and comprehensive training to recruiters.	Unclear

	physiotherapists who were not in equipoise. Concerns that discussing uncertainty with patients could be detrimental to creating trust in their relationship.		
Ritchie 2015 (Cancer)	• Interviews with clinical staff revealed device preferences for certain subgroups of patients.	• Recruiters should gently challenge and acknowledge their own bias in device preference.	Yes
Hamilton 2013 (head and neck cancer)	• Surgeons had strong opinions about whether patients with disease involving the anterior commissure or those with cancer in situ would have better outcomes with a particular modality. • The language describing the treatment processes for the two options was not equivalent: toddling home' and 'nice and simple' for laser surgery compared with 'a bit more labour intensive,' 'a bit further for you to travel' for radiotherapy. In addition, the recruiter's tone appeared apologetic when presenting radiotherapy. • While the EaStER protocol identified locoregional recurrence as the primary	• Principal investigators and recruiters need to think more critically about the concept of scientific equipoise and how that should underpin the RCT.	Yes

	outcome and voice quality posttreatment as the secondary outcome, some recruiting staff felt that this main research question had already been answered.		
Pentecost 2015 (Depression)	• Psychological wellbeing practitioners' preferences for other treatments and their underuse of behavioural activation: Preferences for other treatments affected not only the number of individuals invited but also the number of randomised people who went on to receive at least one BA (behavioural activation) treatment session. • Difficulties in psychological wellbeing practitioners' (PWPs) adapting to recruitment procedures.	• Finding ways of enabling PWPs to engage with study procedures is recommended.	Unclear
Clarke 2015 (childhood intermittent exotropia)	• The explanation of the lack of evidence underlying the effectiveness and timing of intervention served, in many cases, to undermine the parent's confidence in the treating clinician, and by extension, the trial.	• Trial team suggested separation of the role of the treating clinician from the main recruiter to the trial. This proved extremely beneficial in aiding the process of recruitment and should be be considered in a future study.	Yes
Hilton 2015 (stress urinary	• Apparent inconsistency between lack of personal equipoise over the value of invasive urodynamic testing on the one	• No changes were suggested (the majority of respondents regarded the basic research question as being important	

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incontinence in women)	hand, and the majority view that the basic research question was important and associated with a high degree of willingness to randomise patients into a definitive RCT on the other hand.	(70%), and most would be prepared to randomise patients into a definitive RCT to address this (60%).	
Crawley 2013 (children with chronic fatigue syndrome)	• Discussion of the interventions tended to be weighted towards the Lightning Process rather than the specialist medical care during recruitment consultations.	• No specific change reported to address this issue.	
Moynihan 2012 (bladder cancer)	• An explanation of equipoise was usually perceived to be absent in the information process. • The need to believe in expert physicians and an inability to accept medical uncertainty is documented. • Physicians find the concept of equipoise difficult, both because of personal preference, and the difficulties of explaining the uncertainty prevailing in any form of randomization	• Attention to be focused on training trialists who are involved in recruitment to complicated trials, both in terms of communication processes and on the assimilation of complex trial pathways to avoid a palpable breakdown in communication.	Unclear

Audrey 2011 (Cancer)	• Audio recording of recruitment consultations revealed that treatments were not presented or interpreted equally. Surgery and radiotherapy were described in detail as aggressive, curative treatments while monitoring was portrayed briefly as a more passive process of watching and waiting.	• Recruiters were asked to change the order in which the treatments were presented (active monitoring, surgery, and radiotherapy) and to describe their respective advantages and disadvantages in equivalent detail. • Issues of randomization and clinical equipoise were clarified for both patients and recruiters.	Yes
Paramasivan 2011 (Prostate cancer)	• Centers sometimes appeared to take on a 'collective' preference - one that represented the views of most staff in the center. • Surgery was translated as the 'gold standard' and thus led to the reinforcement of treatment preferences that were already strong because of the differences perceived between the arms.	• No specific changes planned to address these barriers.	
Palmer 2016 (joint hypermobility syndrome)	• Physiotherapists anticipated that it may be difficult to 'persuade' patients that clinical equipoise existed and felt that this was an issue related to recruitment.	• Training and monitoring of trial personnel to ensure notions of equipoise are delivered and reinforced consistently is likely to improve recruitment rates to a future RCT.	Unclear

Citation	Findings associated with code: Patient treatment preferences	Changes planned before the full trial	Were the proposed changes clearly linked to coded data?
Paramasivan 2017 (complex obesity)	• Patients tended to decline study participation, often choosing bypass surgery.	• Do not indicate patient preference anywhere on the notes. • Move beyond initial probing questions in relation to patient preferences toward rectifying any erroneous views. • Request patients who appear to have a preference or decision about trial participation to 'keep an open mind' until they had heard all the relevant information.	Yes
Griffin 2016 (hip impingement)	• Concerns about patient reactions and preferences at the start of the trial.	• The patient should have the opportunity to talk to a researcher for longer and should be able to ask questions and raise concerns.	Yes
Hilton 2015 (stress urinary incontinence)	• Although most eligible women were willing to be randomised, some had a previously undeclared preference for avoiding IUT and expressed relief at being allocated to the control group.	No specific changes planned to address this barrier.	
Hamilton 2013 (head and neck cancer)	• **Non-equivalence of the treatment processes:** Surgeons and nurses reported that they were convinced that many patients opted for laser	• Principal investigators and recruiters must try to elicit and understand patient views and preferences. • The need to gently challenge preferences that are based on inaccurate information.	Yes

	surgery, because it was perceived as more convenient. • **Patient preferences and the role of recruiters:** Many patients were referred by surgeons specifically for either laser surgery or radiotherapy, and so had definite expectations as to which treatment they would receive. This made it very difficult for the recruiters to introduce the idea of participating in the EaStER trial.	• The need for training recruiters to enable them to explain the need for randomisation and the rationale for the RCT to patients.	
Clarke 2015 (childhood intermittent exotropia)	• Recruitment was hampered by strong parental preferences.	• To account for parental preferences, a future trial will incorporate a preference arm or accept that recruitment will inevitably be restricted to those parents who are prepared to consider surgery as a treatment.	Yes
Audrey 2011 (Cancer)	• Patients often expressed lay views that cancer should be removed or came with media information that was biased in favor of radical treatments.	• No specific changes planned to address this barrier.	

Paramasivan 2011 (transitional cell carcinoma of the bladder)	• Recruiters and investigators repeatedly mentioned that they were convinced that a major barrier to recruitment to SPARE was the existence of clear treatment preferences among patients.	• No specific changes planned to address this barrier.	
McEachan 2016 (Childhood obesity)	• Some control group women interviewed expressed disappointment at being allocated to the control group.	• No specific changes planned to address this barrier	
Palmer 2016 (joint hypermobility syndrome)	• Regardless of their prior experiences and understanding of equipoise, many participants still hoped to be randomized into the advice and physiotherapy arm, hoping that 'something' rather than 'nothing' would be more beneficial.	• No specific changes planned to address this barrier	
Citation	**Findings associated with code: Issues related to the control group**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**
Nair 2014 (lung cancer)	• Some participants struggled with understanding the rationale for having a control group and said that allocation to the control arm of the study would put them off from participating.	**Changes made to the study design or Participant Information Leaflet (PIL)**	Yes

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	• Comments from some participants demonstrated a lack of understanding of the scientific nature of the study and the need for a control or comparison group. • some people who understood the need for a control group, found it hard to appreciate the need for this in a screening trial.	• **T**he control group will be changed to non-test group, which is what participants were most comfortable with". • 'Whenever a new test is developed, we need to find out if it works. We do this by having a group of people who have the test and a group of people who do not. Both groups need to be similar so that we can compare what happens to the people in each group.' • 'If you are in the non-test group, the information you give us will be really important in helping us find out if the new lung cancer blood test works, by comparing what happens to both groups.	
Audrey 2011 (cancer)	• The non-radical treatment option (control) caused difficulties for both patients and recruiters. Although this option included regular review, recruiters often used the term 'watchful waiting' with the potential for interpretation as 'no treatment'.	• Issues identified by the qualitative research led to changes in the study information, randomisation, terminology used and presentation of the non-radical arm. • The non-radical arm was renamed 'active monitoring' with additional emphasis placed on the regular scrutiny of PSA tests and the availability of radical intervention if required or requested. As a result of these changes, recruiting staff were able to express confidence in this treatment option.	Yes

Kendrick 2017 (depression)	• One standard care patient pointed out that he could not grasp an understanding of the purpose of the control arm. • Many standard care patients believed that they were to have a chest X-ray well into the trial period. One patient stated that she had only entered onto the trial for the purpose of having a chest X-ray. • Some patients felt that they would not have the best treatment if they were randomized to standard care.	• Patients should be supported to take the necessary time to ensure understanding of patient information sheets before signing consent, especially with regard to clinical equipoise and that they will not necessarily benefit from participation. • A lack of skills in introducing research could be addressed through more training in a smaller group of practices.	Yes
Palmer 2016 (joint hypermobility syndrome)	• Both patients and health professionals felt that the content of the control arm, consisting of a one-off advice session, may not be perceived as equitable to the physiotherapy intervention arm.	• Patients and health professionals offered a number of suggestions for augmenting the content of the control arm, including providing ongoing support through group meetings, gym membership and the provision of general, not targeted, exercises, so the two arms were perceived as more equitable.	Yes
Citation	**Findings associated with code: Communicating study information and associated terminology**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**
Griffin 2016 (hip impingement)	• Graphic descriptions of surgery that may have put patients off randomisation.	• Providing frequent and comprehensive training to recruiters.	Unclear

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	• Presenting trial information in an order that is confusing for patients. • Surgeons going beyond their protocol brief, to explain the trial rather than referring patients on to the trial recruiter for this information.		
Aventin 2016 (Sexual health)	• The baseline questionnaire was too long and some did not feel comfortable answering questions relating to sexuality.	• At an individual level, researchers should ensure that data collection documentation is clear to parents and pupils, perhaps involving steering group members in ensuring clarity.	Yes
Crawley 2013 (chronic fatigue syndrome)	• Patient information sheets were perceived as long, difficult to understand, repetitive in places and not visually appealing to 12 to 18-year olds.	• Consider using different patient information sheets for children aged 12 to 14 years than those used for older teenagers.	Yes
Moynihan 2012 (transitional cell carcinoma of the bladder)	• Patients displayed what may be perceived as 'poor understanding' of trial procedures and concepts. Patients' accounts suggested that information giving was often sub-optimal and/or understanding unverified. • An explanation of equipoise was usually perceived to be absent in the information process.	• Attention to be focused on training trialists who are involved in recruitment to complicated trials, both in terms of communication processes and on the assimilation of complex trial pathways.	Unclear

	• Patients across the sample failed to understand the 'language' of trial procedures. • Research overload, information overload and a perceived lack of information affected decision making.		
Marshman 2012 (dental caries)	• Finding an appropriate form of words to explain aspects of the trial to parents and children was difficult for some dentists.	• No specific changes planned to address this barrier.	
Audrey 2011 (cancer)	• Patients may have interpreted trial and clinical terminology quite differently than intended by practitioners and this was evident in the early stages of ProtecT when, for example, 'trial' was sometimes interpreted as 'try and see'.	• Issues identified by the qualitative research led to changes in the study information, randomisation, terminology used and presentation of the non-radical arm. • Recruiters were asked to change the order in which the treatments were presented (active monitoring, surgery, and radiotherapy) and to describe their respective advantages and disadvantages in equivalent detail. • Recruiters were asked to replace 'trial' with 'study'.	Yes
Paramasivan 2011 (transitional cell carcinoma of the bladder)	• Recruiters and investigators agreed that the SPARE trial was difficult to explain. • Recruiters indicated that they found the quantity of information problematic as well as its complexity.	• The construction of a simpler version of the study flowchart which was then issued to recruiters so that they could provide a clearer articulation of the trial. • The consent for chemotherapy was separated from the consent for SPARE in response to recruiters indicating that	Yes

		patients were given too much information about various aspects of the trial at the same time. • The recruitment study team drafted a new, shorter and clearer PIS which removed the 'loaded' terminology, explained the simplified study outline and included the new flowchart.	
Ellis 2016 (lung cancer)	• For some participants, the questionnaire items probed areas that they had not thought about or had chosen not to think about. • Carers also expressed some discontent with the questionnaires and this was seen as a potential barrier to recruitment.	• The number of questionnaires to be used in the subsequent trial will be decreased.	Yes
Citation	**Findings associated with code: issues around the eligibility criteria**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**
Hilton 2015 (stress urinary incontinence)	• Interpretation of eligibility criteria differed between centers (**Authors' judgement**).	• Ensure clarity over inclusion/exclusion criteria Running screening training exercises might be considered for a future definitive trial to ensure similar screening standards and practices and an 'assumed eligibility' approach in all centers.	Yes
Bhattacharya 2011 (older population unintentionally	• There was less clarity regarding the minimum age for recruiting patients to the study. Maintaining the minimum recruitment age at 75 years as initially	• A lower age band for recruitment is necessary.	Yes

non-adherent to medication)	proposed resulted in over one-third of patients being ineligible for study participation		
Hamilton 2013 (head and neck cancer)	• Surgeons applied the inclusion/exclusion criteria variably, thereby reducing the available number of eligible patients and creating differences between centers.	• Issues related to inclusion/ exclusion criteria, may require close examination and regular meetings to discuss and resolve evolving issues.	Yes
Clarke 2015 (childhood intermittent exotropia)	• Difficulty in confirming eligibility at the initial screening visit • Subsequent blockage of appointment slots by children who needed rescreening for eligibility, contributed to a failure to recruit to target.	• A future trial will consider a limit on the upper age at which participants would be included.	Yes
Paramasivan 2011 (transitional cell carcinoma of the bladder)	• Some recruiters thought there was leeway for interpretation of the inclusion/exclusion criteria in partnership with the main trial team.	• No changes planned to address this issue (The possibility of relaxing certain inclusion criteria was discussed with the TMG but it was decided that these could not be changed without invalidating the aims of the RCT).	
Ellis 2016 (lung cancer)	• Those involved in the recruitment process reported that the inclusion/exclusion criterion was too restrictive. As a result, it was felt that many patients who may have benefited from participation in the trial were excluded.	• No changes planned to address this barrier (eligibility criteria will remain the same for the subsequent trial	

Citation	Findings associated with code: Practical barriers	Changes planned before the full trial	Were the proposed changes clearly linked to coded data?
Griffin 2016 (hip impingement)	• Difficulty in implementing procedures due to the multicenter nature of the pilot.	• Regular visits to the centers by the PI and other TGM members to keep momentum • Delivery of a slick and easy-to-implement recruitment process to be the least disruptive to routine clinical practice. • Providing frequent and comprehensive training to recruiters. • Modifying the support to teams in other centers according to their research experience. • Setting recruitment targets and engendering a healthy competition between centers. • Follow up with messages and regular newsletters about the need to recruit. • Contacts between research and clinical departments about recruitment opportunities should be encouraged.	Yes
Hamlet 2017 (young people with appearance-altering conditions)	• Barriers of the primary care environment (time-limited consultations, high workload, competing studies)	• No specific changes to address these barriers.	
Aventin 2016 (Sexual health)	• Perceived lack of time for potential study participants to take part.	• Environmental facilitators of recruitment: approaching schools attending RSE training days, highlighting the innovative nature of the intervention, flexibility in terms of	Yes

	• Involvement in another research projects.	how and when the research was conducted in individual schools, the provision of support to schools by facilitation of the project by dedicated researchers, providing a clear outline of the roles and responsibilities of the school (and research team) from the outset and facilitating discussion on the benefits and perceived barriers to taking part.	
Gabbay 2017 (Debt Counselling for Depression)	• Delayed practice recruitment due to higher administrative issues. • Staffing and workload Complexity of primary care services	• The study failed to reach its recruitment target and was terminated early during the internal pilot phase, and, therefore, it did not progress to main trial.	
Lawton 2017 (postpartum haemorrhage)	• Staff reluctance to forgo written consent procedures	• Staff who are inexperienced in using alternatives to prospective written consent may benefit from training and support to increase their confidence and willingness to use alternative consent approaches. This training and support could focus on raising staff awareness and understanding of ethical review processes and of how, and why, they are legally protected when alternatives to prospective written consent are used.	Yes
Trevelyan 2016 (phantom limb syndrome)	• Failure to identify suitable participants due to units not operating in full capacity.	• A future trial would need to ensure that trial centers allocated adequate time and personnel. • Applying multicentered approach to recruitment.	Yes
Blekken 2015 (fecal incontinence)	• Staff discontinuity • Insufficient time • Large care staff • sub-optimal use of skill-mix	• For the main study, the plan is to include personal meetings with the director of health and social affairs and the care managers of the NHs. • One of the RNs from the pilot study will also be invited to share her experience and to answer questions about participating.	Unclear

		• The economic compensation and the recommendation of releasing the responsible RNs from daily work. • Recruitment of a local opinion leader and using the unit as a cluster will improve study feasibility by increasing the number of potential clusters, which impacts power more than increasing individuals enrolled.	
Pentecost 2015 (depression)	• Staff attrition: randomised participants' not seeing study psychological wellbeing practitioners.	• Finding ways of enabling PWPs to engage with study procedures is recommended.	Unclear
Clarke 2015 (childhood intermittent exotropia)	• There was a lag in recruitment due to the delay in the subsequent appointment for the recruitment clinic.	• The use of research nurses in all centers should be considered in a future study. • Separation of the role of the treating clinician from the main recruiter to the trial.	Unclear
Marshman 2012 (dental caries)	• Shortage in radiographs and its impact on the number of eligible participants. • Time constraints and busy schedule.	• Practitioners should be advised that patients will require longer appointments than normal for involvement in the trial and would prefer appointments out of school time. • The recommendation for recruitment of whole practices, with participation of all members of the practice team rather than individual practitioners.	Yes
Ellis 2016 (lung cancer)	• Inconvenient time frame between providing consent and receiving the first intervention.	• The timeframe between consent and delivery of the first RDSI session has been expanded to 2 weeks.	Yes

Latter 2018 (cancer patients at the end of life)	• Organisational change, team staffing levels, nurse workloads and variable flow of palliative care referrals. • Nurses' unfamiliarity with recruitment. • Incompatibility of recruitment procedures with nursing.	• No specific changes planned to address these barriers.	
Citation	**Findings associated with code: commitment of staff and participants to the trial**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**
Paramasivan 2011 (transitional cell carcinoma of the bladder)	• Recruiters believed that some teams or members were very committed to SPARE but that others were indifferent or even antagonistic to it, and this created additional difficulties because patients developed strong preferences for one arm or the other.	• Clinical centers were asked to identify two Lead Recruiters (LRs) per site whose responsibilities would be to act as the focus for SPARE recruitment activity.	Yes
Latter 2018 (cancer patients at the end of life)	• Recruiting fewer dyads than anticipated affected nurses' engagement and the priority they gave to the study.	• No specific changes reported	
Citation	**Findings associated with code: Beliefs and expectations about trial participation**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**

Hamlet 2017 (young people with appearance-altering conditions)	• A 'conspiracy of silence': Beliefs that young people would prefer not to discuss appearance-related concerns with their GP. • Participants seemed hesitant approaching the topic directly.	• This study highlights the potential need for training to educate primary care staff to broach the topic of a visible difference confidently, both within and outside the parameters of research. Training, with a particular focus on how to talk to young people who might be experiencing appearance concerns, could facilitate doctor–patient communication about the psychosocial challenges of living with a condition or injury that alters appearance and, in turn, patient disclosure.	Yes
Van Den Berg 2017 (chest pain)	• Some participants did feel that being in pain on arrival, feeling overwhelmed, or anxious about the situation meant that they did not feel ready to commit at the time of the very first approach. • **Concerns about being experimented on:** some participants felt being generally sceptical of clinical research and initially felt anxious about participation**.**	• Waive verbal consent for initial trial procedures that do not affect the participant. • Waiting until the patient's condition is more settled and they can provide appropriate written informed consent. • The need to explore shared decision making to cater for a wide spectrum of perspectives.	Yes
Trevelyan 2016 (phantom limb syndrome)	• Intensity of Phantom Limb Pain (PLP) was a major barrier.	• Consider lowering or excluding the severity of PLP.	Yes
Ritchie 2015 (Cancer)	• Patient self-preservation (the need to retain control of choice of device or treatment schedules).	• Recruiters should gently challenge patients' preconceptions, as well as recognising and acknowledging their own bias in device preference.	Yes

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Hamilton 2013 (head and neck cancer)	• **Lay beliefs:** The oncology centre/hospital where radiotherapy was performed had a negative image and was seen as a 'place to die'.	• No specific changes planned to address this barrier.	
Nair 2014 (cancer)	• Participants felt stigmatized (because of their smoking status) by some of the language used in the PILs. • The perception held by some participants that the trial is designed to encourage people to stop smoking.	• **"**We removed all mention of providing smoking cessation information and advice from the Patient information leaflets". • 'Lung cancer can happen to anyone, including the young and old and people who do not smoke, but the risk is higher in those over 50 and those who have smoked.'	Yes
Moynihan 2012(transitional cell carcinoma of the bladder)	• The patients' sense of alienation was evident. Feelings of isolation, loss of control and powerlessness underwrote involvement in the trial process.	• Attention to be focused on training trialists who are involved in recruitment to complicated trials, both in terms of communication processes and on the assimilation of complex trial pathways. • It is suggested that health professionals consider facilitating a context in which patients feel fully included in the trial enterprise.	Unclear
Ellis 2016 (lung cancer)	• Many patients who were identified as being suitable to participate tended to deny their symptoms, having become normalised and adjusted their lives accordingly and therefore were ineligible.	• No specific changes planned to address this barrier.	

Kendrick 2017(depression)	• One participant expressed anxiety about a poor medical outcome seemingly influenced by media reporting of a previous trial, while another patient was worried that she may have lung cancer. • One participant thought that she had been invited to take part in the trial because of her smoking status or history of smoking and the fact that she may have lung cancer highlighting a smoking stigma.	• Patients should be assured that the aim of the study is not to stop smoking, as it seems that this may limit recruitment due to smoking stigmatization.	Yes
Latter 2018(cancer patients at the end of life)	• Nurses 'protecting' patients and carers from additional burden or distress. • Nurses' avoidance of difficulty and disappointment: some nurses described pre-judging patients' and carers' willingness to participate, to avoid invitations being declined, which they found discouraging.	• No specific changes reported to address these barriers.	
Citation	**Findings associated with code: Integration of the trial into clinical practice**	**Planned changes before the full trial**	**Were the proposed changes clearly linked to coded data?**
Paramasivan 2017(complex obesity)	• Well-established routines for clinical service provision led to the trial being presented to patients as an 'add-on'	• Mention the study in the opening statements of the surgical consultations. • Express enthusiasm for the study.	Yes

	extra rather than an integral part of existing clinical services.		
Griffin 2016 (hip impingement)	• Teams experienced issues such as remembering to approach patients at each possible opportunity, or the need not to discuss surgery before diagnosis was confirmed. • Some research associates expressed their concern about talking to patients about the audio recording of the consultation. • Various sites expressed concern about patients being referred for 'surgery' instead of 'treatment'. Some centres use a conservative approach and, therefore, patients tend to go for physiotherapy first before arriving at a surgeon appointment. Recruiters said they would find it difficult to approach these patients or to feel confident they would agree to take part in the trial.	• Delivery of a slick and easy-to-implement recruitment process to be the least disruptive to routine clinical practice. • Providing frequent and comprehensive training to recruiters.	Unclear
Paramasivan 2011(transitional cell carcinoma of the bladder)	• The pathway that potential trial participants followed from a diagnosis of bladder cancer to being recruited to the SPARE trial proved extremely difficult because of the number of people who might come into contact with the patient during their visits and sometimes the different clinical	• Clinical centers were asked to identify two Lead Recruiters (LRs) per site whose responsibilities would be to act as the focus for SPARE recruitment activity. • The LRs were also advised to see if they could arrange a specific 'recruitment appointment' about 7-10 days after the chemotherapy discussion, with the aim of providing full	Yes

	(surgery or oncology, or local /regional) centres that might be involved.	information about the trial and obtaining consent for participation. • It was also recommended that trial participants should be referred to the respective specialists after randomization rather than before to ensure consistency of information.	
Ritchie 2015 (Cancer)	• Potential delays from referral to treatment. • Additional service provision and increased workload.	• The remit of the funded role of trial Champion has been developed to encompass not only recruitment and randomisation but also coordination and facilitation of device insertion appointments and communication.	Unclear
Citation	**Findings associated with code: Participation burden**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**
Lawton 2017 (postpartum haemorrhage)	• The burden of completing and signing consent form.	• No specific changes planned to address this issue	
Clarke 2015 (childhood intermittent exotropia)	• For parents and clinicians, the initial screening appointment presented a challenge, in that it had to encompass many points within a limited time. • The initial two visits, for screening and recruitment, often gave insufficient time for parents to fully consider participation in the trial.	• The use of research nurses in all centers should be considered in a future study. • Separation of the role of the treating clinician from the main recruiter to the trial.	Unclear

Nair 2014 (cancer)	• The main obstacle to participation appeared to be the need for flexible appointments. • work commitments among some of the younger participants were seen as a potential barrier.	• Those expressing interest in the study are sent the full PIL and at least 24 hours after anticipated receipt are phoned to discuss the study, answer questions, undertake a preliminary eligibility assessment and to arrange a recruitment visit at a time suitable to the patient. • Appointment reminders by phone, text message or email.	Unclear
Moynihan 2012 (transitional cell carcinoma of the bladder)	• Patients spontaneously indicated the need to 'work' their way around NHS waiting times and hospital administration. • Patients often criticized their need to 'work' against 'bad administration', sometimes affecting trial decisions.	• It is suggested that health professionals consider facilitating a context in which patients feel fully included in the trial enterprise.	Unclear
Citation	**Findings associated with code: Confidence about approaching patients**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**
Griffin 2016 (hip impingement)	• Research associates shared their concerns about not being able to answer patient questions and obtain consent without a surgeon or other senior clinician signing the form for them. • Long periods between recruitment clinics represented a challenge for research associates to maintain	• Providing frequent and comprehensive training to recruiters. • Modifying the support to teams in other centers according to their research experience.	Unclear

	confidence and knowledge about the UK FASHIoN trial.		
Hamlet 2017 (young people with appearance-altering conditions)	• Participants seemed hesitant approaching the topic directly.	• Training, with a particular focus on how to talk to young people who might be experiencing appearance concerns, could facilitate doctor–patient communication about the psychosocial challenges of living with a condition or injury that alters appearance and, in turn, patient disclosure.	Yes

S6: Facilitators for recruitment

Citation	Findings associated with code: Altruism and personal gain	Changes planned before the full trial	Were the proposed changes clearly linked to coded data?
Hamlet 2017 (young people with appearance-altering conditions)	• Participants reported a personal interest in the topic, which increased its pertinence and served as a motivator for recruitment.	• No changes reported	
Van Den Berg 2017 (Chest pain)	• Participation seemed motivated by altruism and the expectation that their participation may benefit both them and their families. • Participants also perceived that the research may bring direct personal benefits.	• No changes reported	
Bhattacharya 2011 (older people unintentionally non-adherent to medication)	• Patients wanted to take part to help others, to help themselves, to give payback to the NHS.	• No changes reported	
Notley 2015 (psychological difficulties)	• Participants expressed keenness to be involved in research, for altruistic reasons.	• No changes reported	
Hilton 2015 (stress urinary incontinence)	• Altruistic factors motivated participation.	• No changes reported	

Citation	**Findings associated with code: Communicating study information**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**
Aventin 2016 (sexual health)	• Promoting the social benefits and credibility of the research aims, help school decision-makers recognise the importance of the research projects goals and objectives. recruitment presentations by the research team using video testimonials from participants who took part in the pilot study and face-to-face contact with school management and teachers were important in this regard. • Ensuring that pupils are provided with adequate information about their roles and responsibilities, and given an opportunity to meet with the research staff before data collection will also be beneficial to pupil recruitment.	• No changes reported	
Hilton 2015 (stress urinary incontinence)	• The information provided about the study was clear and informative and there was enough information for women to be able to make a decision about taking part. • Good understanding of the study	• No changes reported	

Van Den Berg 2017 (Chest pain)	• Participants were provided with sufficient and clearly presented information and given the opportunity to ask for clarification about what participation in the MACS trial involved. They valued good interpersonal skills of the research staff	• No changes reported	
Notley 2015 (psychological difficulties)	• 11 participants displayed a sound understanding of the randomization process. • There was a thorough understanding of the rationale for the processes or measures used.	• No changes reported	
Realpe 2016 (hip impingement)	Analysis of the recruitment consultations provided evidence of a logical sequence for information sharing which seemed to facilitate recruitment for both recruiting clinicians and patients (Six step model): • Step 1: explain what the condition is to the patient • Step 2: reassure the patient that they will receive best treatment • Step 3; explain that there is uncertainty about which treatment is the best • Step 4; explain the purpose of the study	• The six-step recruitment model will be used to train and support recruiters in the large number of new centers in the full-scale trial.	Yes

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	• Step 5; give the patient a balanced view about the advantages and disadvantages of each treatment being compared. • Step 6; explain the study procedures.		
Hilton 2015 (stress urinary incontinence)	• Supplementary information from trial and clinic staff was seen as important.	• No changes reported	
Crawley 2013 (chronic fatigue syndrome)	• Sufficient information was provided during recruitment consultation, families were able to ask questions, understood what the study was about and what would happen if they decided to participate.	• No changes reported	
Citation	**Findings associated with code: Patients' social networks and positive experience of research**	**Changes planned before the full trial**	
Van Den Berg 2017 (chest pain)	• Participants positive experience was sufficient to recommend participation in clinical research to others.	• No changes reported	
Thompson 2016 (haemodialysis patients)	• Patients' social networks in the unit were an effective means of disseminating information. • Hearing other participants discuss their participation in the trial were effective means of promoting participation in the study.	• No changes reported	

S7: Barriers to retention

Citation	Findings associated with: Burden of follow-up questionnaires	Changes planned before the full trial	Were the proposed changes clearly linked to coded data?
Gabbay 2017 (Depression)	• With regard to feasibility and acceptability of the outcome measures, it was apparent that the number of outcome measures (and their form and content) was problematic for some participants – adding considerably to the time taken for completion of interviews. Furthermore, several participants questioned the forced choice responses of questionnaires, which did not capture the reality of their experience.	• The study failed to reach its recruitment target and was terminated early during the internal pilot phase, and, therefore, it did not progress to main trial.	
Hilton 2015 (stress urinary incontinence)	• Repeating questionnaires at 6 months when many women had few, if any, symptoms to report was sometimes felt to be burdensome and irrelevant; this is in keeping with the number of blank follow-up questionnaires returned.	• The need to complete and return questionnaires even if there are few symptoms was emphasized. • Modify questionnaires to allow 'short-cutting' of irrelevant areas to reduce respondent burden. • A further possibility is to link questionnaire completion at follow-up to the face-to-face clinic review.	• Yes
Crawley 2013 (chronic fatigue syndrome)	• The number of questionnaires used at follow-up was considered a burden by the	• Measures to improve outcome data collection using a variety of strategies, including telephone	• Unclear

	majority of children and parents interviewed and observed. • Parents felt the timing of questionnaires did not allow time for change, as they were too close together.	follow-up, would need to be implemented in a full study.	
Gray 2013 (male obesity)	• Focus group participants found difficulties with some of the wording in the questionnaires.	• Fieldworkers should be given full training in assisting men with questionnaire completion if required (e.g., if participants have literacy problems).	• Yes
McEachan 2016 (infant obesity)	• Some of the measurement tools were found to be burdensome to complete.	• Maintaining regular contact with participants throughout follow-up. • A future trial should ensure that a range of communication channels are used to maximise retention. • Strike a balance between collecting valid and reliable data and overly burdening participants, which may lead to missing data, withdrawal or trial attrition.	• Yes
Tsianakas 2016 (recurrent or metastatic cancer)	• All outcome measures were judged appropriate except the Scottish Physical Activity Questionnaire (SPAQ). Eight participants reported it was repetitive and difficult to complete.	• Alternative methods for measuring the intensity, duration and frequency of physical activity in any future study are recommended.	• Yes
Ellis 2016 (lung cancer)	• Patients and carers expressed some discontent with the questionnaires and this was seen as a potential barrier to retention.	• The number of questionnaires to be used in the subsequent trial will be decreased.	• Yes

Kendrick 2017 (depression)	• Some patients reported problems with the data collection questionnaires. For example, one patient had difficulties regarding the clarity of a particular question asking whether she was anxious or depressed. • Two patients pointed out that they thought that the patient questionnaire was intrusive.	• No specific changes reported to address these barriers.	
Myall 2015 (cancer-related fatigue)	• Few participants found the questionnaires at 3-time points burdensome. • Several participants who were ≥18 months post diagnosis felt some questions were not relevant. For example, items about health service use and seeking help from health professionals were more suited to those with a current diagnosis and were an unwelcome reminder of potential problems they may encounter. • Several participants considered the psychological aspect of cancer was missing and should be included in the questionnaires. • Questionnaires requested the same information more than once. For some this was a source of anxiety and revealed additional decision-making work spending time deliberating over responses.	• The need for less generic and more specific information was considered important. While RESTORE needs to retain a broad reach, improved signposting to resources dealing with a variety of cancers and relevant to users at various distances from diagnosis and treatment, and inclusion of more wide-ranging patients' stories, offer some ways RESTORE could be tailored to address the informational needs of a diverse range of users. This could reduce the potential for information to be viewed as an unwelcome reminder of their cancer.	• Unclear

Citation	**Findings associated with: Practical barriers**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**
McEachan 2016 (infant obesity)	• One issue for both participants and facilitators was setting up the groups in a convenient location. • Some participants reported making journeys that required considerable effort	• No specific changes reported to address these barriers.	
Kendrick 2017 (depression)	• A small minority of patients found the process of getting a chest X-ray difficult. One patient said that she had to pay for the parking costs and using public transport would be too problematic.	• Patients should be reassured that participation in the trial should cause the patient the least amount of inconvenience, especially in terms of travel necessities.	Unclear

S8: CERQual Evidence Profile_ Recruitment barriers

Summary of review finding (individual changes across each of the contributing studies are presented in table 2)	**Studies contributing to the review finding.**	**Adequacy**	**Coherence**	**CERQual assessment of confidence in the evidence**	**Explanation of CERQual assessment**
1- **Changes planned before the full trial to address issues with randomisation** The changes reported included explaining the process of randomisation in a clear way to study participants to deal with lack of understanding and confusion. Changes were also made to simplify and clarify the randomisation period.	(1-6)	Minor concerns about adequacy (one study reported no changes to address this barrier)	Moderate concerns about coherence (3 studies with well-grounded changes relevance, two studies with unclear fit)	Moderate confidence	6 studies with moderate concerns about adequacy and coherence. No or very minor concerns about methodological limitations and relevance.
2- **Changes planned before the full trial to address issues with clinical equipoise**: Changes included feedback sessions to make recruiters aware of instances where they inadvertently used loaded terminology, providing frequent training to recruiters and to	(3,4,7-16)	Minor concerns about adequacy (3 study reported no changes to address this barrier)	Moderate concerns about coherence (6 studies with well-grounded changes,6 studies with unclearly linked changes)	Moderate confidence	12 studies with moderate concerns about coherence. No or minor concerns about methodological limitations, adequacy and relevance.

present treatment options in a balanced way.					
3- Changes planned before the full trial to address issues with patient treatment preferences: Changes were made toward rectifying any erroneous views, gently challenge patient treatment preferences and request patients to 'keep an open mind' until they had heard all the relevant information.	(3,5,7,8,12,13,16-18)	Moderate concerns about adequacy(5 study reported no changes to address this barrier)	Moderate concerns about coherence (4 studies with with well-grounded changes,5 studies with with unclearly-linked changes)	Moderate confidence	9 studies with moderate concerns about adequacy and coherence. No or minor concerns about methodological limitations and relevance.
Changes planned before the full trial to address issues related to the control group: • Changes were made to the study design or Participant Information Leaflet (PIL) ''The control group will be changed to non-test group'', changes made to the presentation of the non-radical arm which was	(3,6,16,19)	No or very minor concerns about adequacy	No or very minor concerns about coherence	High confidence	4 studies with no or very minor concerns about methodological limitations, coherence, adequacy and relevance.

renamed 'active monitoring' and suggestions for augmenting the content of the control arm so the two arms were perceived as more equitable.					
Changes planned before the full trial to address issues around the eligibility criteria: • Changes were made to ensure clarity over inclusion/exclusion criteria in all centers, considering a lower age band for recruitment or a limit on the upper age at which participants would be included.	(12,13,17,18,20,21)	No or very minor concerns about adequacy	No or very minor concerns about coherence	High confidence	6 studies with no or very minor concerns about methodological limitations, coherence, adequacy and relevance
Changes planned before the full trial to address practical barriers: Changes included regular visits to the centres by the PI and other TGM members to keep momentum, delivery of a slick and easy-to-implement recruitment	(8,11,12,21-29)	Moderate concerns about adequacy (3 studies reported no changes to address these barriers)	Moderate concerns about coherence (5 studies with well-grounded changes and 3 studies with unclearly-linked changes)	Moderate confidence	12 studies with moderate concerns about adequacy and coherence. No or very minor concerns about methodological limitations and relevance.

process to be the least disruptive to routine clinical practice, providing frequent and comprehensive training to recruiters and to ensure that trial centres allocated adequate time and personnel.					
Changes planned before the full trial to address participation burden: Changes included the use of research nurses in all centres, separation of the role of the treating clinician from the main recruiter to the trial, appointment reminders by phone, text message or email and facilitating a context in which patients feel fully included in the trial enterprise.	(12,15,19,30)	Moderate concerns about adequacy (one study reported no changes to address these barriers)	Moderate concerns about coherence (one study with well-grounded changes and 3 studies with unclearly-linked changes)	Moderate confidence	4 studies with moderate concerns about adequacy and coherence. No or very minor concerns about methodological limitations and relevance.
Changes planned before the full trial to address barriers related to communicating study information and associated terminology: Changes were made to ensure that data collection documentation is clear to study participants, changing the order in which the treatments were	(3,8,14,15,18,21,23, 28)	Minor concerns about adequacy (one study reported no changes to address these barriers)	Minor concerns about coherence (5 studies with well-grounded changes and 2 studies with unclearly-linked changes)	High confidence	8 studies with minor concerns about adequacy and coherence. No or very minor concerns about methodological limitations and relevance.

presented and to describe their respective advantages and disadvantages in equivalent detail and drafting a new, shorter and clearer PIS which removed the 'loaded' terminology.					
Changes planned before the full trial to address barriers related to beliefs and expectations: Changes included highlighting the potential need for training to educate primary care staff to broach the topic of a visible difference confidently, waive verbal consent for initial trial procedures that do not affect the participant and removing all mention of providing smoking cessation information and advice from the Patient information leaflets" to avoid smoking stigma.	(6,9,15,17,21,22,26, 29,31,32)	Moderate concerns about adequacy (3 studies reported no changes to address these barriers)	Minor concerns about coherence (6 studies with well-grounded changes and one study with unclearly linked changes)	High confidence	10 studies with moderate concerns about adequacy. Minor or very minor concerns about methodological limitations, coherence and relevance.

Changes planned before the full trial to address barriers related to Integration of the trial into clinical practice: Changes reported were the need to mention the study in the opening statements of the surgical consultations, express enthusiasm for the study, delivery of a slick and easy-to-implement recruitment process to be the least disruptive to routine clinical practice, ensure that trial participants will be referred to the respective specialists after randomization rather than before to ensure consistency of information, and providing frequent training to recruiters.	(7-9,18)	No or very concerns about adequacy	Minor concerns about coherence (3 studies with well-grounded changes and one study with unclearly linked changes)	High confidence	4 studies with no or minor concerns about methodological limitations, coherence, adequacy and relevance.
Changes planned before the full trial to address barriers related to Confidence about approaching patients: Modifying the support to teams in other centers according to their research experience and the need for training to educate primary care staff to broach the topic of a visible difference confidently,	(8,22)	No or very concerns about adequacy	No or very concerns about coherence	High confidence	2 studies with no or very minor concerns about methodological limitations, coherence, adequacy and relevance.

both within and outside the parameters of research.					
Changes planned before the full trial to address barriers related to assiduousness and commitment of recruiters: Clinical centers were asked to identify two Lead Recruiters (LRs) per site whose responsibilities would be to act as the focus for SPARE recruitment activity.	(4,29)	Moderate concerns about adequacy (one study reported no changes to address these barriers)	Moderate concerns about coherence (only one study with well-grounded changes)	Moderate confidence	2 studies with moderate concerns about adequacy and coherence. No or very minor concerns about methodological limitations and relevance.
Changes planned before the full trial to address issues around the invitation to participate: Changes included sending postal invitation letter with a summary of the main points at the front of the PIL; and, where necessary or appropriate invitation during consultation with GP/Practice Nurse, placing posters in GP waiting rooms and finding ways of enabling psychological wellbeing practioners' to engage with study procedures.	(11,19)	Minor concerns about adequacy	Moderate concerns about coherence (one study with well-grounded changes)	Moderate confidence	2 studies with moderate concerns about coherence. No or very minor concerns about methodological limitations, adequacy, and relevance.

S9: CERQual Evidence Profile_ Retention barriers

Summary of review finding	**Studies contributing to the review finding.**	**Adequacy**	**coherence**	**CERQual assessment of confidence in the evidence**	**Explanation of CERQual assessment**
Changes planned before the full trial to address burden of follow-up questionnaires: The need to complete and return questionnaires even if there are few symptoms was emphasized, modifying questionnaires to allow 'short-cutting' of irrelevant areas to reduce respondent burden, link questionnaire completion at follow-up to the face-to-face clinic review and the use of a variety of strategies, including telephone follow-up to maximise retention.	(1-9)	Minor concerns about adequacy (only one study reported no changes to address these barriers)	Minor concerns about coherence (7 studies with well-grounded changes and one study with unclearly linked changes)	High confidence	9 studies with minor concerns about adequacy and coherence. No or very minor concerns about methodological limitations and relevance.

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Using qualitative methods in pilot and feasibility trials to inform recruitment and retention processes in full-scale randomised trials: a qualitative evidence synthesis

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Abstract

Objectives To systematically review published pre-trial qualitative research studies and explore how their findings were used to inform recruitment and retention processes in full-scale trials.

Design Qualitative evidence synthesis using thematic analysis.

Data sources and eligibility criteria We conducted a comprehensive search of databases; Dissertation Abstracts International, CINAHL, Embase, MEDLINE, Sociological Abstracts and Psycinfo. We included all reports of pre-trial qualitative data on recruitment and retention in clinical trials up to March, 2018.

Data extraction and synthesis Two authors independently extracted data using a predefined data extraction form that captured study aims, design, methodological approach, and main findings, including barriers and facilitators to recruitment and or retention. The synthesis was undertaken using Thomas and Harden's thematic synthesis method and reported following the ENTREQ guidelines. Confidence was assessed using GRADE-CERQual approach.

Results Thirty-five papers (connected to 31 feasibility studies) from three different countries, published between 2010 and 2017 were included. All studies were embedded in pilot or feasibility studies to inform design aspects in preparation for a subsequent full-scale trial. Twelve themes were identified as recruitment barriers and three as recruitment facilitators. Two themes were identified as barriers for retention and none as retention facilitators. The findings from qualitative research in feasibility or pilot trials are often not explicitly linked to proposed changes to the recruitment and retention strategies to be used in the future or planned full-scale trial.

Conclusions Many trial teams do pre-trial qualitative work with the aim of improving recruitment and retention in future full-scale trials. Just over half of all reports of such work do not clearly show how their findings will change the recruitment and retention strategy of the future trial. The scope of pre-trial work needs to expand beyond looking for problems and also look for what might help and spend more time on retention.

Strengths and limitations of this study

- Our comprehensive search strategy optimises the likelihood that we have identified relevant studies published in the time period in principal journals.
- Although we did not apply a quality assessment checklist to individual included studies to consider the relationship between quality and maximising the value of pre-trial qualitative research, the systematic methodology and the use of GRADE-CERQual assessment of confidence in the findings is a strength of the review.
- The review was based on what was written in published research and this may not reflect the breadth of qualitative research that is undertaken in practice.
- Most of the included studies were UK-based, that means it is uncertain whether and to what extent the findings apply to the trial environment outside the UK.

Introduction:

Recruitment of participants to, and their retention in, randomised controlled trials (RCTs) is a key determinant of research efficiency, but both can be challenging (1). Reviews of clinical trials funded by the UK Medical Research Council (MRC) and the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme have shown that the proportion of trials achieving their original recruitment target was in the range of 31%–56%, and some suffered loss to follow up of up to 77% (2-4). Despite a substantial body of literature on strategies to improve recruitment and retention in clinical trials, the quality of this evidence is lacking (5-9). The Cochrane Review on strategies to improve recruitment to RCTs found only three interventions with a high Grading of Recommendations Assessment, Development and Evaluation (GRADE) rated evidence and the corresponding review on interventions to improve retention found no high certainty evidence (5, 10).

Given the lack of certainty around effective strategies to improve recruitment and retention, trialists are increasingly integrating qualitative methods within randomised trials to unpack the complex processes involved (11, 12). However, much of the qualitative work to date has been on intervention development and often done when the full trial is ongoing (13), which means it can sometimes be too late to prevent or rectify a problem that has already happened. In its framework for the evaluation of complex interventions the UK MRC strongly recommended that trialists use qualitative methods prior to running a full-scale trial to understand barriers to participation and to estimate response rates (14). Briel and colleagues suggested that 89% of obstacles leading to the discontinuation of RCTs could be avoided if issues were identified and addressed during the trial planning stages (15). Likewise, a recent thematic synthesis of 45 qualitative studies (16) exploring adult patients' experiences with RCT participation identified the diverse psychological, physical, and financial burdens experienced by patients across the whole

process of the trial. The consideration of these modifiable factors at the pre-trial stage (i.e. research conducted or embedded with feasibility or pilot trials to inform trial design and conduct before recruitment to the full-scale trial starts , such as the volume, timing, complexity, or format of trial information or the organisation of participants' follow-up, could help to deliver more efficient RCTs and timely delivery of trial results (16, 17).

Qualitative research conducted during the pre-trial stage could have a role in improving efficiency by identifying problems with recruitment or retention early and then suggesting solutions for the full-scale trial (18, 19). O'Cathain and colleagues noted, however, that pre-trial qualitative research is underutilised, despite its potential to optimise trial design and recruitment (20). A recent meta-epidemiological study conducted to determine how often pilot studies planned to use qualitative data to inform the design and feasibility of a larger trial also highlighted that qualitative data collection was planned for in less than half of the protocols of pilot trials (92/227) in PubMed between 2013 and 2017 (21). A recent methodological review of 160 publications (123 protocols and 37 completed trials) on the reporting of progression criteria from external pilot trials to definitive RCTs reported that recruitment and retention were the most frequent indicators contributing to progression criteria (22). However, progression criteria were mostly reported as distinct thresholds (eg, achieving a specific target; 133/160, 83%) with less than a third of the planned and completed pilot trials that included qualitative research reported how these findings would contribute towards progression criteria (34/108, 31%).

The aim of this qualitative evidence synthesis (QES) was to explore how pre-trial qualitative research with trial participants, recruiters, clinicians, chief investigators and trial managers was used to inform recruitment and retention processes in full-scale randomised trials. Understanding how existing studies have employed qualitative methods at the pre-trial stage to inform recruitment and retention in future full-scale trials has the potential to identify how the

value of pre-trial work could be maximised and highlight key aspects for others to focus on when considering this type of work.

Methods

This systematic evidence synthesis is reported in accordance with the Enhancing Transparency in Reporting the Synthesis of Qualitative Research (ENTREQ) statement (23). The protocol was developed but was considered outside of scope by PROSPERO as it does not address health outcomes.

Search strategy

Searches were conducted on key electronic databases from inception to 4 March 2018: Dissertation Abstracts International, CINAHL, Embase, MEDLINE, Sociological Abstracts, Psycinfo, SSCI (Social Science Citation Index), the Cochrane Library and Health Technology Assessment. There were no language, date or geographic restrictions. The MEDLINE search strategy is included in supplementary document 1.

Different search strategies were used alongside electronic databases as using multiple search methods is more likely to locate relevant qualitative studies than relying solely on bibliographic databases (24). Methods applied included following up reference lists, hand searching and contacting experts or authors.

Inclusion/Exclusion criteria

Types of studies

We included all primary qualitative studies embedded in health-related feasibility or pilot studies. We also included studies using mixed methods if a clearly identifiable qualitative component

was present. Qualitative studies that explored recruitment and/or retention issues in a feasibility or pilot study to inform a subsequent, fully powered, Phase III randomised trial were included. Pre-trial qualitative studies that indicated progress to a full-scale trial was not feasible due to poor recruitment were also included.

Participants

All studies focusing on the perceptions and experiences of trial participants (e.g., patients, carers, or parents) who took part in a healthcare related pilot or feasibility RCT were included.

We also included studies reporting on the perceptions of stakeholders directly or indirectly involved in recruiting or retaining participants to RCTs (including chief investigators, trial managers, clinicians, research nurses, funders and research ethics committees).

Intervention/phenomena of interest

The body of research for which qualitative research was used to explore ways of optimising recruitment and or retention in RCTs at the pre-trial stage. All studies focusing on the perceptions and experiences of trial participants, recruiters, chief investigators, and other trial stakeholders were included.

Evaluation

To identify perceived barriers and facilitators to recruitment and or retention and the changes made to inform the design of a definitive trial.

Study selection

Titles and abstracts were screened by two reviewers independently (AE reviewed all studies along with either ST or KG) and disagreements were resolved by discussion. The full texts of potentially eligible studies were obtained and screened by two reviewers independently to confirm inclusion. Disagreements were resolved by discussion with a third opinion being sought if necessary.

Data extraction

Two reviewers independently (AE along with either ST, KG or HB) extracted data from eligible full-text papers using a prespecified data extraction form that included study aims, design, methodological approach adopted and main findings, including barriers and facilitators to recruitment and or retention. This was piloted on a subset of relevant studies and modified where necessary. All qualitative findings from the primary studies relevant to the research question were extracted. Findings were defined as any qualitative data describing a new concept, theme, sub-theme or finding statement, presented in forms including, but not limited to, text, tables, diagrams, supplementary files located anywhere in the paper. Participant quotations (first order constructs) and authors' interpretations (second order constructs) reported in the results/findings sections of included papers were extracted.

Quality appraisal of included studies

The application of quality criteria to qualitative research is widely debated (25). In this QES we are not concerned with the methodological quality of the included qualitative work *per se* but its contribution to planning the future full-scale trial. We therefore defined quality as the contribution of the pre-trial qualitative research to the full-scale trial endeavour (recruitment and retention) and whether the findings were used explicitly (as reported in the publications) to inform the plan

of action before moving onto a full-scale trial. Quality assessment of the included studies against a specific checklist was not applied.

Data synthesis

We followed the detailed methods for thematic synthesis outlined by Thomas and Harden (26). Coding and analysis were limited to the qualitative findings extracted from the primary studies; we did not code the whole of each included study because most of it was not relevant to our research question (see 'Data extraction'). First, we inductively line-by-line coded the results/findings and discussion sections covering any text reported as direct/verbatim participant quotes as well as the authors' interpretation of their data. Second, after extracting the reported barriers and facilitators to recruitment and retention, we created a codebook that was grouped into common themes. Team members (AE, KG, KH) then independently coded each extracted barrier and facilitator with the themes from the codebook. If new codes emerged, they were added iteratively to the codebook and the barriers and facilitators were re-themed accordingly. Third, the three reviewers (AE, KG, KH) met to reach consensus on the codes and themes, with further interpretative discussion focused on the research question to generate analytical themes. Throughout the coding process, the review authors met regularly to cross-check newly generated codes and themes against the data, discuss interpretation, and synthesise the analytical themes.

As our primary aim was to assess the practical significance of pre-trial qualitative research, we looked at each paper to identify whether qualitative findings were linked to any proposed changes to the recruitment and retention plan of action for subsequent full-scale trials.

Assessment of the certainty in evidence

The Confidence in the Evidence from Reviews of Qualitative research (CERQual) approach was used to to assess our confidence in the review finding (27). The CERQual approach is based on four components which include: the methodological limitations of included studies, the coherence of the review findings, the adequacy of data contributing to the review findings and the relevance of the included studies to the review question.

Each review finding was assessed by two reviewers (AE, KG) and concerns regarding any of the four components were noted. Four levels were used to describe the overall assessment of confidence in a review finding- high, moderate, low or very low. All review findings started off by default as 'high confidence' and were then 'rated down' by one or more levels if there were concerns regarding any of the CERQual components.

For CERQuaL assessment, we had no concerns regarding methodological limitations and relevance for the body of data contributing to each review finding. Our goal was not to judge whether some absolute standard of methodological quality had been achieved, but rather to indicate how and if findings from the qualitative research were transformed into an action plan to inform recruitment or retention processes for the full-scale trial. Considering that, a specific methodological quality checklist was deemed unnecessary as high or low scores would not affect our confidence in how and if qualitative findings informed the design of a subsequent full-scale trial. For the sake of brevity these two components were not included in the CERQual evidence profile.

Patient and public involvement statement

Patients and the public were not involved in the design, conduct, reporting or dissemination of our research.

Results

Thirty-five studies (connected to 31 feasibility studies) met the pre-specified inclusion criteria and were included in this QES. For some feasibility studies, there was more than one paper reporting findings from qualitative investigations. We included all relevant studies for comprehensiveness and to make sure we captured all perspectives from stakeholders involved.

No additional papers were identified from reference searches, review papers or reports. Figure 1 shows details of studies screened, excluded and included.

Characteristics of the included studies

All the included studies were published in English (19, 28-61) and were conducted in three high-income countries: the UK (n=33), Canada (n=1) and Norway (n=1). The majority of included studies (n=33/ 94%) were funded by UK organisations with two non-UK funded studies. Of the UK studies, %70 (n=23) were funded by the National Institute for Health Research (NIHR).

Each study included between 10 and 69 participants, with findings from 917 people in total reported across the papers. Contributing to the sample were: trial participants (629, 69%), clinicians and recruiters (234, 26%), family carers (26, 3%) and members of the Trial Management Group (19, 2%). Supplementary document 2 details the characteristics of the studies included in the review.

The setting of the feasibility studies in which the qualitative research was embedded included a range of clinical contexts such as; cancer (n=11), mental health (n=5), obesity (n=3), sexual and reproductive health (n=3), chronic fatigue (n=2), musculoskeletal conditions (n=2), pain (n=2), incontinence (n=2), tooth decay (n=1), childhood intermittent exotropia (n=1), renal disease (n=1), non-adherence to medications (n=1) and appearance-related distress (n=1). As expected, the clinical context differed as did the interventions under investigation; two studies (28, 38) were Clinical Trials of an Investigational Medicinal Product (CTIMP) and 29 were non-CTIMP studies. These interventions were also broadly categorised as: surgical (n = 6) and non-surgical (n=25).

All the included studies were embedded in pilot or feasibility trials to inform design aspects in preparation for a subsequent full-scale trial. The main data collection and analysis methods used were interviews (n = 31; 88%) and thematic analysis (n = 25; 71%). Audio recording of recruitment consultations and non-participant observations of consultations were used in six of the included studies (31, 45, 46, 50, 54, 55).

Findings

Twelve themes were identified as recruitment barriers and three as recruitment facilitators, whereas only two themes were identified as barriers for retention and none as retention facilitators (Table 1). The findings from the included studies focused more on recruitment than retention and researchers tended to focus on problems (barriers) rather than what might help (facilitators). The link between pre-trial qualitative findings and proposed changes to the recruitment and retention strategies to be used in any future full-scale trial were not always clear (supplementary document 3).

The findings that led to the identification of the barriers and facilitators highlighted in Table 1 and their link to the proposed changes for the full-scale trial are presented below in more detail.

Table 1 Summary of findings for themes linked to recruitment and retention barriers and facilitators.

	Barriers	Facilitators
Recruitment	1- Lack of clarity or understanding of randomisation	1- Personal gain and making a difference
	2- Lack of clinical equipoise	2- Communicating study information
	3- Strong patient treatment preferences	3- Social networks and experience of research
	4- Issues related to the control group	
	5- Communicating study information and associated terminology	
	6- Issues around the eligibility criteria	
	7- Practical barriers	
	8- Commitment of staff and participants to the trial	
	9- Beliefs and expectations about trial participation	
	10- Mismatch between the trial protocol and clinical care pathways	
	11- Participation burden	
	12- Lack of confidence in approaching study participants	
Retention	1- Burden of follow-up questionnaires	None identified
	2- Practical barriers	

Barriers to recruitment

A total of 12 recruitment barriers were identified. Supplementary document 4 outlines the findings associated with each theme and their link to the proposed changes for the full-scale trial.

Participant level factors

1. Lack of clarity or understanding of randomisation

Six studies (19, 52, 54, 55, 57, 60) outlined the influence of randomisation as a major barrier to recruitment. Trial participants believed the concept of randomisation was often not clear or perceived haphazardly and some struggled to understand the need for randomisation (19, 52). Despite explaining random allocation, some participants were still uncertain whether they would be selected based on some personal or illness characteristics (19, 60).

> *"How do they choose? Say, likes of five will go for the test and five will'nae, how do they actually choose?" (Patient) (19)*

Link between randomisation findings and changes proposed for the full-scale trial

The changes planned before the full trial to deal with issues around clarity of the randomisation process were clearly linked to coded data in three of the six studies (19, 54, 55). To clarify the concept of randomisation, one study reported that randomisation will be explained to participants in the following way: ''To try and make sure both groups are the same, each person is put into a group at random. This is the fairest way of deciding who gets the test and means everyone will have a 50/50 chance of being put in either group'' (19). In other cases, randomisation period was simplified and clarified and recruiters were encouraged to elicit

patients' lay views and explain that randomisation offered a way of resolving the dilemma of treatment choice (54, 55).

Two studies reported changes that were not explicitly linked to the qualitative findings (52, 60). In one study, authors suggested that the focus would be on training trialists who are involved in recruitment to complicated trials, both in terms of communication processes and on the assimilation of complex trial pathways (52). To resolve misunderstanding about the process of random allocation, one study reported that the study team needs to spend more time at participating practices training them in the recruitment process; patients should be supported to take the necessary time to ensure understanding of patient information sheets before signing consent (60). In one study, no changes to address the lack of understanding of randomisation were reported (57).

2. Strong patient treatment preferences

Patient treatment preferences was a theme in nine studies (29, 31, 32, 35, 45, 49, 54, 55, 57). Recruitment was hampered by strong preferences with patients often wanting the intervention and then expressing disappointment at being allocated to the control group (29, 31, 32, 35, 49, 54, 57).

Recruiters' perception of unequal treatment processes was also common, and they believed that many patients opted for one treatment because it was perceived as more convenient (45). In two studies (45, 54), recruiters assumed that patients came with media information that was biased in favour of the intervention (radical treatment) and often expressed lay views that cancer should be surgically removed.

''I still think to leave everyone, if you told in that group 'right half of you are going to go to physio [therapy] and half advice.' I think wouldn't you feel a little bit jipped, knowing 'wait a minute how come I'm not going to get anything'?" (Patient) (29)

Link between treatment preferences findings and changes proposed for the full-scale trial

The changes proposed before the full trial to address patient treatment preferences were clearly linked to qualitative data in four studies (31, 32, 45, 49). Changes reported were: recruiters were asked to move beyond initial probing questions in relation to patient preferences toward rectifying any erroneous views and to ask patients who appear to have a preference to 'keep an open mind' until they had heard all the relevant information (31), the need to gently challenge preferences that are based on inaccurate information and training recruiters to enable them to explain the need for randomisation and the rationale for the RCT to patients (45) and the incorporation of a preference arm in a future trial to account for parental preferences (49).

In five studies, no specific changes were reported to account for strong patient treatment preferences (29, 35, 54, 55, 57).

3. Issues related to the control group

Participants' lack of understanding the rationale for having a control group was a dominant theme in four studies (19, 29, 54, 60). Some participants struggled with understanding the need for a control group and said that allocation to the control arm of the study would put them off from participating (19). The perceived inequity in the content of the control arm was a major barrier to recruitment as some patients felt that they would not receive the best treatment if they were allocated to standard care (29, 60). In one study, the presentation of the control arm

caused difficulties for both patients and recruiters with the potential for interpretation as 'no treatment' (54).

> *"Participant: Aye. If I was one of the 50% when they said, "Right, we're gonna take a sample from you and test it", then yeh, but if I was one of the 50% that didn't get picked (the control group), then no. I would rather not know, actually. No." (Patient) (19)*

Link between control group findings and changes proposed for the full-scale trial

The changes proposed before the full trial to address the issues related to the control group were clearly linked to qualitative data in all four studies (19, 29, 54). The changes reported were: modification of the Participant Information Leaflet (PIL) where the control group will be changed to non-test group, which is what participants were most comfortable with (19), giving participants the necessary time to ensure understanding of patient information sheets before signing consent, especially with regard to clinical equipoise and that they will not necessarily benefit from participation (60) and augmenting the content of the control arm so that the trial arms could be perceived as more equitable (29).

4. Participation burden

The burden imposed by participation in the trial was a prominent theme in four studies (19, 38, 49, 52). The experience of completing and signing a consent form at the time of enrolment was burdensome in one study (38). In two studies, limited appointment time for the initial screening and the need for flexible appointments presented a challenge for participants to fully consider participation in the trial (19, 49). In the study by Moynihan (2012), patients commented on how poor administration and the need to 'work' their way around NHS waiting times prevented them from being fully included in the trial enterprise (52).

''Well, your appointments would have to be flexible, because people are still working. Not myself, I'm retired, but there are always people working who might not be able to get time off work'' (Patient) (19)

Link between participation burden findings and changes proposed for the full-scale trial

The changes proposed before the full trial to account for participation burden were not clearly linked to qualitative data in three studies (19, 49, 52). The changes proposed included facilitating a context in which patients feel fully included in the trial enterprise (52), separation of the role of the treating clinician from the main recruiter to the trial (49) and providing a phone call to potential participants to discuss the study after anticipated receipt of the full PIL (19).

In one study, no specific changes were reported to address this barrier (38).

5. Beliefs and expectations about trial participation

Pre-existing beliefs and expectations amongst study participants hindered recruitment efforts in ten studies (19, 30, 33, 36, 39, 42, 45, 52, 59, 60).

Participants' beliefs that undermined involvement in the trial process were: feelings of anxiety about a poor medical outcome and scepticism about being experimented on (36, 60), negative image about the hospital 'a place to die' (45), social desirability perception that the trial was designed to encourage people to stop smoking (19, 60), feelings of isolation and powerlessness (52) and a sense of denial (participants tended to deny their symptoms and therefore were ineligible) (59). In other cases, nurses believed they needed to protect patients from additional burden (which implicitly they believed the trial would cause) and this was cited as a main recruitment barrier (30).

"You've got to explain everything and they don't want to go to X hospital because they think once they go to—that's where the oncology centre is -so they think when they go there, they die, because that's where you go to die" (Recruiter).(45)

Link between beliefs and expectations findings and changes proposed for the full-scale trial

The changes proposed before the full trial to address pre-existing beliefs and expectations were clearly linked to qualitative data in six studies (19, 33, 36, 39, 42, 60). The changes proposed included asking recruiters to gently challenge patients' preconceptions (42) and to wait until the patient's condition is more settled before providing appropriate written informed consent (36).

One study reported changes which were not explicitly linked to coded data (52). In three studies, no specific changes were planned to address these issues (30, 45, 59).

Clinician/recruiter factors

6. Lack of clinical equipoise

Twelve studies outlined the influence of lack of clinical equipoise as a major barrier to recruitment (29, 31, 32, 35, 42, 45, 48-50, 52, 54, 55). Recruiters and clinical staff found it difficult to maintain equipoise as interviews revealed treatment preferences for certain subgroups of patients and this affected not only the number of individuals approached and invited but also the number of randomised participants (31, 35, 42, 45, 48). In many cases the explanation of the lack of evidence underlying the effectiveness and timing of intervention served to undermine the participant's confidence in the treating clinician, and by extension, the trial (32, 49).

Audio recording of recruitment consultations revealed that the terminology used by recruiters created unbalanced presentations of treatment options for which one treatment was presented at greater length and more favourably than the other and this was a strong indicator for the lack of trial equipoise (31, 32, 45, 50, 54, 55).

> *"I share the concerns and doubts that many of the patients do, i.e. that it won't work and it's difficult to sell a treatment when you yourself don't really believe it's going to make any difference" (Principal investigator) (32)*

Link between clinical equipoise findings and changes proposed for the full-scale trial

Changes planned before the full trial to maintain clinical equipoise were explicitly linked to qualitative data in six studies (29, 31, 42, 45, 49, 54). Changes reported were: Feedback sessions to be used to make recruiters aware of instances where they inadvertently used loaded terminology (31), asking recruiters to gently challenge and acknowledge their own bias in device preference (42), highlighting the need for principal investigators and recruiters to think more critically about the concept of scientific equipoise and how that should underpin the RCT (45), separation of the role of the treating clinician from the main recruiter to the trial (49), changing the order in which the treatments were presented and to describe their respective advantages and disadvantages in equivalent detail (54), training and monitoring of trial personnel to ensure notions of equipoise are delivered and reinforced consistently (29).

Three studies suggested changes to maintain clinical equipoise but were not clearly linked to qualitative data (32, 48, 52). These changes involved providing frequent and comprehensive training to recruiters (36,39) and finding ways of enabling practitioners to engage with study procedures (41). In three studies, no specific changes to maintain clinical equipoise were reported (35, 50, 55).

7. Communicating study information and associated terminology

Presentation of trial information was a major barrier to recruitment and this was evident in eight studies (32, 34, 50, 52-55, 59). In many cases, patients failed to understand the language of trial procedures or interpreted trial and clinical terminology quite differently than as intended by practitioners (for example, 'trial' was interpreted as 'try and see') (31, 52, 54). In other cases, recruiters and investigators agreed that the trial was difficult to explain and indicated that they found the quantity and content of trial information problematic (31, 53). There were also cases where study documentation was perceived as long, difficult to understand or repetitive in places and this affected decision making (34, 50). In the study by Griffin (2016), graphic description of surgery was thought to have put patients off randomisation and surgeons tended to go beyond their protocol brief, to explain the trial rather than referring patients on to the trial recruiter for this information (32).

> *"There's always a risk from the traction that it may stretch the nerves down the leg, so that could leave you with some numbness. If you're very unlucky it could leave you with a little bit of weakness there" (Principal investigator) (32)*

Link between communication findings and changes proposed for the full-scale trial

The changes proposed before the full trial to address the problems related to the communication of study information and associated terminology were explicitly linked to qualitative data in five studies (34, 50, 54, 55, 59). The changes reported were: changing the order in which the treatments were presented and describing their respective advantages and disadvantages in equivalent detail (32), construction of a simpler version of the study flowchart and drafting a new, shorter and clearer participant information sheets which removed the 'loaded' terminology (50, 55).

Two studies suggested changes to improve trial presentation but were not clearly linked to qualitative data (32, 52). These changes involved providing frequent and comprehensive training to recruiters on the assimilation of complex trial pathways (32, 52). In one study, no specific changes were reported to address this barrier (53).

8. Issues around the eligibility criteria

Another recurring theme that hampered recruitment efforts was the complexity trial staff faced in applying the eligibility criteria, which appeared in six studies (35, 41, 45, 49, 55, 59). In some cases, interpretation of the eligibility criteria differed between centres; there was less clarity over the minimum age for recruiting participants to the study and recruiters thought there was leeway for interpretation of the inclusion/exclusion criteria in partnership with the trial team (35, 41, 45, 55). In other cases, highly restrictive eligibility criteria and the difficulty to confirm eligibility for the trial at the initial screening visits hindered recruitment efforts (49, 59).

> *"I personally don't have a problem (with applying the eligibility criteria), but that's because I deal with trials all the time (...), but I think with some of my colleagues, both juniors within oncology and colleagues in surgery are not as familiar with trials, maybe have a little more difficulty in interpretation" (Recruiter). (55)*

Link between eligibility findings and changes proposed for the full-scale trial

The changes proposed before the full trial to address the problems related the complexity of applying the eligibility criteria were clearly linked to qualitative data in four studies (35, 41, 45, 49). The changes reported were: running screening training exercises to ensure similar screening standards and practices and an 'assumed eligibility' approach in all centres (35), close examination and regular meetings to discuss and resolve evolving issues (45) and

considering a limit on the upper age at which participants would be included (49). Two studies reported no changes to address this issue (55, 59).

9. Commitment to the trial

Variable staff commitment to the trial was a major barrier to recruitment in two studies (30, 55). Recruiters believed that some trial members were very committed to the trial but others were less dedicated or even antagonistic to it, and this contributed to the development of strong patient treatment preferences to one arm or the other (55). In other cases, recruitment of fewer than anticipated dyads affected nurses' commitment and the priority given to the trial (30).

> *"when we were doing the training it's just right there. And then it slips to tenth place. And if you haven't recruited, it's twentieth place because you're doing this, this and this" (Recruiter) (30).*

Link between staff commitment findings and changes proposed for the full-scale trial

The changes proposed before the full trial to address variable commitment by both participants and staff were clearly linked to qualitative data in one study (55) where clinical centres were asked to identify two Lead Recruiters (LRs) per site whose responsibilities would be to act as the focus for trial recruitment activity. The remaining study reported no changes to account for this barrier (30).

10. Lack of confidence in approaching study participants

Lack of confidence in approaching study participants or the topic of interest hindered recruitment in two studies (32, 33). In one study (32), time lag between recruitment clinics posed a challenge for research staff to preserve confidence and knowledge about the study. Research

staff also showed their concerns about not being able to respond to patients' questions and ask for consent without a senior clinician or surgeon signing the form for them (33).

> *"The gaps can be quite big between the patients, so I go back to my notes and reread everything again just before I'm going to see them so it's fresh in my mind because otherwise you're likely to forget" (Recruiter) (32).*

Link between 'lack of confidence in approaching participants' findings and changes proposed for the full-scale trial

The changes proposed before the full trial to account for the lack of confidence in approaching study participants were clearly linked to qualitative data in one study (33). The study highlighted the need for training primary care staff to address the lack of confidence in raising the sensitive issue of appearance-altering conditions.

For the remaining study, reported changes were not clearly linked to qualitative data (32). The study proposed providing frequent and comprehensive training to recruiters and modifying the support to teams in other centres according to their research experience.

Contextual/situational factors

11. Practical barriers

Practical barriers to recruitment was a major recurring theme in twelve studies (30, 32-34, 37-39, 43, 48, 49, 53, 59). Commonly cited barriers were: difficulty in implementing procedures owing to the multi-centre nature of the pilot (32), barriers of the primary care environment (33, 37) (time-limited consultations, high workload and competing studies), widespread reluctance in

practice to forgo written consent procedures at the time of trial enrolment (62), staffing issues (staff attrition, insufficient time, sub-optimal use of skill-mix) (30, 39, 43, 48) and delay in recruitment appointments (49).

> *"I then had a full caseload, so I wasn't taking on any new patients for quite a long time. […] We've had the consultants doing first visits and I would follow on afterwards because we've been so short staffed' (Recruiter) (30)*

Link between practical barriers findings and changes proposed for the full-scale trial

The changes proposed before the full trial to address practical barriers were clearly linked to qualitative data in five studies (34, 38, 39, 53, 59). The proposed changes included allowing flexibility in terms of how and when the research was conducted (34), ensuring that future trial centres are allocated adequate time and personnel (39), advising practitioners that patients will require longer appointments than normal for involvement in the trial (53).

Four studies reported changes to address this barrier but these were not clearly linked to qualitative data (32, 43, 48, 49). In three studies, no changes to address practical barriers were reported (30, 33, 37).

12. Mismatch between the trial protocol and clinical care pathways

Integrating the trial into clinical practice was considered a particular challenge hindering recruitment in four studies (31, 32, 42, 55). In some cases, the trial was presented as an 'add-on' rather than an integral part of existing clinical services (31, 32). In other cases, the pathway that potential participants had to follow from diagnosis to being recruited to the trial proved extremely complex (55).

"I think what we didn't appreciate was the number of the different pathways with which people actually come into that system, and the complexity (...) in terms of the treating centres and the randomising centres and all the different centres that are involved in an individual patient's care" (Principal Investigator) (35).

Link between integration findings and changes proposed for the full-scale trial.

The changes proposed before the full trial to account for poor trial integration into clinical care pathways were clearly linked to qualitative data in two studies (31, 55). Clinicians were asked to mention the study in the opening statements of the surgical consultations and to express enthusiasm for the study (31).Two studies proposed changes that were not explicitly linked to coded data (32, 42). These involved providing frequent and comprehensive training to recruiters (32) and recruiting a trial Champion to encompass coordination and facilitation of appointments and communication (42).

Facilitators of recruitment

A total of three recruitment facilitators were identified. Supplementary document 5 outlines the findings associated with each theme and their link to the proposed changes for the full-scale trial.

1. Personal gain and making a difference

Potential participants' sense of obligation and altruism was a major factor that impacted positively on their decisions to participate in five studies (33, 35, 36, 41, 44). Altruism was often cited as an important motivating factor, contributing to improved care for others in the future (35, 36, 41). In other cases, participants were motivated by having a personal interest in the topic and perceived that research may bring direct personal benefit (33, 36, 41).

''I know that's sort of a I´ thing to say, but it's true, I mean I'm not try'..., for sympathy, but I have had a terrible time, and I don't want other people to have it like, if you know, if I have children I wouldn't want them to have go through that I went through, and um, in generally I just, you know, want to take part in it for other people''(Patient) (44)

Link between altruism findings and changes proposed for the full-scale trial

No changes were reported in the five studies to take advantage of the conditional altruism expressed by participants and its potential impact on recruitment before the full-scale trial starts.

2. Communicating study information

Providing clear and informative study information to potential participants was an important facilitator for recruitment in six studies (34-36, 44, 46, 50). In many cases, providing clear and informative study information and ensuring study participants had a thorough understanding of the study were important factors to facilitate a decision about taking part (34-36, 44, 50) (34,47,50,61,62). In the study by Realpe, a logical sequence for information sharing (six step recruitment model) emerged after analysis of recruitment consultations and this seemed to facilitate recruitment (46).

''So everything was really well explained you know, so yeah I mean I can't fault it really, no I was well impressed with it all'' (Patient) (35)

Link between information communication findings and changes proposed for the full-scale trial

The changes planned before the full-scale to take advantage of providing clear study information were reported in only one study (46). The study proposed a six-step recruitment model (specifying: explain the condition, reassure patients about receiving treatment, establish

uncertainty, explain the study purpose, give a balanced view of treatments, and explain study procedures) to train and support recruiters in the large number of new centers in the full-scale trial.

3. Social networks and experience of research

Patients' social networks and positive experience of research helped to promote study participation in two studies (36, 40).

> *''So, I think because a lot of them are friends here, so they talk, and, you know, if you're doing that, "What do you think about it?" So, they ask each other.…Cause a lot of things happen that way here, cause they listen to what other patients talk to nurses about, then they think, "Oh, okay, I'll try that, too"' (patient) (40)*

Link between networks and experiences findings and changes proposed for the full-scale trial

No changes were reported in the two studies that identified social networks as influential for recruitment before the full-scale trial starts.

Barriers to retention

Two retention barriers were identified. Supplementary document 6 outlines the findings associated with each theme and their link to the proposed changes for the full-scale trial.

1. Burden of follow-up questionnaires

Nine studies outlined that the burden of follow-up questionnaires was a major barrier to retention (35, 37, 47, 50, 51, 57-60). Across a variety of contexts, questionnaire structure was

perceived to be burdensome and this encompassed many forms: forced choice responses of questionnaires which did not capture the reality of patients' experiences (37), lack of clarity and difficulties with some of the wording in the questionnaires (51, 60), repetitive and difficult-to-complete questionnaires (47, 58). In two studies, the timing of questionnaires was perceived to be burdensome and irrelevant because it did not allow time for change when many patients had few, if any symptoms to report (35, 50).

> *"I didn't understand a lot of the questions so she [researcher] was having to interpret them . . . and that probably it probably went longer than what it should have done" (patient) (37)*

Link between questionnaire burden findings and changes proposed for the full-scale trial

The changes proposed before the full trial to address the burden of follow-up questionnaires were clearly linked to qualitative data in five studies (35, 51, 57-59). The changes reported involved modifying questionnaires to allow 'short-cutting' of irrelevant areas to reduce respondent burden (35), reducing the number of questionnaires in the subsequent trial (59) and training fieldworkers in assisting participants with questionnaire completion if required (51).

In two studies, changes reported were not clearly linked to coded data (47, 50). These involved identifying measures to improve outcome data collection using a variety of strategies. Two studies reported no changes to address this barrier (37, 60).

2. Practical barriers

Practical issues appeared to hinder participant retention in two studies (57, 60). Some participants reported that making journeys to the site required considerable effort (57, 60). A small minority of patients found the process of getting a chest X-ray difficult. Some

participants had to pay for the parking costs and using public transport seemed to be too problematic (60).

Link between practical barriers findings and changes proposed for the full-scale trial

One study reported changes to account for practical barriers but were not clearly linked to qualitative data (60). The study reported that patients should be reassured that participation in the trial should cause them the least amount of inconvenience. In one study, no changes to address practical barriers were reported (57).

Facilitators for retention

There were no facilitators for retention reported in the included studies.

GRADE-CERQual assessment

The CERQual Evidence profile is presented in supplementary documents 7 and 8 which highlights each review finding along with its CERQual assessment.

Discussion

Embedded qualitative investigations to illuminate barriers to recruitment and retention prior to a full-scale trial have increased in the last decade (20, 63). This systematic qualitative evidence synthesis was based on findings from 35 studies. The review provides important insights on how the findings of qualitative research methods at the pre-trial stage were used to inform changes to the recruitment and retention plan of future full-scale trials.

The systematic synthesis identified an assortment of recruitment barriers (n=12) but only identified two barriers to retention. There were only three facilitators for recruitment, and there were no facilitators for retention. The findings of included studies tended to focus more on the challenges to recruitment and retention rather than the facilitators. Perhaps researchers are instinctively more interested in what is not working well (the barriers) and trying to make changes to remove those barriers. However, it is also important for researchers to take advantage of what facilitated recruitment and retention at the pre-trial stage and to ensure 'what worked well' stays working well in the full-scale trial and that should be reflected in the reporting. Of the three recruitment facilitators identified, few studies (46, 59) explicitly reported how these facilitators would be used to improve the recruitment process in the subsequent full-scale trial. It is hard to believe that there are no facilitators for retention in the included studies; perhaps researchers were not looking for, or reporting, this.

The focus on recruitment may have meant that retention was overlooked, something that is in line with findings from a qualitative interview study with stakeholders from five trials (64). The study identified that extensive work on recruitment targets was deemed detrimental to retention activities and highlighted the need for efficient training and support for trial staff involved in retention practices and a wider recognition of the importance of retention from funding organisations. A recent evidence synthesis of qualitative studies identified only 11 studies that had explored any aspect of trial retention with participants who had not completed the trial until the end (65). While it may be hard to re-engage with former participants to understand why trials fail to retain them, the lack of knowledge about this issue is striking. To date, very few interventions have been shown to improve retention in RCTs, with only moderate certainty evidence available for the use of monetary incentives with a prompts or reminder to improve responses to postal questionnaires (10). Yet, none of the retention interventions to date has been informed by evidence on the perspectives of participants and/or former participants from a

range of trials and what they experience as barriers and enablers to trial retention. A recent qualitative study with participants from several host trials provided participant reported evidence of behavioral reasons investigating two retention behaviours: questionnaire return and follow-up clinic attendance (66). Barriers frequently reported in relation to both target behaviours stemmed from participants' knowledge, beliefs about their capabilities and the consequences of performing (or not performing) the behavior. The findings can be used to develop participant-centered behavioural interventions where uncertainties remain about the most effective ways to increase retention. The study also highlighted that it is critical that researchers consider barriers and enablers of retention at the pretrial stage to prevent problems before they arise. Lawrie et al (67) applied a behavioural framework to understand the barriers and enablers to questionnaire return within the C-Gall trial. The study outlined practical considerations other researchers may wish to consider to increase questionnaire return rate, such as managing participants' expectations of trial-related activities (e.g., how many questionnaires they will be expected to complete), highlighting the negative consequences of participant drop- out, tailoring the administration of questionnaires to suit individual preferences and circumstances and providing support where required.

The most common recruitment barriers reported in the included studies were lack of understanding the concept of randomisation, preference for a particular treatment option, and lack of clinical equipoise. The use of innovative qualitative data collection methods provided an in-depth understanding of recruitment processes, how the trial was presented, and how patients were responding to the trial. Audio recording of recruitment consultations is a good example that provides specific recruiter feedback and opportunities to change practices (46). The approach was successfully implemented in six of the included studies (31, 45, 46, 50, 54, 55). Exploring patient preferences, presenting information while being aware of framing effects, and avoiding the use of loaded terminology were identified as practical actions that recruiters

could take to improve recruitment. The qualitative analysis of recruitment consultations highlighted communication practices that helped the multicentre pilot UK FASHIoN trial to achieve a 70% recruitment rate, although it had been assumed at the outset that it would be extremely difficult (46). On the other hand, retention was rarely discussed during clinical trial consultations. An embedded mixed-methods with a purposive sample of audio-recorded trial consultations obtained from four sites of a large multicenter UK-based surgical RCT revealed that there was no discussion of retention across 79% of consultations. If retention was discussed, it only made up 3% (at best) of the consultation content (68).

The changes reported in the included studies to address recruitment barriers mainly aimed to clarify the concept of randomisation to study participants, maintain clinical equipoise, challenge patient treatment preferences and ensure clarity around the eligibility criteria. The changes reported to address retention barriers centered around identifying ways to ease the burden of follow-up questionnaires. However, in many cases, the link between the changes proposed for the full-scale trial and the pre-trial qualitative findings was not explicit. This was the case in nearly 50% of the included studies, meaning that capitalising on the value of pre-trial qualitative research when reporting these studies was not clear despite findings suggesting there was a problem that needed to be addressed. This might be because of limited article word count in papers reporting the results of the qualitative work alongside the pilot trial results, where very little space was allocated to the qualitative component and its impact was usually reported rather than demonstrated. It could also, of course, be because the proposed changes were not related to the pre-trial qualitative findings. It is impossible to tell from many published reports.

The findings from our QES are in line with recently published studies on how qualitative work prior to an RCT can be invaluable in informing study design, especially for new interventions. A pre-trial qualitative work with health care professionals conducted to refine the design and

delivery of the Prepare for Kidney Care RCT identified challenges related to its design and recruitment and allowing changes to be made to the trial design in advance of the trial commencing (18). Likewise, clinicians' views of patient-initiated follow-up in head and neck cancer were explored in a qualitative study to Inform the PETNECK2 trial (69). This study highlighted clinicians' concerns that patients have unmet psychosocial needs during follow-up and that head and neck cancer community need to consider alternative follow-up protocols and justification for the PETNECK2 study.

Quality of the evidence and certainty of the findings

Since the main aim of this qualitative evidence synthesis was to explore the practical utility of using qualitative research methods at the pre-trial stage with the aim of maximising the chances of recruitment and retention success in a future full-scale trial, CERQual assessment of the overall confidence in the evidence was applied to assess whether qualitative findings were used to inform changes to the recruitment and retention plan. We considered a little less than half of the findings as of high certainty because the findings showed high levels of coherence and adequacy, while we assessed the remaining findings to be of moderate certainty because of concerns regarding both the coherence of the findings and the adequacy of data in the underlying studies. This means that for over half of the included studies, the contribution of pre-trial qualitative research to the decision-making process and how it informed recruitment and retention processes for any subsequent full-scale trial was not explicit.

Limitations and strengths of the review

This qualitative synthesis brings together the evidence-base of barriers and facilitators to recruitment and retention identified in pre-trial qualitative work together with an assessment of the practical utility of pre-trial qualitative research in informing the recruitment and retention plan

before the commencement of a full-scale trial. The comprehensive search strategy optimises the likelihood that we have identified all relevant studies published in the time period. Although we did not apply a quality assessment checklist to individual included studies to consider the relationship between quality and maximising the value of pre-trial qualitative research, the systematic methodology and the use of GRADE-CERQual assessment of confidence in the findings is a strength of the review (70).

There are however limitations. The review was based on what was written in published research and this may not reflect the breadth of qualitative research that is undertaken in practice. Every effort was made to contact corresponding authors to obtain a full account of qualitative data where information was lacking in the published report, or when researchers reported that a stand-alone article based on qualitative research will be published separately but was not yet available. However, not all authors provided these data, in which case it means the synthesis was limited to the findings and quotes published in the qualitative reports. Of the 35 included studies, 33 were UK based (the other two were conducted in Canada and Norway) and this resonates with the fact that both recruitment and retention are among the top three methodological research priorities in the UK (71). It does, however, mean it is uncertain whether and to what extent the findings apply to the trial environment outside the UK. The geographical spread of studies included in our QES is in line with the Cochrane review on factors that impact on recruitment to randomised trials (72). Of the 29 studies included in the review, 16 studies were conducted in the UK, six in other European countries (Austria n = 1, Denmark n = 1, Germany n = 2, Sweden n = 1, the Netherlands n = 1); three in the USA; and one each in Australia, Canada, New Zealand and Tanzania.

Suggestions for good practice and maximising value

While pre-trial qualitative research can be very illuminating in identifying barriers and facilitators to recruitment and retention, researchers need to clearly report how and if the findings from the qualitative research will be used to optimise their recruitment and retention approaches in the full-scale trial. This qualitative evidence synthesis highlights the inefficient use of pre-trial qualitative research; despite identifying an assortment of barriers to recruitment or retention, researchers failed, in most cases, to articulate how their qualitative findings would be put into a clear action plan to optimise the conduct of a future full-scale trial. The key issues identified by qualitative research need to be discussed with trial stakeholders and used in support of making practical changes to the trial design, presentation, or amendments to the study protocol and that should be made explicit in the reporting. This could help make a stronger case when submitting funding applications for a planned full-scale trial and reassure funders that extensions will not be required. Examples of involving stakeholders at all phases of trial planning and conduct have proven effective in increasing both recruitment and retention (73). Crocker et al also investigated the impact of patient and public involvement (PPI) on rates of enrolment and retention in clinical trials (74). On average, PPI interventions modestly but significantly increased the odds of participant enrolment in the main analysis (odds ratio 1.16, 95% confidence interval and prediction interval 1.01 to 1.34). In exploratory subgroup analyses, the involvement of people with lived experience of the condition under study was significantly associated with improved enrolment (odds ratio 3.14 *v* 1.07; P=0.02). The findings for retention were inconclusive owing to the paucity of eligible studies.

This evidence synthesis provides some pointers for how researchers can improve their approach to pre-trial qualitative work. Below we have suggested two summary recommendations that may help to maximise the value of undertaking this type of work:

1. **Plan the qualitative research with the full-scale trial in mind**

Researchers need to think about the recruitment and retention challenges their planned trial is likely to face and design the pre-trial qualitative research to specifically address these, while of course allowing for a degree of openness and flexibility to address possible emerging issues as the trial progresses. Researchers need to prioritise the practical importance of qualitative research and its potential to optimise the conduct of the full-scale trial.

2. **Be clear that changes were made to the recruitment or retention plan**

In some cases, there was a clear link between qualitative findings and a particular change being made to the recruitment or retention plan for the full-scale trial. In others, there was no explicit link between findings and changes, or the lack of changes. For these the influence of pre-trial qualitative work on the recruitment or retention plans for the full-scale trial remained unclear, either because of poor reporting or because there was no link. Researchers should provide a clear statement of their findings and the linked changes, if any, to the recruitment and retention plan for the full-scale trial.

A good example of how barriers to recruitment and the corresponding changes were reported in a study is that by Paramasivan et al 2017 ‘‘Enabling recruitment success in bariatric surgical trials: pilot phase of the By-Band-Sleeve study’’ (31). This study was highlighted as a good example because qualitative findings were clearly reported, and the decision-making process was made explicit with regards to how the findings were transformed into actions to mitigate against recruitment problems before the commencement of a full-scale trial.

Conclusion

Many trial teams do pre-trial qualitative work with the aim of improving, among other things, recruitment, and retention in future full-scale trials. Just over half of all reports of such work do not clearly show how their findings will change the recruitment and retention strategy of the future trial. The scope of pre-trial work needs to expand beyond looking for problems and also look for what might help and spend more time on retention.

Contributors AE, ST and KG conceptualised and designed the review. CF conducted the search. AE, ST and KG reviewed titles, abstracts, and full-text papers for eligibility. AE extracted data from all the included studies along with either ST or KG or HB. Data synthesis was carried out by one researcher (AE) and verified by two researchers (KG, KH) for meaning and content. AE drafted the paper, and all authors reviewed drafts and approved the final version.

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Figure legends/caption

Figure 1- PRISMA flow diagram

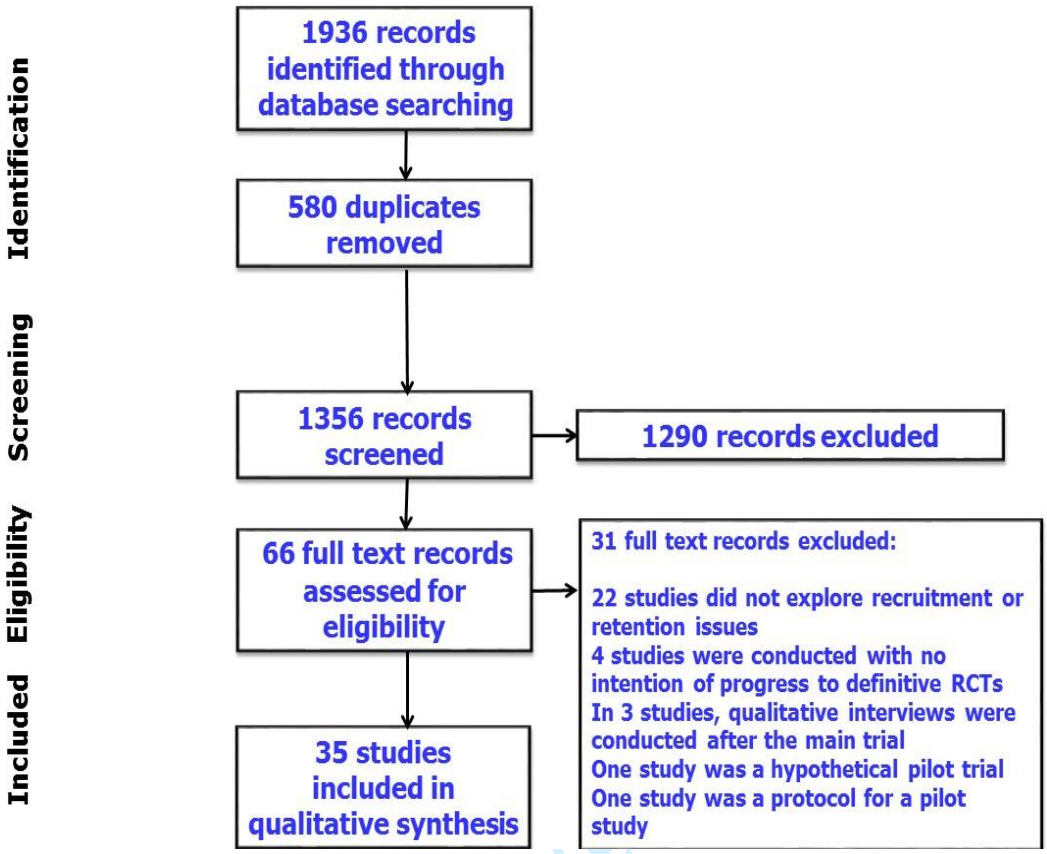

Figure 1 PRISMA flow diagram

MEDLINE MULTI-FILE SEARCH STRATEGY

Database: Embase Classic+Embase <1947 to 2018 Week 9>, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>

OVID Multi-file Search URL: https://shibboleth.ovid.com/

Search Strategy:

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1 qualitative research/ (89507)

2 qualitative research.tw,kw. (33140)

3 (qualitative adj3 method$).tw. (52706)

4 (qualitative method? or qualitative methodology).kw. (2407)

5 (qualitative adj3 stud$).tw. (94525)

6 qualitative study.kw. (2277)

7 focus groups/ use ppez (25522)

8 focus group?.tw,kw. (80757)

9 grounded theory/ (5381)

10 grounded theory.tw,kw. (20998)

11 narrative analys?s.tw,kw. (2073)

12 process evaluation.tw,kw. (5813)

13 mixed method?.tw,kw. (27752)

14 mixed method$.mp. (28575)

15 mixed methodology.tw,kw. (675)

16 (in depth adj4 interview$).tw. (40998)

17 in depth interview?.kw. (159)

18 ((semi structured or semistructured) adj5 interview$).tw. (87381)

19 semi structured interview?.kw. (250)

20 qualitative interview$.tw. (17258)

21 qualitative interview?.kw. (396)

22 (interview$ and theme$).tw. (58848)

23 interview?.kw. (6522)

24 (interview$ and audio recorded).tw. (4755)
25 qualitative case stud$.tw. (1950)
26 descriptive case stud$.tw. (476)
27 qualitative case study.kw. (22)
28 descriptive case study.kw. (0)
29 qualitative exploration.tw,kw. (1893)
30 qualitative evaluation.tw,kw. (6656)
31 qualitative intervention.tw,kw. (25)
32 qualitative approach.tw,kw. (7695)
33 qualitative inquiry.tw,kw. (1168)
34 qualitativ$ analys$.tw. (32509)
35 qualitative analysis.kw. (1173)
36 (qualitative adj3 data).tw. (34073)
37 qualitative data.kw. (132)
38 discourse analysis.tw,kw. (3297)
39 discursive.tw,kw. (3255)
40 phenomenological.tw,kw. (30851)
41 thematic analysis.tw,kw. (24656)
42 ethnograph$.tw. (18785)
43 ethnography.kw. (1721)
44 action research.tw,kw. (7591)
45 ethno?methodology.tw,kw. (156)
46 social construction.tw,kw. (1763)
47 or/1-46 (426888)
48 Patient Dropout/ use ppez (8077)
49 Patient Dropouts/ use emcz (539)
50 Patient Recruitment/ use ppez (62890)
51 Research Subjects/ use emcz (5835)
52 Patient Selection/ (145510)

53 Informed Consent/ (125958)

54 patient recruitment.kw. (179)

55 attrition.kw. (1400)

56 patient retention.kw. (32)

57 ((recruit$ or participat$ or take part or dropout$ or drop$ out$ or withdr?wl$ or barrier$ or retention or response$ or respond$ or attrition) adj4 trial?).tw. (58536)

58 or/48-57 (333454)

59 47 and 58 (8081)

60 Feasibility Study/ use emcz (88085)

61 Feasibility Studies/ use ppez (63390)

62 Pilot Projects/ use ppez (113723)

63 Pilot Study/ use emcz (119757)

64 feasibility.tw. (357698)

65 pilot.tw. (320772)

66 pre trial$.tw. (1487)

67 ((early or develop$) adj3 phase).tw. (110286)

68 vanguard.tw. (1626)

69 ("proof of principle" or "proof of concept").tw. (62696)

70 or/60-69 (741610)

71 59 and 70 (983)

72 71 not abstract.pt. (799)

73 limit 72 to English language (832) MEDLINE 422 EMBASE 351

74 remove duplicates from 73 (504)

S4: ***Characteristics of included studies.***

Study ID	Country	Clinical area	Study aim/ objective	Participants	Method of data collection	Method of analysis
Michie 2014	UK	Sexual and reproductive health	To determine the feasibility of a larger study designed to ascertain if pharmacy-based interventions can increase the uptake of effective contraception after emergency contraception.	12 women, four from each arm of the pilot study and the pharmacists involved	Semi-structured interviews	Thematic analysis
Palmer 2016	UK	Joint hypermobility syndrome	To explore Patients' and health professionals' perspectives on the intervention and the proposed trial (a parallel two-arm pilot RCT comparing 'advice' with 'advice and physiotherapy'.	25 patients (three men and 22 women; aged 19–60 years) 16 health professionals (three men and 13 women; 0–30 years post qualification; 14 physiotherapists and two podiatrists)	Seven focus groups were conducted with patients and health professionals before the pilot trial Interviews with participants and health professionals and short telephone interviews with six patients who declined to take part in the trial.	Thematic analysis
Latter 2018	UK	Cancer	To evaluate participants' experiences of Cancer Carers Medicines Management and trial procedures.	12 nurses and 9 family carers	Face-to-face semi-structured qualitative interviews	Framework approach

Paramasivan 2017	UK	Severe and complex obesity	To improve information provision and recruitment organization in the pilot phase of the By-Band-Sleeve study (gastric bypass versus gastric band versus sleeve gastrectomy)	12 in-depth staff interviews, 84 audio recordings of patient consultations, 19 non-participant observations of consultations and patient screening data	Interviews, audio recordings of recruitment consultations and non-participant observations of consultations	Thematic analysis using constant comparative methods
Griffin 2016	UK	Femoroacetabular impingement syndrome	To understand the recruitment process in a feasibility study of a randomised controlled trial of arthroscopic surgery for hip impingement compared with best conservative care (UK FASHIoN) so that any difficulties related to design, or conduct can be identified, and changes put in place.	Ten interviews conducted with members of the TMG, Twenty-one interviews with clinicians and research associates	Face-to-face In-depth interviews	Constant comparison and case study approaches
Hamlet 2017	UK	Appearance-related distress, teasing or bullying	To explore GP and nurses' experiences of recruiting to a trial exploring the feasibility of evaluating YP Face IT, a novel online psychosocial intervention to support young people with appearance-altering conditions.	Nine different GPs and two nurses	Focus groups, face-to-face or telephone interviews	Thematic analysis

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Aventin 2016	UK	Sexual health	To determine the facilitators and barriers to recruitment and retention to a school-based sexual-health cluster randomised trial	Principals, vice-principals, teachers, pupils and parents recruited to the study	Semi-structured interviews and focus groups	Thematic analysis
Hilton 2015	UK	Stress urinary incontinence	To explore women's understandings and experiences of the consent process and their decision to participate in the pilot RCT to assess the feasibility of a future trial of invasive urodynamic testing prior to surgery for stress urinary incontinence in women (INVESTIGATE-I)	29 women who had participated in the pilot study.	Semi-structured interviews	Framework analysis
Van Den Berg 2017	UK	Cardiac chest pain	To explore patient attitudes and potential barriers to participation in a full-scale randomised trial comparing use of the Manchester Acute Coronary Syndromes (MACS) decision rule with standard care	10 participants	Semi-structured interviews (two interviews were undertaken face to face and eight by telephone).	Framework analysis
Gabbay 2017	UK	Depression and debt	To explore participants' experience of involvement in the trial (Debt Counselling for Depression in Primary Care: an adaptive randomised	23 patients, 7 GPs and 4 CAB (Citizens Advice Bureau) advisors who participated in the trial	Semi-structured interviews	Thematic analysis

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			controlled pilot trial (DeCoDer study), including the acceptability of trial processes and outcome measures. To access narrative voices of those involved in the design and delivery of the trial, including the different roles played by each team member.			
Lawton 2017	UK	Women who have a retained placenta	To explore women's and staff experiences of, and views about, the recruitment and consent procedures used during the pilot phase of a peripartum trial conducted in an emergency setting.	Interviews with staff (n = 27) and participating women (n = 22).	Semi-structured interviews	Thematic analysis
Trevelyan 2016	UK	Phantom limb pain (PLP)	To inform the development of an appropriate and feasible protocol for use in a definitive multicenter RCT assessing the effectiveness of acupuncture for treating lower limb amputees with PLP.	13 patients	Semi-structured interviews	Thematic analysis
Thompson 2016	Canada	End-stage renal disease	To better understand feasibility of a main study	25 patients and 11 staff were interviewed	Semi-structured interviews	Thematic analysis

			evaluating the efficacy of cycling and resistance exercise each performed during the haemodialysis treatment on QoL			
Bhattacharya 2016	UK	Older people with unintentional non-adherence to medications	To gain opinions on each stage of a trial assessing the effectiveness and cost-effectiveness of medication organisation devices compared with usual care for older people in a community setting to identify what worked well and less well with a view to optimising definitive study design.	Two mixed focus groups of RCT participants (Eight) and a range of health-care professionals (Seven) involved in the delivery of the RCT.	Focus groups	Thematic analysis
Ritchie 2015	UK	Cancer	To provide in-depth, explanatory information to inform the main trial (the Cancer and Venous Access (CAVA) RCT comparing the clinical and cost-effective-ness of three venous access devices for chemotherapy delivery.	Three patient focus groups (each comprising three patients) and 23 interviews with clinical staff were conducted.	Focus groups and semi-structured interviews	Thematic analysis
Blekken 2015	Norway	Fecal incontinence	To improve the design of a planned cluster-randomised controlled trial of two educational programs for	One focus group interview (n = 7) and 4 individual interviews.	Focus groups and semi-structured interviews	Thematic analysis

			care staff concerning nursing home patients' fecal incontinence			
Notley 2015	UK	Mental health difficulties	To explore individual experiences of participating in a pilot trial of social recovery cognitive–behavioural therapy.	13 participants	Face-to-face qualitative semi-structured interviews	Thematic analysis
Hamilton 2013	UK	Cancer	To investigate the factors contributing to poor recruitment to the EaStER trial ''Early Stage glottic cancer: Endoscopic excision or Radiotherapy'' feasibility study.	Surgeons and nurse recruiters	Semi-structured interviews, focus groups and audio-recordings of recruitment encounters	Thematic analysis
Realpe 2016	UK	Femoroacetabular impingement syndrome	To understand the recruitment process during a pilot RCT comparing surgical and nonsurgical interventions for hip impingement (UK FASHIoN) so that any difficulties related to design or conduct can be identified and changes put in place.	12 consultations with 60 patients were recorded	Audio-recording of recruitment consultations	Thematic analysis and focused conversation analysis.
Foster 2016	UK	Cancer related fatigue	To test the proof of concept and inform the design of an effectiveness trial (RESTORE, an exploratory RCT of a web-based intervention to	19 participants	Semi-structured telephone interviews.	Content analysis

			enhance self-efficacy to manage cancer-related fatigue)			
Pentecost 2015	UK	Depression	To inform the design of a full-scale trialto assess the effectiveness of combining behavioural activation with physical activity promotion for adults with depression.	Nine psychological wellbeing practitioners and 15 participants	Semi-structured interviews	Thematic analysis
Clarke 2015	UK	Intermittent Exotropia X	To inform the design and conduct of a future full randomised controlled trial comparing eye muscle surgery against active monitoring for childhood intermittent exotropia.	parents and treatment orthoptists	Semi-structured interviews	Thematic analysis
Crawley 2013	UK	Chronic fatigue syndrome	To explore the feasibility and acceptability of the recruitment, randomisation and interventions in a trial of specialist medical care and the Lightning Process in children with chronic fatigue syndrome.	13 mothers and 12 children on three occasions	In-depth interviews and audio recordings of recruitment consultations	Thematic analysis
Gray 2013	UK	Obesity	To elicit men's experiences of participation in a pilot trial of weight management for overweight and obese men	Four focus groups total of 26 men sampled purposively from a list of volunteers to include men	Focus groups	Framework approach

			delivered through professional football clubs.	of different ages and baseline BMIs		
Nair 2014	UK	Lung Cancer	To explore the potential barriers and facilitators that would impact recruitment to a trial evaluating the effectiveness of screening using a blood test for the early detection of lung cancer (the ECLS trial).	32 people who matched the inclusion/exclusion criteria for the trial took part in four focus groups	Focus groups	Thematic analysis
Moynihan 2012	UK	Transitional Cell Carcinoma (TCC) of the bladder	The aim was to illuminate problems in the context of randomisation in a trial comparing selective bladder preservation against surgery in muscle invasive bladder cancer (SPARE)	24 patients (accepters and decliners to randomization	Semi-structured interviews	Thematic analysis
Marshman 2012	UK	Tooth decay	To describe service providers' and users' perspectives on the pilot trial to identify improvements to the conduct and design of the FiCTION (Filling Children's Teeth: Indicated Or Not?) main trial.	Individual interviews were held with 4 dentists and a group interview was held with 17 dental team members. Face-to-face interviews were held with 4 parents and children and 5 telephone interviews were conducted with parents	Individual/group interviews face-to-face and telephone interviews	Framework approach
Audrey 2011	UK	Localized prostate cancer	The purpose of ASPECTS (Aspirin and Esomeprazole	45 patients	In-depth interviews and audio recording of	Framework approach

			Chemoprevention in Barrett's metaplasia) was to explore patients' experiences of palliative chemotherapy treatments as part of ASPECTS (Aspirin and Esomeprazole Chemoprevention in Barrett's metaplasia) trial.		recruitment consultations	
Paramasivan 2011	UK	Transitional cell carcinoma of the bladder	To explore reasons for low recruitment and attempt to improve recruitment rates to the SPARE (Selective bladder Preservation Against Radical Excision) trial by implementing changes suggested by qualitative findings.	9 recruiters and 9 non-recruiters were interviewed across four centers.	Audio recording of discussions between potential RCT participants and recruitment staff In-depth interviews with Trial Management Group	Simple counts, cross tabulations and content analysis
Forbes 2010	UK	Breast cancer	To explore women's views of the design of a large pragmatic randomised controlled trial of the policy of offering a health professional-delivered intervention to promote early presentation with breast symptoms in older women	69 women participating in 7 focus groups and 17 in-depth interviews	Focus groups and in-depth interviews	Thematic analysis

McEachan 2016	UK	Childhood obesity	To inform progression to a definitive trial comparing Healthy and Active Parenting Programme for early Years intervention and usual care	14 parents (across intervention and control groups) 7 telephone interviews with women who were randomised to the intervention group but who did not attend any sessions	Semi-structured interviews and focus groups	Thematic analysis
Tsianakas 2017	UK	Recurrent or metastatic cancer	To explore the acceptability of CanWalk intervention, randomisation process and outcome measures.	10 participants (5 per group; 6 men and 4 women; 5 >65 years; 9 White British or Irish)	Semi-structured telephone interviews	Thematic analysis
Ellis 2017	UK	lung cancer	To elicit the views and perceptions of those who participated in a randomised controlled feasibility trial testing a non-pharmacological intervention, Respiratory Distress Symptom Intervention (RDSI)	11 lung cancer patients, 3 caregivers and 7 researchers involved in recruitment	Semi-structured interviews	Thematic analysis
Kendrick 2017	UK	Depression	To determine key elements of the best design for a trial of patient-reported outcome measures (PROMs) for monitoring primary care patients with depression.	14 patients and 13 practice staff.	Semi-structured interviews	Thematic analysis

Myall 2015	UK	Cancer-related fatigue	To assess feasibility and acceptability of RESTORE, an exploratory RCT of a web-based intervention to enhance self-efficacy to manage cancer-related fatigue (CRF) following primary cancer treatment	19 patients	Semi-structured telephone interviews	Framework approach

The link between qualitative findings and changes proposed to recruitment and retention for the full-scale trial for each barrier and facilitator

	Barriers (number of studies contributing to the review finding)	Were there any changes planned for the full-scale trial based on pre-trial qualitative data? Yes, Unclear, No (the number of studies contributing to the review finding)	Facilitators	Were there any changes planned for the full-scale trial based on pre-trial qualitative data? (Yes, Unclear, No)
Recruitment	1- Lack of clarity or understanding of randomisation (n=6/35[1])	Yes (3/6) Unclear (n=2/6) No (n=1/6)	1- Altruism and personal gain (n=5/35[1])	No changes reported

[1] There were 35 included studies in total.

2-	Lack of clinical equipoise (n=12/35)	Yes (n=5/12) Unclear (n=4/12 (33%) No (n=3/12)	2- Communicating study information (n=7/35)	Yes (n=1/7) No (n=6/7)
3-	Strong patient treatment preferences (n=9/35)	Yes (n=4/9 (44%) No (n=5/9)	3- Social networks and experience of research (n=2/35)	No changes reported
4-	Issues related to the control group (n=4/35)	Yes (n=4/4)		
5-	Communicating study information and associated terminology (n= 8/35)	Yes (n=5/8) Unclear (n=2/8) No (n=1/8)		

6- Issues around the eligibility criteria (n=6/35)	Yes (n=4/6) No (n=2/6)
7- Practical barriers (n=12/35)	Yes (n=5/12) Unclear (n=4/12) No (n=3/12)
8- Commitment of staff and participants to the trial (n= 2/35)	Yes (n=1/2) No (n=1/2)
9- Beliefs and expectations (n= 10/35)	Yes (n=6/10) Unclear (n=1/10) No (n=3/10)

	10- Mismatch between the trial protocol and clinical care pathways (n= 4/35)	Yes (n=2/4) Unclear (n=2/4)	
	11- Participation burden (n= 4/35)	Unclear (n=3/4) No (n=1/4)	
	12- Lack of confidence in approaching study participants (n= 2/35)	Yes (n=1/2) Unclear (n=1/2)	
Retention	1- Burden of follow-up questionnaires (n= 9/35[1])	Yes (n=5/9) Unclear (n=2/9) No (n=2/9)	None identified
	2- Practical barriers (n= 2/35)	Unclear (n=1/2) No (n=1/2)	

S5: Barriers to recruitment

Participant level factors			
Study ID (clinical area)	**1. Findings associated with code: Lack of clarity or understanding of randomisation**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**
Nair 2014 (Lung Cancer)	• Some participants struggled to understand the concept or need for randomisation. • Despite explaining random allocation, some participants were still uncertain whether they would be selected based on some personal or illness characteristics.	• Randomisation will be explained to participants in the following way: 'To try and make sure both groups are the same, each person is put into a group at random. This is the fairest way of deciding who gets the test and means everyone will have a 50/50 chance of being put in either group'.	Yes
Moynihan 2012 (Transitional Cell Carcinoma (TCC) of the bladder)	• Often randomisation was perceived haphazardly as patients strove to make sense of their involvement in the trial process while questioning scientific principles.	• Attention to be focused on training trialists who are involved in recruitment to complicated trials, both in terms of communication processes and on the assimilation of complex trial pathways.	Unclear
Audrey 2011 (Prostate cancer)	• Patients and recruiters had difficulty with randomization. Patients commonly expressed lay views that cancer should be removed, told stories of friends or relatives who had died of advanced disease, or brought media	• It was necessary to emphasize that recruiters must be genuinely uncertain about the best treatment, believe the patient to be suitable for all three treatments, and be confident in these beliefs. • Recruiters were encouraged to elicit patients' lay views and then discuss differences with ProtecT study information.	• Yes

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	information that was often biased in favor of radical treatments.	explain that randomisation offered a way of resolving the dilemma of treatment choice.	
Paramasivan 2011 (Transitional cell carcinoma of the bladder)	• The complexity of the trial design led to confusion among some patients and recruiters about the timing of randomization.	• The randomization period was simplified and clarified so that patients could be randomized at any time before the three cycles of chemotherapy rather than during the second cycle.	• Yes
McEachan 2016 (Childhood obesity)	• Many women said they were unsure about why they had been approached to take part in the study and some said they did not realise the intervention was aimed at overweight/obese women. • Some control group women interviewed expressed disappointment at being allocated to the control group.	• No changes reported to address this barrier	• No

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Kendrick 2017 (Depression)	• Many patients were confused as to the process of randomization with some believing that the process of being assigned to an arm of the trial was decided by the doctor in view of their past medical history or their smoking status. • It was apparent that several of the standard care patients had not adequately understood management allocation prior to agreeing to participate in the trial. • Some patients felt that they would not have the best treatment if they were randomized to standard care indicating a lack of understanding of trial equipoise.	• Practices should be cluster randomized to streamline recruitment and follow-up, so all patients in each are treated the same, by whichever GP or PN they see. • The study team needs to spend more time at participating practices training them in the recruitment process. • Patients should be supported to take the necessary time to ensure understanding of patient information sheets before signing consent, especially with regard to clinical equipoise and that they will not necessarily benefit from participation.	Unclear
Study ID (clinical area)	**Findings associated with code: Strong patient treatment preferences**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**
Paramasivan 2017 (complex obesity)	• Patients tended to decline study participation, often choosing bypass surgery.	• Do not indicate patient preference anywhere on the notes. • Move beyond initial probing questions in relation to patient preferences toward rectifying any erroneous views. • Request patients who appear to have a preference or decision about trial participation to 'keep an open mind' until they had heard all the relevant information.	Yes

Griffin 2016 (hip impingement)	• Concerns about patient reactions and preferences at the start of the trial.	• The patient should have the opportunity to talk to a researcher for longer and should be able to ask questions and raise concerns.	Yes
Hilton 2015 (stress urinary incontinence)	• Although most eligible women were willing to be randomised, some had a previously undeclared preference for avoiding IUT and expressed relief at being allocated to the control group.	No specific changes planned to address this barrier.	
Hamilton 2013 (head and neck cancer)	• **Non-equivalence of the treatment processes:** Surgeons and nurses reported that they were convinced that many patients opted for laser surgery, because it was perceived as more convenient. • **Patient preferences and the role of recruiters:** Many patients were referred by surgeons specifically for either laser surgery or radiotherapy, and so had definite expectations as to which treatment they would receive. This made it very difficult for the recruiters to introduce the idea of participating in the EaStER trial.	• Principal investigators and recruiters must try to elicit and understand patient views and preferences. • The need to gently challenge preferences that are based on inaccurate information. • The need for training recruiters to enable them to explain the need for randomisation and the rationale for the RCT to patients.	Yes

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Clarke 2015 (childhood intermittent exotropia)	• Recruitment was hampered by strong parental preferences.	• To account for parental preferences, a future trial will incorporate a preference arm or accept that recruitment will inevitably be restricted to those parents who are prepared to consider surgery as a treatment.	Yes
Audrey 2011 (Cancer)	• Patients often expressed lay views that cancer should be removed or came with media information that was biased in favor of radical treatments.	• No specific changes planned to address this barrier.	
Paramasivan 2011 (transitional cell carcinoma of the bladder)	• Recruiters and investigators repeatedly mentioned that they were convinced that a major barrier to recruitment to SPARE was the existence of clear treatment preferences among patients.	• No specific changes planned to address this barrier.	
McEachan 2016 (Childhood obesity)	• Some control group women interviewed expressed disappointment at being allocated to the control group.	• No specific changes planned to address this barrier	
Palmer 2016 (joint hypermobility syndrome)	• Regardless of their prior experiences and understanding of equipoise, many participants still hoped to be randomized into the advice and physiotherapy arm, hoping that 'something' rather than 'nothing' would be more beneficial.	• No specific changes planned to address this barrier	
Study ID (clinical area)	**Findings associated with code: Issues related to the control group**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**

Nair 2014 (lung cancer)	• Some participants struggled with understanding the rationale for having a control group and said that allocation to the control arm of the study would put them off from participating. • Comments from some participants demonstrated a lack of understanding of the scientific nature of the study and the need for a control or comparison group. • some people who understood the need for a control group, found it hard to appreciate the need for this in a screening trial.	**Changes made to the study design or Participant Information Leaflet (PIL)** • **T**he control group will be changed to non-test group, which is what participants were most comfortable with". • 'Whenever a new test is developed, we need to find out if it works. We do this by having a group of people who have the test and a group of people who do not. Both groups need to be similar so that we can compare what happens to the people in each group.' • 'If you are in the non-test group, the information you give us will be really important in helping us find out if the new lung cancer blood test works, by comparing what happens to both groups.	Yes
Audrey 2011 (cancer)	• The non-radical treatment option (control) caused difficulties for both patients and recruiters. Although this option included regular review, recruiters often used the term 'watchful waiting' with the potential for interpretation as 'no treatment'.	• Issues identified by the qualitative research led to changes in the study information, randomisation, terminology used and presentation of the non-radical arm. • The non-radical arm was renamed 'active monitoring' with additional emphasis placed on the regular scrutiny of PSA tests and the availability of radical intervention if required or requested. As a result of these changes, recruiting staff were able to express confidence in this treatment option.	Yes

Kendrick 2017 (depression)	• One standard care patient pointed out that he could not grasp an understanding of the purpose of the control arm. • Many standard care patients believed that they were to have a chest X-ray well into the trial period. One patient stated that she had only entered onto the trial for the purpose of having a chest X-ray. • Some patients felt that they would not have the best treatment if they were randomised to standard care.	• Patients should be supported to take the necessary time to ensure understanding of patient information sheets before signing consent, especially with regard to clinical equipoise and that they will not necessarily benefit from participation. • A lack of skills in introducing research could be addressed through more training in a smaller group of practices.	Yes
Palmer 2016 (joint hypermobility syndrome)	• Both patients and health professionals felt that the content of the control arm, consisting of a one-off advice session, may not be perceived as equitable to the physiotherapy intervention arm.	• Patients and health professionals offered a number of suggestions for augmenting the content of the control arm, including providing ongoing support through group meetings, gym membership and the provision of general, not targeted, exercises, so the two arms were perceived as more equitable.	Yes
Study ID (clinical area)	**Findings associated with code: Participation burden**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**
Lawton 2017 (Postpartum haemorrhage)	• The burden of completing and signing consent form.	• No specific changes planned to address this issue	

Clarke 2015 (childhood intermittent exotropia)	• For parents and clinicians, the initial screening appointment presented a challenge, in that it had to encompass many points within a limited time. • The initial two visits, for screening and recruitment, often gave insufficient time for parents to fully consider participation in the trial.	• The use of research nurses in all centers should be considered in a future study. • Separation of the role of the treating clinician from the main recruiter to the trial.	Unclear
Nair 2014 (cancer)	• The main obstacle to participation appeared to be the need for flexible appointments. • work commitments among some of the younger participants were seen as a potential barrier.	• Those expressing interest in the study are sent the full PIS and at least 24 hours after anticipated receipt are phoned to discuss the study, answer questions, undertake a preliminary eligibility assessment and to arrange a recruitment visit at a time suitable to the patient. • Appointment reminders by phone, text message or email	Unclear
Moynihan 2012 (transitional cell carcinoma of the bladder)	• Patients spontaneously indicated the need to 'work' their way around NHS waiting times and hospital administration. • Patients often criticized their need to 'work' against 'bad administration', sometimes affecting trial decisions.	• It is suggested that health professionals consider facilitating a context in which patients feel fully included in the trial enterprise.	Unclear
Study ID (clinical area)	**Findings associated with code: Beliefs and expectations about trial participation**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**
Hamlet 2017 (young people	• A 'conspiracy of silence': Beliefs that young people would prefer not to	• This study highlights the potential need for training to educate primary care staff to broach the topic of a visible	Yes

with appearance-altering conditions)	discuss appearance-related concerns with their GP. • Participants seemed hesitant approaching the topic directly.	difference confidently, both within and outside the parameters of research. Training, with a particular focus on how to talk to young people who might be experiencing appearance concerns, could facilitate doctor–patient communication about the psychosocial challenges of living with a condition or injury that alters appearance and, in turn, patient disclosure.	
Van Den Berg 2017 (chest pain)	• Some participants did feel that being in pain on arrival, feeling overwhelmed, or anxious about the situation meant that they did not feel ready to commit at the time of the very first approach. • **Concerns about being experimented on:** some participants felt being generally sceptical of clinical research and initially felt anxious about participation**.**	• Waive verbal consent for initial trial procedures that do not affect the participant. • Waiting until the patient's condition is more settled and they can provide appropriate written informed consent. • The need to explore shared decision making to cater for a wide spectrum of perspectives.	Yes
Trevelyan 2016 (phantom limb syndrome)	• Intensity of Phantom Limb Pain (PLP) was a major barrier.	• Consider lowering or excluding the severity of PLP.	Yes
Ritchie 2015 (Cancer)	• Patient self-preservation (the need to retain control of choice of device or treatment schedules).	• Recruiters should gently challenge patients' preconceptions, as well as recognising and acknowledging their own bias in device preference.	Yes

Hamilton 2013 (head and neck cancer)	• **Lay beliefs:** The oncology centre/hospital where radiotherapy was performed had a negative image and was seen as a 'place to die'.	• No specific changes planned to address this barrier.	
Nair 2014 (cancer)	• Participants felt stigmatized (because of their smoking status) by some of the language used in the PILs. • The perception held by some participants that the trial is designed to encourage people to stop smoking.	• **"**We removed all mention of providing smoking cessation information and advice from the Patient information leaflets". • 'Lung cancer can happen to anyone, including the young and old and people who do not smoke, but the risk is higher in those over 50 and those who have smoked.'	Yes
Moynihan 2012(transitional cell carcinoma of the bladder)	• The patients' sense of alienation was evident. Feelings of isolation, loss of control and powerlessness underwrote involvement in the trial process.	• Attention to be focused on training trialists who are involved in recruitment to complicated trials, both in terms of communication processes and on the assimilation of complex trial pathways. • It is suggested that health professionals consider facilitating a context in which patients feel fully included in the trial enterprise.	Unclear
Ellis 2016 (lung cancer)	• Many patients who were identified as being suitable to participate tended to deny their symptoms, having become normalised and adjusted their lives accordingly and therefore were ineligible.	• No specific changes planned to address this barrier.	

Kendrick 2017(depression)	• One participant expressed anxiety about a poor medical outcome seemingly influenced by media reporting of a previous trial, while another patient was worried that she may have lung cancer. • One participant thought that she had been invited to take part in the trial because of her smoking status or history of smoking and the fact that she may have lung cancer highlighting a smoking stigma.	• Patients should be assured that the aim of the study is not to stop smoking, as it seems that this may limit recruitment due to smoking stigmatization.	Yes
Latter 2018 (cancer patients at the end of life)	• Nurses 'protecting' patients and carers from additional burden or distress. • Nurses' avoidance of difficulty and disappointment: some nurses described pre-judging patients' and carers' willingness to participate, to avoid invitations being declined, which they found discouraging.	• No specific changes reported to address these barriers.	

Clinician/recruiter factors			
Study ID (clinical area)	**Findings associated with code: clinical equipoise**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**
Paramasivan 2017 (Complex obesity)	• Recruiters found it difficult to maintain equipoise. • Audio recordings revealed that the terminology used by recruiters in the appointments favoured bypass and they tended to present it more positively than band surgery)	• Feedback sessions used to make recruiters aware of instances where they inadvertently used loaded terminology.	Yes
Griffin 2016 (hip impingement)	• Lack of equipoise in research teams: five surgeons (36%) and two physiotherapists (10%) showed a lack of active clinical equipoise when faced with real-life case scenarios or discussing involvement with a pilot RCT. One surgeon has a fundamental disbelief in femoroacetabular impingement, so that a trial of its treatment lacks relevance for them. • Unbalanced presentations of treatment options for which surgery has been presented at greater length and more favourably than either choosing conservative care or	• Providing frequent and comprehensive training to recruiters.	Unclear

	participating in the RCT (surgeons tend to talk most about what they are most familiar with). • Some surgeons favoured surgery as the optimal treatment for FAI (n = 2), which is the case for the two physiotherapists who were not in equipoise. Concerns that discussing uncertainty with patients could be detrimental to creating trust in their relationship.		
Ritchie 2015 (Cancer)	• Interviews with clinical staff revealed device preferences for certain subgroups of patients.	• Recruiters should gently challenge and acknowledge their own bias in device preference.	Yes
Hamilton 2013 (head and neck cancer)	• Surgeons had strong opinions about whether patients with disease involving the anterior commissure or those with cancer in situ would have better outcomes with a particular modality. • The language describing the treatment processes for the two options was not equivalent: toddling home' and 'nice and simple' for laser surgery compared with 'a bit more labour intensive,' 'a	• Principal investigators and recruiters need to think more critically about the concept of scientific equipoise and how that should underpin the RCT.	Yes

	bit further for you to travel' for radiotherapy. In addition, the recruiter's tone appeared apologetic when presenting radiotherapy. • While the EaStER protocol identified locoregional recurrence as the primary outcome and voice quality posttreatment as the secondary outcome, some recruiting staff felt that this main research question had already been answered.		
Pentecost 2015 (Depression)	• Psychological wellbeing practitioners' preferences for other treatments and their underuse of behavioural activation: Preferences for other treatments affected not only the number of individuals invited but also the number of randomised people who went on to receive at least one BA (behavioural activation) treatment session. • Difficulties in psychological wellbeing practitioners' (PWPs) adapting to recruitment procedures.	• Finding ways of enabling PWPs to engage with study procedures is recommended.	Unclear

Clarke 2015 (childhood intermittent exotropia)	• The explanation of the lack of evidence underlying the effectiveness and timing of intervention served, in many cases, to undermine the parent's confidence in the treating clinician, and by extension, the trial.	• Trial team suggested separation of the role of the treating clinician from the main recruiter to the trial. This proved extremely beneficial in aiding the process of recruitment and should be be considered in a future study.	Yes
Hilton 2015 (stress urinary incontinence in women)	• Apparent inconsistency between lack of personal equipoise over the value of invasive urodynamic testing on the one hand, and the majority view that the basic research question was important and associated with a high degree of willingness to randomise patients into a definitive RCT on the other hand.	• No changes were suggested (the majority of respondents regarded the basic research question as being important (70%), and most would be prepared to randomise patients into a definitive RCT to address this (60%).	
Crawley 2013 (children with chronic fatigue syndrome)	• Discussion of the interventions tended to be weighted towards the Lightning Process rather than the specialist medical care during recruitment consultations.	• No specific change reported to address this issue.	
Moynihan 2012 (bladder cancer)	• An explanation of equipoise was usually perceived to be absent in the information process. • The need to believe in expert physicians and an inability to accept medical uncertainty is documented. • Physicians find the concept of equipoise difficult, both because of	• Attention to be focused on training trialists who are involved in recruitment to complicated trials, both in terms of communication processes and on the assimilation of complex trial pathways to avoid a palpable breakdown in communication.	Unclear

	personal preference, and the difficulties of explaining the uncertainty prevailing in any form of randomization		
Audrey 2011 (Cancer)	• Audio recording of recruitment consultations revealed that treatments were not presented or interpreted equally. Surgery and radiotherapy were described in detail as aggressive, curative treatments while monitoring was portrayed briefly as a more passive process of watching and waiting.	• Recruiters were asked to change the order in which the treatments were presented (active monitoring, surgery, and radiotherapy) and to describe their respective advantages and disadvantages in equivalent detail. • Issues of randomization and clinical equipoise were clarified for both patients and recruiters.	Yes
Paramasivan 2011 (Prostate cancer)	• Centers sometimes appeared to take on a 'collective' preference - one that represented the views of most staff in the center. • Surgery was translated as the 'gold standard' and thus led to the reinforcement of treatment preferences that were already strong because of the differences perceived between the arms.	• No specific changes planned to address these barriers.	

Palmer 2016 (joint hypermobility syndrome)	• Physiotherapists anticipated that it may be difficult to 'persuade' patients that clinical equipoise existed and felt that this was an issue related to recruitment.	• Training and monitoring of trial personnel to ensure notions of equipoise are delivered and reinforced consistently is likely to improve recruitment rates to a future RCT.	Unclear
Study ID (clinical area)	**Findings associated with code: Communicating study information and associated terminology**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**
Griffin 2016 (hip impingement)	• Graphic descriptions of surgery that may have put patients off randomisation. • Presenting trial information in an order that is confusing for patients. • Surgeons going beyond their protocol brief, to explain the trial rather than referring patients on to the trial recruiter for this information.	• Providing frequent and comprehensive training to recruiters.	Unclear
Aventin 2016 (Sexual health)	• The baseline questionnaire was too long and some did not feel comfortable answering questions relating to sexuality.	• At an individual level, researchers should ensure that data collection documentation is clear to parents and pupils, perhaps involving steering group members in ensuring clarity.	Yes

Crawley 2013 (chronic fatigue syndrome)	• Patient information sheets were perceived as long, difficult to understand, repetitive in places and not visually appealing to 12 to 18-year olds.	• Consider using different patient information sheets for children aged 12 to 14 years than those used for older teenagers.	Yes
Moynihan 2012 (transitional cell carcinoma of the bladder)	• Patients displayed what may be perceived as 'poor understanding' of trial procedures and concepts. Patients' accounts suggested that information giving was often sub-optimal and/or understanding unverified. • An explanation of equipoise was usually perceived to be absent in the information process. • Patients across the sample failed to understand the 'language' of trial procedures. • Research overload, information overload and a perceived lack of information affected decision making.	• Attention to be focused on training trialists who are involved in recruitment to complicated trials, both in terms of communication processes and on the assimilation of complex trial pathways.	Unclear
Marshman 2012 (dental caries)	• Finding an appropriate form of words to explain aspects of the trial to parents and children was difficult for some dentists.	• No specific changes planned to address this barrier.	

Audrey 2011 (cancer)	• Patients may have interpreted trial and clinical terminology quite differently than intended by practitioners and this was evident in the early stages of ProtecT when, for example, 'trial' was sometimes interpreted as 'try and see'.	• Issues identified by the qualitative research led to changes in the study information, randomisation, terminology used and presentation of the non-radical arm. • Recruiters were asked to change the order in which the treatments were presented (active monitoring, surgery, and radiotherapy) and to describe their respective advantages and disadvantages in equivalent detail. • Recruiters were asked to replace 'trial' with 'study'.	Yes
Paramasivan 2011 (transitional cell carcinoma of the bladder)	• Recruiters and investigators agreed that the SPARE trial was difficult to explain. • Recruiters indicated that they found the quantity of information problematic as well as its complexity.	• The construction of a simpler version of the study flowchart which was then issued to recruiters so that they could provide a clearer articulation of the trial. • The consent for chemotherapy was separated from the consent for SPARE in response to recruiters indicating that patients were given too much information about various aspects of the trial at the same time. • The recruitment study team drafted a new, shorter and clearer PIS which removed the 'loaded' terminology, explained the simplified study outline and included the new flowchart.	Yes
Ellis 2016 (lung cancer)	• For some participants, the questionnaire items probed areas that they had not thought about or had chosen not to think about.	• The number of questionnaires to be used in the subsequent trial will be decreased.	Yes

	• Carers also expressed some discontent with the questionnaires, and this was seen as a potential barrier to recruitment.		
Study ID (clinical area)	**Findings associated with code: issues around the eligibility criteria**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**
Hilton 2015 (stress urinary incontinence)	• Interpretation of eligibility criteria differed between centers (**Authors' judgement**).	• Ensure clarity over inclusion/exclusion criteria Running screening training exercises might be considered for a future definitive trial to ensure similar screening standards and practices and an 'assumed eligibility' approach in all centers.	Yes
Bhattacharya 2011 (older population unintentionally non-adherent to medication)	• There was less clarity regarding the minimum age for recruiting patients to the study. Maintaining the minimum recruitment age at 75 years as initially proposed resulted in over one-third of patients being ineligible for study participation	• A lower age band for recruitment is necessary.	Yes
Hamilton 2013 (head and neck cancer)	• Surgeons applied the inclusion/exclusion criteria variably, thereby reducing the available number of eligible patients and creating differences between centers.	• Issues related to inclusion/ exclusion criteria, may require close examination and regular meetings to discuss and resolve evolving issues.	Yes
Clarke 2015 (childhood intermittent exotropia)	• Difficulty in confirming eligibility at the initial screening visit	• A future trial will consider a limit on the upper age at which participants would be included.	Yes

	• Subsequent blockage of appointment slots by children who needed rescreening for eligibility, contributed to a failure to recruit to target.		
Paramasivan 2011 (transitional cell carcinoma of the bladder)	• Some recruiters thought there was leeway for interpretation of the inclusion/exclusion criteria in partnership with the main trial team.	• No changes planned to address this issue (The possibility of relaxing certain inclusion criteria was discussed with the TMG but it was decided that these could not be changed without invalidating the aims of the RCT).	
Ellis 2016 (lung cancer)	• Those involved in the recruitment process reported that the inclusion/exclusion criterion was too restrictive. As a result, it was felt that many patients who may have benefited from participation in the trial were excluded.	• No changes planned to address this barrier (eligibility criteria will remain the same for the subsequent trial	
Study ID (clinical area)	**Findings associated with code: commitment to the trial**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**
Paramasivan 2011 (transitional cell carcinoma of the bladder)	• Recruiters believed that some teams or members were very committed to SPARE but that others were indifferent or even antagonistic to it, and this created additional difficulties because patients developed strong preferences for one arm or the other.	• Clinical centers were asked to identify two Lead Recruiters (LRs) per site whose responsibilities would be to act as the focus for SPARE recruitment activity.	Yes

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Latter 2018 (cancer patients at the end of life)	• Recruiting fewer dyads than anticipated affected nurses' engagement and the priority they gave to the study.	• No specific changes reported	
Citation	**Findings associated with code: Lack of confidence in approaching study participants**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**
Griffin 2016 (hip impingement)	• Research associates shared their concerns about not being able to answer patient questions and obtain consent without a surgeon or other senior clinician signing the form for them. • Long periods between recruitment clinics represented a challenge for research associates to maintain confidence and knowledge about the UK FASHIoN trial.	• Providing frequent and comprehensive training to recruiters. • Modifying the support to teams in other centers according to their research experience.	Unclear
Hamlet 2017 (young people with appearance-altering conditions)	• Participants seemed hesitant approaching the topic directly.	• Training, with a particular focus on how to talk to young people who might be experiencing appearance concerns, could facilitate doctor–patient communication about the psychosocial challenges of living with a condition or injury that alters appearance and, in turn, patient disclosure.	Yes

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Contextual/situational factors			
Study ID (clinical area)	**Findings associated with code: Practical barriers**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**
Griffin 2016 (hip impingement)	• Difficulty in implementing procedures due to the multicenter nature of the pilot.	• Regular visits to the centers by the PI and other TGM members to keep momentum • Delivery of a slick and easy-to-implement recruitment process to be the least disruptive to routine clinical practice. • Providing frequent and comprehensive training to recruiters. • Modifying the support to teams in other centers according to their research experience. • Setting recruitment targets and engendering a healthy competition between centers. • Follow up with messages and regular newsletters about the need to recruit. • Contacts between research and clinical departments about recruitment opportunities should be encouraged.	Yes
Hamlet 2017 (young people with appearance-altering conditions)	• Barriers of the primary care environment (time-limited consultations, high workload, competing studies)	• No specific changes to address these barriers.	

Aventin 2016 (Sexual health)	• Perceived lack of time for potential study participants to take part. • Involvement in another research projects.	• Environmental facilitators of recruitment: approaching schools attending RSE training days, highlighting the innovative nature of the intervention, flexibility in terms of how and when the research was conducted in individual schools, the provision of support to schools by facilitation of the project by dedicated researchers, providing a clear outline of the roles and responsibilities of the school (and research team) from the outset and facilitating discussion on the benefits and perceived barriers to taking part.	Yes
Gabbay 2017 (Debt Counselling for Depression)	• Delayed practice recruitment due to higher administrative issues. • Staffing and workload Complexity of primary care services	• The study failed to reach its recruitment target and was terminated early during the internal pilot phase, and, therefore, it did not progress to main trial.	
Lawton 2017 (postpartum haemorrhage)	• Staff reluctance to forgo written consent procedures	• Staff who are inexperienced in using alternatives to prospective written consent may benefit from training and support to increase their confidence and willingness to use alternative consent approaches. This training and support could focus on raising staff awareness and understanding of ethical review processes and of how, and why, they are legally protected when alternatives to prospective written consent are used.	Yes
Trevelyan 2016 (phantom limb syndrome)	• Failure to identify suitable participants due to units not operating in full capacity.	• A future trial would need to ensure that trial centers allocated adequate time and personnel. • Applying multicentered approach to recruitment.	Yes
Blekken 2015 (fecal incontinence)	• Staff discontinuity • Insufficient time	• For the main study, the plan is to include personal meetings with the director of health and social affairs and the care managers of the NHs.	Unclear

	• Large care staff • sub-optimal use of skill-mix	• One of the RNs from the pilot study will also be invited to share her experience and to answer questions about participating. • The economic compensation and the recommendation of releasing the responsible RNs from daily work. • Recruitment of a local opinion leader and using the unit as a cluster will improve study feasibility by increasing the number of potential clusters, which impacts power more than increasing individuals enrolled.	
Pentecost 2015 (depression)	• Staff attrition: randomised participants' not seeing study psychological wellbeing practitioners.	• Finding ways of enabling PWPs to engage with study procedures is recommended.	Unclear
Clarke 2015 (childhood intermittent exotropia)	• There was a lag in recruitment due to the delay in the subsequent appointment for the recruitment clinic.	• The use of research nurses in all centers should be considered in a future study. • Separation of the role of the treating clinician from the main recruiter to the trial.	Unclear
Marshman 2012 (dental caries)	• Shortage in radiographs and its impact on the number of eligible participants. • Time constraints and busy schedule.	• Practitioners should be advised that patients will require longer appointments than normal for involvement in the trial and would prefer appointments out of school time. • The recommendation for recruitment of whole practices, with participation of all members of the practice team rather than individual practitioners.	Yes

Ellis 2016 (lung cancer)	• Inconvenient time frame between providing consent and receiving the first intervention.	• The timeframe between consent and delivery of the first RDSI session has been expanded to 2 weeks.	Yes
Latter 2018 (cancer patients at the end of life)	• Organisational change, team staffing levels, nurse workloads and variable flow of palliative care referrals. • Nurses' unfamiliarity with recruitment. • Incompatibility of recruitment procedures with nursing.	• No specific changes planned to address these barriers.	
Study ID (clinical area)	**Findings associated with code: Mismatch between the trial protocol and clinical care pathways**	**Planned changes before the full trial**	**Were the proposed changes clearly linked to coded data?**
Paramasivan 2017(complex obesity)	• Well-established routines for clinical service provision led to the trial being presented to patients as an 'add-on' extra rather than an integral part of existing clinical services.	• Mention the study in the opening statements of the surgical consultations. • Express enthusiasm for the study.	Yes
Griffin 2016 (hip impingement)	• Teams experienced issues such as remembering to approach patients at each possible opportunity, or the need not to discuss surgery before diagnosis was confirmed. • Some research associates expressed their concern about talking to patients	• Delivery of a slick and easy-to-implement recruitment process to be the least disruptive to routine clinical practice. • Providing frequent and comprehensive training to recruiters.	Unclear

	about the audio recording of the consultation. • Various sites expressed concern about patients being referred for 'surgery' instead of 'treatment'. Some centres use a conservative approach and, therefore, patients tend to go for physiotherapy first before arriving at a surgeon appointment. Recruiters said they would find it difficult to approach these patients or to feel confident they would agree to take part in the trial.		
Paramasivan 2011(transitional cell carcinoma of the bladder)	• The pathway that potential trial participants followed from a diagnosis of bladder cancer to being recruited to the SPARE trial proved extremely difficult because of the number of people who might come into contact with the patient during their visits and sometimes the different clinical (surgery or oncology, or local /regional) centres that might be involved.	• Clinical centers were asked to identify two Lead Recruiters (LRs) per site whose responsibilities would be to act as the focus for SPARE recruitment activity. • The LRs were also advised to see if they could arrange a specific 'recruitment appointment' about 7-10 days after the chemotherapy discussion, with the aim of providing full information about the trial and obtaining consent for participation. • It was also recommended that trial participants should be referred to the respective specialists after randomization rather than before to ensure consistency of information.	Yes
Ritchie 2015 (Cancer)	• Potential delays from referral to treatment.	• The remit of the funded role of trial Champion has been developed to encompass not only recruitment and randomisation but also coordination and facilitation of device insertion appointments and communication.	Unclear

	• Additional service provision and increased workload.		

S6: Facilitators for recruitment

Citation	Findings associated with code: Altruism and personal gain	Changes planned before the full trial	Were the proposed changes clearly linked to coded data?
Hamlet 2017 (young people with appearance-altering conditions)	• Participants reported a personal interest in the topic, which increased its pertinence and served as a motivator for recruitment.	• No changes reported	
Van Den Berg 2017 (Chest pain)	• Participation seemed motivated by altruism and the expectation that their participation may benefit both them and their families. • Participants also perceived that the research may bring direct personal benefits.	• No changes reported	
Bhattacharya 2011 (older people unintentionally non-adherent to medication)	• Patients wanted to take part to help others, to help themselves, to give payback to the NHS.	• No changes reported	
Notley 2015 (psychological difficulties)	• Participants expressed keenness to be involved in research, for altruistic reasons.	• No changes reported	
Hilton 2015 (stress urinary incontinence)	• Altruistic factors motivated participation.	• No changes reported	

Citation	**Findings associated with code: Communicating study information**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**
Aventin 2016 (sexual health)	• Promoting the social benefits and credibility of the research aims, help school decision-makers recognise the importance of the research projects goals and objectives. recruitment presentations by the research team using video testimonials from participants who took part in the pilot study and face-to-face contact with school management and teachers were important in this regard. • Ensuring that pupils are provided with adequate information about their roles and responsibilities, and given an opportunity to meet with the research staff before data collection will also be beneficial to pupil recruitment.	• No changes reported	
Hilton 2015 (stress urinary incontinence)	• The information provided about the study was clear and informative and there was enough information for women to be able to make a decision about taking part. • Good understanding of the study	• No changes reported	

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Van Den Berg 2017 (Chest pain)	• Participants were provided with sufficient and clearly presented information and given the opportunity to ask for clarification about what participation in the MACS trial involved. They valued good interpersonal skills of the research staff	• No changes reported	
Notley 2015 (psychological difficulties)	• 11 participants displayed a sound understanding of the randomization process. • There was a thorough understanding of the rationale for the processes or measures used.	• No changes reported	
Realpe 2016 (hip impingement)	Analysis of the recruitment consultations provided evidence of a logical sequence for information sharing which seemed to facilitate recruitment for both recruiting clinicians and patients (Six step model): • Step 1: explain what the condition is to the patient • Step 2: reassure the patient that they will receive best treatment • Step 3; explain that there is uncertainty about which treatment is the best • Step 4; explain the purpose of the study	• The six-step recruitment model will be used to train and support recruiters in the large number of new centers in the full-scale trial.	Yes

	• Step 5; give the patient a balanced view about the advantages and disadvantages of each treatment being compared. • Step 6; explain the study procedures.		
Hilton 2015 (stress urinary incontinence)	• Supplementary information from trial and clinic staff was seen as important.	• No changes reported	
Crawley 2013 (chronic fatigue syndrome)	• Sufficient information was provided during recruitment consultation, families were able to ask questions, understood what the study was about and what would happen if they decided to participate.	• No changes reported	
Citation	**Findings associated with code: Patients' social networks and positive experience of research**	**Changes planned before the full trial**	
Van Den Berg 2017 (chest pain)	• Participants positive experience was sufficient to recommend participation in clinical research to others.	• No changes reported	
Thompson 2016 (haemodialysis patients)	• Patients' social networks in the unit were an effective means of disseminating information. • Hearing other participants discuss their participation in the trial were effective means of promoting participation in the study.	• No changes reported	

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S7: Barriers to retention

Citation	Findings associated with: Burden of follow-up questionnaires	Changes planned before the full trial	Were the proposed changes clearly linked to coded data?
Gabbay 2017 (Depression)	• With regard to feasibility and acceptability of the outcome measures, it was apparent that the number of outcome measures (and their form and content) was problematic for some participants – adding considerably to the time taken for completion of interviews. Furthermore, several participants questioned the forced choice responses of questionnaires, which did not capture the reality of their experience.	• The study failed to reach its recruitment target and was terminated early during the internal pilot phase, and, therefore, it did not progress to main trial.	
Hilton 2015 (stress urinary incontinence)	• Repeating questionnaires at 6 months when many women had few, if any, symptoms to report was sometimes felt to be burdensome and irrelevant; this is in keeping with the number of blank follow-up questionnaires returned.	• The need to complete and return questionnaires even if there are few symptoms was emphasized. • Modify questionnaires to allow 'short-cutting' of irrelevant areas to reduce respondent burden. • A further possibility is to link questionnaire completion at follow-up to the face-to-face clinic review.	• Yes
Crawley 2013 (chronic fatigue syndrome)	• The number of questionnaires used at follow-up was considered a burden by the	• Measures to improve outcome data collection using a variety of strategies, including telephone	• Unclear

	majority of children and parents interviewed and observed. • Parents felt the timing of questionnaires did not allow time for change, as they were too close together.	follow-up, would need to be implemented in a full study.	
Gray 2013 (male obesity)	• Focus group participants found difficulties with some of the wording in the questionnaires.	• Fieldworkers should be given full training in assisting men with questionnaire completion if required (e.g., if participants have literacy problems).	• Yes
McEachan 2016 (infant obesity)	• Some of the measurement tools were found to be burdensome to complete.	• Maintaining regular contact with participants throughout follow-up. • A future trial should ensure that a range of communication channels are used to maximise retention. • Strike a balance between collecting valid and reliable data and overly burdening participants, which may lead to missing data, withdrawal or trial attrition.	• Yes
Tsianakas 2016 (recurrent or metastatic cancer)	• All outcome measures were judged appropriate except the Scottish Physical Activity Questionnaire (SPAQ). Eight participants reported it was repetitive and difficult to complete.	• Alternative methods for measuring the intensity, duration and frequency of physical activity in any future study are recommended.	• Yes
Ellis 2016 (lung cancer)	• Patients and carers expressed some discontent with the questionnaires and this was seen as a potential barrier to retention.	• The number of questionnaires to be used in the subsequent trial will be decreased.	• Yes

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Kendrick 2017 (depression)	• Some patients reported problems with the data collection questionnaires. For example, one patient had difficulties regarding the clarity of a particular question asking whether she was anxious or depressed. • Two patients pointed out that they thought that the patient questionnaire was intrusive.	• No specific changes reported to address these barriers.	
Myall 2015 (cancer-related fatigue)	• Few participants found the questionnaires at 3-time points burdensome. • Several participants who were ≥18 months post diagnosis felt some questions were not relevant. For example, items about health service use and seeking help from health professionals were more suited to those with a current diagnosis and were an unwelcome reminder of potential problems they may encounter. • Several participants considered the psychological aspect of cancer was missing and should be included in the questionnaires. • Questionnaires requested the same information more than once. For some this was a source of anxiety and revealed additional decision-making work spending time deliberating over responses.	• The need for less generic and more specific information was considered important. While RESTORE needs to retain a broad reach, improved signposting to resources dealing with a variety of cancers and relevant to users at various distances from diagnosis and treatment, and inclusion of more wide-ranging patients' stories, offer some ways RESTORE could be tailored to address the informational needs of a diverse range of users. This could reduce the potential for information to be viewed as an unwelcome reminder of their cancer.	• Unclear

Citation	**Findings associated with: Practical barriers**	**Changes planned before the full trial**	**Were the proposed changes clearly linked to coded data?**
McEachan 2016 (infant obesity)	• One issue for both participants and facilitators was setting up the groups in a convenient location. • Some participants reported making journeys that required considerable effort	• No specific changes reported to address these barriers.	
Kendrick 2017 (depression)	• A small minority of patients found the process of getting a chest X-ray difficult. One patient said that she had to pay for the parking costs and using public transport would be too problematic.	• Patients should be reassured that participation in the trial should cause the patient the least amount of inconvenience, especially in terms of travel necessities.	Unclear

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S8: CERQual Evidence Profile_ Recruitment barriers

Summary of review finding (individual changes across each of the contributing studies are presented in table 2)	**Studies contributing to the review finding.**	**Adequacy**	**Coherence**	**CERQual assessment of confidence in the evidence**	**Explanation of CERQual assessment**
1- **Changes planned before the full trial to address issues with randomisation** The changes reported included explaining the process of randomisation in a clear way to study participants to deal with lack of understanding and confusion. Changes were also made to simplify and clarify the randomisation period.	(1-6)	Minor concerns about adequacy (one study reported no changes to address this barrier)	Moderate concerns about coherence (3 studies with well-grounded changes relevance, two studies with unclear fit)	Moderate confidence	6 studies with moderate concerns about adequacy and coherence. No or very minor concerns about methodological limitations and relevance.
2- **Changes planned before the full trial to address issues with clinical equipoise**: Changes included feedback sessions to make recruiters aware of instances where they inadvertently used loaded terminology, providing frequent training to recruiters and to	(3,4,7-16)	Minor concerns about adequacy (3 study reported no changes to address this barrier)	Moderate concerns about coherence (6 studies with well-grounded changes,6 studies with unclearly linked changes)	Moderate confidence	12 studies with moderate concerns about coherence. No or minor concerns about methodological limitations, adequacy and relevance.

present treatment options in a balanced way.					
3- Changes planned before the full trial to address issues with patient treatment preferences: Changes were made toward rectifying any erroneous views, gently challenge patient treatment preferences and request patients to 'keep an open mind' until they had heard all the relevant information.	(3,5,7,8,12,13,16-18)	Moderate concerns about adequacy(5 study reported no changes to address this barrier)	Moderate concerns about coherence (4 studies with with well-grounded changes,5 studies with with unclearly-linked changes)	Moderate confidence	9 studies with moderate concerns about adequacy and coherence. No or minor concerns about methodological limitations and relevance.
Changes planned before the full trial to address issues related to the control group: • Changes were made to the study design or Participant Information Leaflet (PIL) ''The control group will be changed to non-test group'', changes made to the presentation of the non-radical arm which was	(3,6,16,19)	No or very minor concerns about adequacy	No or very minor concerns about coherence	High confidence	4 studies with no or very minor concerns about methodological limitations, coherence, adequacy and relevance.

renamed 'active monitoring' and suggestions for augmenting the content of the control arm so the two arms were perceived as more equitable.					
Changes planned before the full trial to address issues around the eligibility criteria: • Changes were made to ensure clarity over inclusion/exclusion criteria in all centers, considering a lower age band for recruitment or a limit on the upper age at which participants would be included.	(12,13,17,18,20,21)	No or very minor concerns about adequacy	No or very minor concerns about coherence	High confidence	6 studies with no or very minor concerns about methodological limitations, coherence, adequacy and relevance
Changes planned before the full trial to address practical barriers: Changes included regular visits to the centres by the PI and other TGM members to keep momentum, delivery of a slick and easy-to-implement recruitment	(8,11,12,21-29)	Moderate concerns about adequacy (3 studies reported no changes to address these barriers)	Moderate concerns about coherence (5 studies with well-grounded changes and 3 studies with unclearly-linked changes)	Moderate confidence	12 studies with moderate concerns about adequacy and coherence. No or very minor concerns about methodological limitations and relevance.

process to be the least disruptive to routine clinical practice, providing frequent and comprehensive training to recruiters and to ensure that trial centres allocated adequate time and personnel.					
Changes planned before the full trial to address participation burden: Changes included the use of research nurses in all centres, separation of the role of the treating clinician from the main recruiter to the trial, appointment reminders by phone, text message or email and facilitating a context in which patients feel fully included in the trial enterprise.	(12,15,19,30)	Moderate concerns about adequacy (one study reported no changes to address these barriers)	Moderate concerns about coherence (one study with well-grounded changes and 3 studies with unclearly-linked changes)	Moderate confidence	4 studies with moderate concerns about adequacy and coherence. No or very minor concerns about methodological limitations and relevance.
Changes planned before the full trial to address barriers related to communicating study information and associated terminology: Changes were made to ensure that data collection documentation is clear to study participants, changing the order in which the treatments were	(3,8,14,15,18,21,23, 28)	Minor concerns about adequacy (one study reported no changes to address these barriers)	Minor concerns about coherence (5 studies with well-grounded changes and 2 studies with unclearly-linked changes)	High confidence	8 studies with minor concerns about adequacy and coherence. No or very minor concerns about methodological limitations and relevance.

presented and to describe their respective advantages and disadvantages in equivalent detail and drafting a new, shorter and clearer PIS which removed the 'loaded' terminology.					
Changes planned before the full trial to address barriers related to beliefs and expectations: Changes included highlighting the potential need for training to educate primary care staff to broach the topic of a visible difference confidently, waive verbal consent for initial trial procedures that do not affect the participant and removing all mention of providing smoking cessation information and advice from the Patient information leaflets" to avoid smoking stigma.	(6,9,15,17,21,22,26, 29,31,32)	Moderate concerns about adequacy (3 studies reported no changes to address these barriers)	Minor concerns about coherence (6 studies with well-grounded changes and one study with unclearly linked changes)	High confidence	10 studies with moderate concerns about adequacy. Minor or very minor concerns about methodological limitations, coherence and relevance.

Changes planned before the full trial to address barriers related to Integration of the trial into clinical practice: Changes reported were the need to mention the study in the opening statements of the surgical consultations, express enthusiasm for the study, delivery of a slick and easy-to-implement recruitment process to be the least disruptive to routine clinical practice, ensure that trial participants will be referred to the respective specialists after randomization rather than before to ensure consistency of information, and providing frequent training to recruiters.	(7-9,18)	No or very concerns about adequacy	Minor concerns about coherence (3 studies with well-grounded changes and one study with unclearly linked changes)	High confidence	4 studies with no or minor concerns about methodological limitations, coherence, adequacy and relevance.
Changes planned before the full trial to address barriers related to Confidence about approaching patients: Modifying the support to teams in other centers according to their research experience and the need for training to educate primary care staff to broach the topic of a visible difference confidently,	(8,22)	No or very concerns about adequacy	No or very concerns about coherence	High confidence	2 studies with no or very minor concerns about methodological limitations, coherence, adequacy and relevance.

both within and outside the parameters of research.					
Changes planned before the full trial to address barriers related to assiduousness and commitment of recruiters: Clinical centers were asked to identify two Lead Recruiters (LRs) per site whose responsibilities would be to act as the focus for SPARE recruitment activity.	(4,29)	Moderate concerns about adequacy (one study reported no changes to address these barriers)	Moderate concerns about coherence (only one study with well-grounded changes)	Moderate confidence	2 studies with moderate concerns about adequacy and coherence. No or very minor concerns about methodological limitations and relevance.
Changes planned before the full trial to address issues around the invitation to participate: Changes included sending postal invitation letter with a summary of the main points at the front of the PIL; and, where necessary or appropriate invitation during consultation with GP/Practice Nurse, placing posters in GP waiting rooms and finding ways of enabling psychological wellbeing practioners' to engage with study procedures.	(11,19)	Minor concerns about adequacy	Moderate concerns about coherence (one study with well-grounded changes)	Moderate confidence	2 studies with moderate concerns about coherence. No or very minor concerns about methodological limitations, adequacy, and relevance.

S9: CERQual Evidence Profile_ Retention barriers

Summary of review finding	**Studies contributing to the review finding.**	**Adequacy**	**coherence**	**CERQual assessment of confidence in the evidence**	**Explanation of CERQual assessment**
Changes planned before the full trial to address burden of follow-up questionnaires: The need to complete and return questionnaires even if there are few symptoms was emphasized, modifying questionnaires to allow 'short-cutting' of irrelevant areas to reduce respondent burden, link questionnaire completion at follow-up to the face-to-face clinic review and the use of a variety of strategies, including telephone follow-up to maximise retention.	(1-9)	Minor concerns about adequacy (only one study reported no changes to address these barriers)	Minor concerns about coherence (7 studies with well-grounded changes and one study with unclearly linked changes)	High confidence	9 studies with minor concerns about adequacy and coherence. No or very minor concerns about methodological limitations and relevance.

S1 Table. Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ Checklist (Tong, *et al.*, 2012)

Item No.	Guide and Description	Report Location
1. Aim	State the research question the synthesis addresses	Introduction
2. Synthesis methodology	Identify the synthesis methodology or theoretical framework which underpins the synthesis, and describe the rationale for choice of methodology (e.g. meta-ethnography, thematic synthesis, critical interpretive synthesis, grounded theory synthesis, realist synthesis, meta-aggregation, meta-study, framework synthesis)	Methodology of synthesis
3. Approach to searching	Indicate whether the search was pre-planned (comprehensive search strategies to seek all available studies) or iterative (to seek all available concepts until they theoretical saturation is achieved)	Study search strategy
4. Inclusion criteria	Specify the inclusion/exclusion criteria (e.g. in terms of population, language, year limits, type of publication, study type)	Literature search and selection - *Inclusion criteria*
5. Data sources	Describe the information sources used (e.g. electronic databases (MEDLINE, EMBASE, CINAHL, psycINFO), grey literature databases (digital thesis, policy reports), relevant organisational websites, experts, information specialists, generic web searches (Google Scholar) hand searching, reference lists) and when the searches conducted; provide the rationale for using the data sources	Search strategy
6. Electronic Search strategy	Describe the literature search (e.g. provide electronic search strategies with population terms, clinical or health topic terms, experiential or social phenomena related terms, filters for qualitative research, and search limits)	S2 – *search strategy*
7. Study screening methods	Describe the process of study screening and sifting (e.g. title, abstract and full text review, number of independent reviewers who screened studies)	Study selection – S3-*Fig 1 PRISMA flow diagram*
8. Study characteristics	Present the characteristics of the included studies (e.g. year of publication, country, population, number of participants, data collection, methodology, analysis, research questions)	S4 - *Characteristics of included studies*
9. Study selection results	Identify the number of studies screened and provide reasons for study exclusion (e.g. for comprehensive searching, provide numbers of studies screened and reasons for exclusion indicated in a figure/flowchart; for iterative searching describe reasons for study exclusion and inclusion based on modifications to the research question and/or contribution to theory development)	S3-Fig 1 - PRISMA flow diagram
10. Rationale for appraisal	Describe the rationale and approach used to appraise the included studies or selected findings (e.g.	Quality appraisal of included

	assessment of conduct (validity and robustness), assessment of reporting (transparency), assessment of content and utility of the findings)	studies and assessment of the certainty in evidence
11. Appraisal items	State the tools, frameworks and criteria used to appraise the studies or selected findings (e.g. Existing tools: CASP, QARI, COREQ, Mays and Pope [25]; reviewer developed tools; describe the domains assessed: research team, study design, data analysis and interpretations, reporting)	Quality appraisal of included studies and assessment of the certainty in evidence
12. Appraisal process	Indicate whether the appraisal was conducted independently by more than one reviewer and if consensus was required	Quality appraisal of included studies and assessment of the certainty in evidence
13. Appraisal results	Present results of the quality assessment and indicate which articles, if any, were weighted/excluded based on the assessment and give the rationale	S9,10- CERQual Evidence profiles
14. Data extraction	Indicate which sections of the primary studies were analysed and how were the data extracted from the primary studies? (e.g. all text under the headings "results /conclusions" were extracted electronically and entered into a computer software)	Methodology of synthesis – *"all relevant qualitative data"*
15. Software	State the computer software used, if any	None used
16. Number of reviewers	Identify who was involved in coding and analysis	Methodology of synthesis
17. Coding	Describe the process for coding of data (e.g. line by line coding to search for concepts)	Methodology of synthesis
18. Study comparison	Describe how were comparisons made within and across studies (e.g. subsequent studies were coded into pre-existing concepts, and new concepts were created when deemed necessary)	Findings mapped to *Theme Matrix* tables- S,6,7,8
19. Derivation of themes	Explain whether the process of deriving the themes or constructs was inductive or deductive	Inductive process - *Theme Matrix* tables – S,6,7,8
20. Quotations	Provide quotations from the primary studies to illustrate themes/constructs, and identify whether the quotations were participant quotations of the author's interpretation	Findings - *Quotations and all sources given*
21. Synthesis output	Present rich, compelling and useful results that go beyond a summary of the primary studies (e.g. new interpretation, models of evidence, conceptual models, analytical framework, development of a new theory or construct)	Findings and discussion

Correction: *Using qualitative methods in pilot and feasibility trials to inform recruitment and retention processes in full-scale randomised trials: a qualitative evidence synthesis*

Elfeky A, Treweek S, Hannes K, *et al*. Using qualitative methods in pilot and feasibility trials to inform recruitment and retention processes in full-scale randomised trials: a qualitative evidence synthesis. *BMJ Open* 2022;12:e055521. doi: 10.1136/bmjopen-2021-055521

It has been brought to our attention that we attributed data included in our synthesis to a summary paper (*Audrey S. Qualitative research in evidence-based medicine: improving decision-making and participation in randomised controlled trials of cancer treatments. Palliat Med 2011;**25**:758–65*) rather than to the original data source used by Audrey (*Donovan, F. Hamdy, D. Neal, T. Peters, S. Oliver, L. Brindle, D. Jewell, P. Powell, D. Gillatt, D. Dedman, N. Mills, M. Smith, S. Noble, A. Lane and T. S. G. Protect. Prostate Testing for Cancer and Treatment (ProtecT) feasibility study. Health Technology Assessment (Winchester, England). 2003; 7 (14): 1–88*). The former is a commentary article on the findings from the Donovan et al 2003 paper. In addition, we have also identified that a further study (*Stein RC, Dunn JA, Bartlett JMS, Campbell AF, Marshall A, Hall P, et al. OPTIMA prelim: a randomised feasibility study of personalised care in the treatment of women with early breast cancer. Health Technol Assess 2016;20(10)*.) was also omitted.

Both the Donovan *et al* 2003 and Stein *et al* 2016 studies were identified in the original search but through human error were not taken forward for full text assessment. Our investigation of this error also highlighted that the reference lists of included studies had not been checked as per our protocol. We have now extracted data from these two omitted studies and analysed them against the themes identified in the published qualitative evidence synthesis. While the omission of Donovan *et al* 2003 and Stein *et al* 2016 has affected the richness of the accounts within the relevant themes, and potentially the number of studies contributing to individual findings and proposed changes, the omission does not substantively change the overall conclusions of the synthesis. It should be noted that given the commentary article (Audrey 2011) was included in place of the original data source (Donovan *et al* 2003), the original data source (Donovan *et al* 2003) has not been fully credited as contributing to all relevant 'proposed changes to the main trial' topics.

Online supplemental file 2 has been amended to add characteristics of the Protect feasibility study from Audrey et al 2011. It should also be noted that references were incorrectly numbered in online supplemental files 7; 8 and this has also been corrected. online supplemental file 9 is a new file that maps data extracted from Donovan *et al* 2003 and Stein *et al* 2016 to the themes of our qualitative synthesis.

Any future update of this synthesis should use the original source data from Donovan *et al* 2003 rather than the Audrey 2011 summary data and include the Stein *et al* 2016 study.

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The authors and the journal have issued a further correction to this paper. An individual raised queries about the nature of the first correction to this paper. These included (1) the way in which two omitted references were dealt with in the correction and (2) that the addition of new data and its analysis were insufficiently clear and prominent.

BMJ Open has undertaken a post-publication review of this paper to address these issues. We sought advice from two independent methodological experts who had not reviewed the paper previously. The reviewers' comments were then reviewed by the Handling Editor, Editor-in-Chief and the Publication Ethics and Content Integrity Editor. The authors then addressed the comments from the reviewers and the editors and revised their paper further. The authors made the following revisions:

1. The omitted articles, Donovan *et al* (2003) and Stein *et al* (2016) are more clearly referred to within the body of the main paper and referenced accordingly. It was also made clearer that findings from these articles are handled within the online supplemental material, not integrated directly into the qualitative evidence synthesis presented in the main results. The data from the Donovan *et al* (2003) paper were previously indirectly referenced from Audrey *et al* (2011).
2. The authors have added further detail about the addition of new data and its analysis to the methods section and the online supplemental material. The authors more prominently refer the reader to the results in online supplemental files 1–9. The authors have edited the Discussion in the main paper to give more prominence to the additional analyses in online supplemental file 9.

The authors and journal extend their gratitude to the independent methodological experts who helped us with our post publication review.

The previous version of this article and previous versions of its supplemental files are now displayed in the online supplemental file 10. These files are watermarked with 'old version'.

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