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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

Journal:	BMJ Open
Manuscript ID	bmjopen-2021-055521
Article Type:	Original research
Date Submitted by the Author:	17-Jul-2021
Complete List of Authors:	Elfeky, Adel; University of Aberdeen, Health Services Research Unit Treweek, Shaun; University of Aberdeen, Health Services Research Unit Hannes, Karin; KU Leuven, Research Group SoMeTHin'K, Faculty of Social Sciences Bruhn, Hanne; University of Aberdeen, Health Services Research Unit Fraser, Cynthia; University of Aberdeen, Health Services Research Unit Gillies, Katie; University of Aberdeen, Health Services Research Unit
Keywords:	STATISTICS & RESEARCH METHODS, QUALITATIVE RESEARCH, Clinical trials < THERAPEUTICS





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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.

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## 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

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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 fullscale 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

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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.

	Barriers	Facilitators
Recruitment	1- Lack of clarity or understanding of randomisation	1- Personal gain and making 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	5,
Retention	1- Burden of follow-up questionnaires	None identified
	2- Practical barriers	

BMJ Open Table 2 The link between qualitative findings and changes proposed to recruitment and retention for the cull-scale trial for each barrier and facilitator barrier and facilitator. on 18

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Barriers (number of studies contributing to the	Were there any Facilitators	Were the reany changes planned for
review finding and percentage relative to the total	changes	the fullocale trial based on pre-trial
number of included studies)	planned for the	qualitative data? (Yes, Unclear, No)
	full-scale trial	O MY
	based on pre-	
	trial qualitative	d d
	data? (Yes,	fron
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	studies and	n na serie de la composición de la comp
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Page	15	of	106	

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of 106		BMJ Open	.1136/bmjopen-2021-05552	
Recruitment	1- Lack of clarity or understanding of randomisation (n=6/35 <sup>1</sup> (17%))	Yes (3/6 (50%)) Unclear (n=2/6 (33%)) No (n=1/6 (17%))	1- Altruism and personal No chate gain (n=5/35 <sup>1</sup> (14%)) 18 April 2022. Down	les 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%)) No (n=6)	
	<ul><li>3- Strong patient treatment preferences (n=9/35 (26%))</li></ul>	Yes (n=4/9 (44%) No (n=5/9(56%))	3- Social networks and No chage experience of research (n=2/35(6%))	jes reported
	4- Issues related to the control group (n=4/35 (11%))	Yes (n=4/4 (100%))	2024 by guest. F	
There were 35 ir	ncluded studies in total.		guest. Protected by copyright.	
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5- Communicating study information and associa terminology (n= 8/35(23%))	ated Yes (n=5/8 (62%))	5521 on 18 A
	Unclear (n=2/8 (25%))	April 2022
	No (n=1/8 (13%)	Downloade
6- Issues around the eligibility criteria (n=6/35 (1	7%)) Yes (n=4/6(66%))	d from http://bmjopen.
	No (n=2/6 (34%))	/bmjopen.b
7- Practical barriers (n=12/35 (34%))	Yes (n=5/12 (42%))	bmj.com/ on April 19, 2024 by
	Unclear (n=4/12(33%))	April 19, 20
	No (n=3/12 (25%))	124 by guest.
<ul><li>8- Commitment of staff and participants to the trian (n= 2/35(6%))</li></ul>	al Yes (n=1/2 (50%))	st. Protecte
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Page 17 of 106		BMJ Open	.1136/bmj
1 2 3 4 5			.1136/bmjopen-2021-055521 on 18
6 7 8		No (n=1/2 (50%))	521 on 18 Å
9 10 11 12	9- Beliefs and expectations (n= 10/35(28%))	Yes (n=6/10 (60%))	April 2022. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by
13 14 15 16		Unclear (n=1/10(10%))	Downloadec
17 18 19		No (n=3/10 (30%))	from http://
2 <u>0</u> 2 <b>9</b> 22 23	10- Mismatch between the trial protocol and clinical care pathways (n= 4/35(11%))	Yes (n=2/4 (50%))	/bmjopen.b
24 25 26 27		Unclear (n=2/4 (50%))	<u></u>
28 29 30	11- Participation burden (n= 4/35 (11%))	Unclear (n=3/4 (75%))	ı April 19, 2
31 32 33 34		No (n=1/4 (25%))	
35 36 37 38	12- Lack of confidence in approaching study participants (n= 2/35(6%))	Yes (n=1/2 (50%))	guest. Protected by copyright.
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42 43			yright.

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		Unclear (n=1/2 (50%))			
Retention	<ol> <li>Burden of follow-up questionnaires (n= 9/35<sup>1</sup>(26%))</li> </ol>	Yes (n=5/9 (56%))	None identified	April 2022. [	
		Unclear (n=2/9 (22%))		Downloadec	
		No (n=2/9(22%))		d from htt	
	2- Practical barriers (n= 2/35(6%))	Unclear (n=1/2 (50%))	5	tp://bmjope	
		No (n=1/2 (50%))	2/2	n.bmj.cor	
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### **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)

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#### 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).

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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) Page 21 of 106

#### **BMJ** Open

#### 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).

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#### 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

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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

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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,

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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

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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) BMJ Open: first published as 10.1136/bmjopen-2021-055521 on 18 April 2022. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected by copyright

#### 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

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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

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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).

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'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.

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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).

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"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 gualitative 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. 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

**Facilitators of recruitment** 

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

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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 fullscale 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

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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.

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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.

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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

Page 37 of 106

#### **BMJ** Open

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.

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## 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

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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.

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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.

**Contributors** AE, ST and KG conceptualised and designed the review. 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.

**Funding** This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Not required.

1 2 3	Provenance and peer review Net commissioned: externally peer reviewed
4	Provenance and peer review Not commissioned; externally peer reviewed.
5 6 7	Data sharing statement No original data were generated for this study.
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Sı Table. Enhancin	g transparency in reporting the synthesis of qualitative
research: ENTREQ	Checklist (Tong, et al., 2012)

	Q Checklist (Tong, et al., 2012)	D
ltem No.	Guide and Description	Report Location
1. Aim 2. Synthesis methodology	State the research question the synthesis addresses 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)	Introduction 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 criteric
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 o 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 - PRISM 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

limitations of included studies

Appraisal of the

methodological

included studies -

Appraisal of the

methodological limitations of

included studies

S8,9- CERQual

Evidence profiles

Methodology of

synthesis – "all

qualitative data"

Methodology of

Methodology of

Findings mapped

to Theme Matrix

Inductive process

- *Theme Matrix* tables – S5,6,7

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CASP

assessment of conduct (validity and robustness),

State the tools, frameworks and criteria used to

tools: CASP, QARI, COREQ, Mays and Pope [25];

reviewer developed tools; describe the domains

Indicate whether the appraisal was conducted

independently by more than one reviewer and if

content and utility of the findings)

and interpretations, reporting)

the assessment and give the rationale

entered into a computer software)

coding to search for concepts)

when deemed necessary)

interpretation

construct)

constructs was inductive or deductive

State the computer software used, if any

consensus was required

assessment of reporting (transparency), assessment of

appraise the studies or selected findings (e.g. Existing

assessed: research team, study design, data analysis

Present results of the quality assessment and indicate which articles, if any, were weighted/excluded based on

Indicate which sections of the primary studies were

analysed and how were the data extracted from the

"results /conclusions" were extracted electronically and

Describe the process for coding of data (e.g. line by line

across studies (e.g. subsequent studies were coded into

pre-existing concepts, and new concepts were created

Explain whether the process of deriving the themes or

illustrate themes/constructs, and identify whether the

quotations were participant quotations of the author's

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

Provide quotations from the primary studies to

primary studies? (e.g. all text under the headings

Identify who was involved in coding and analysis

Describe how were comparisons made within and

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## 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:

- qualitative research/ (89507)
- qualitative research.tw,kw. (33140)
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- grounded theory.tw,kw. (20998)
- narrative analys?s.tw,kw. (2073)
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### **BMJ** Open

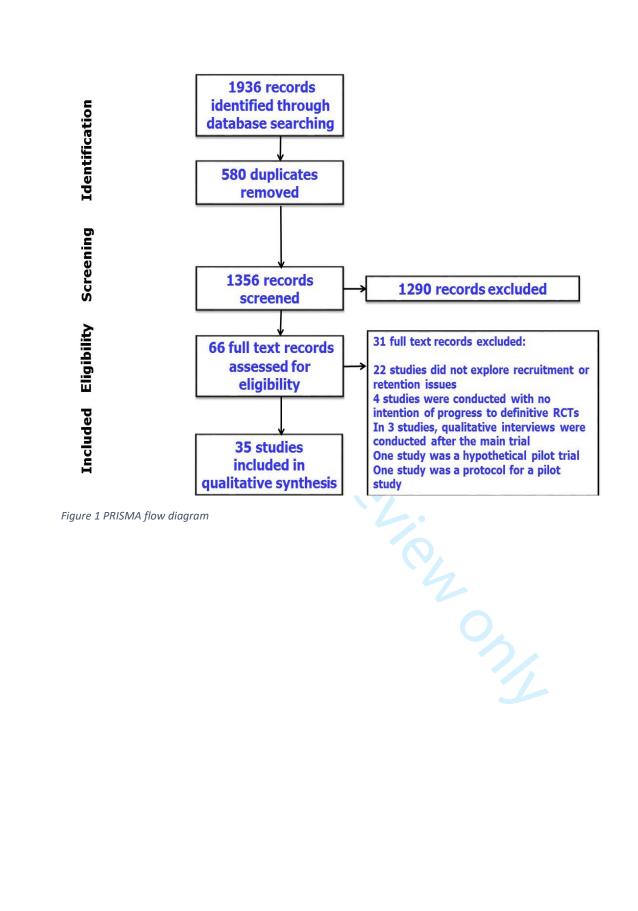
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51	Research Subjects/ use emcz (5835)
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- 73 limit 72 to English language (832) MEDLINE 422 EMBASE 351
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# S4: Characteristics of included studies.

			BMJ Open		.1136/bmjopen-2021-05	Page 54 of
	I	cluded studies.			<b>.</b>	
Study ID	Country	Clinical area	Study aim/ objective	Participants	Method of data	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 participants 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 interviers	Framework approach
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Page 55	of	106
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f 106			BMJ Open		.1136/bmjopen	
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 usir 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-too 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 geoups, face- to-faceor 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-stuctured interviews and focus groupse	Thematic analysis
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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 attitudes and potential barriers to participate in the scale randomised trial.       10 participants       Semi-structured interviews (two interviews were undertaken face to face ang eight by telephone).       Framework analysis         Gabbay 2017       UK       Depression and debt       To explore experience of involvement in the acceptability of trial processes and outcome measures       23 patients, 7 GPs and Semi-structured interviews were undertaken face to face ang eight by telephone).       Thematic analysis				BMJ Open		.1136/bmjope	Page 56 of 106
Van Den Berg 2017UKCardiac chest painTo explore patient attitudes and potential barriers to participation in a full- scale randomised trial.10 participantsSemi-structured interviews (two interviews were undertaken face to face and eight by telephone).Framework analysisGabbay 2017UKDepression and debtTo explore participants' experience of involvement in the trial, including the acceptability of trial processes and outcome measures23 patients, 7 GPs and 4 CAB (Citizens Advice Bureau) advisors who participated in the trialThematic analysisTo access narrative voices of those involved in the design and delivery of the trialTo access narrative trialSemi-structured interviewsThematic analysis	Hilton 2015	UK		understandings and experiences of the consent process and their decision to participate in the pilot	participated in the	Semi-structured interviews	Framework analysis
A CAB (Citizens Advice Bureau) advisors who participated in the trial, including the acceptability of trial processes and outcome measures       interviews         To access narrative voices of those involved in the design and delivery of the trial including the trial including the acceptability of the trial including the acceptability of the trial including	-	UK	Cardiac chest pain	To explore patient attitudes and potential barriers to participation in a full-	10 participants	Semi-structured interviews (two interviews were undertaken face to face ang eight by	Framework analysis
by each team member.	Gabbay 2017	UK	Depression and debt	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	4 CAB (Citizens Advice Bureau) advisors who participated in the	nervingen.bmj.com/ on April 19, 2024 by guest. Protected	Thematic analysis

Page 57 of 106

					1136/bmjopen-2	
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 21 on 18 April 2	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 jopen.bmj.com/ 9 Ap	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 gg, 2024 by guest. Protected by copyright	Thematic analysis

		BMJ Open		1136/bmjopen-	Page 58 of 10
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-stouctured interviews on 18 April 2022	Thematic analysis
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-stsuctured interviews	Thematic analysis
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
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
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 by copyright	Thematic analysis and focused conversation analysis.
	Norway UK UK	NorwayFecal incontinenceUKMental health difficultiesUKCancerUKFemoroacetabular	UKCancerTo provide in-depth, explanatory information to inform the main trialNorwayFecal incontinenceTo improve the quality of the planned trialUKMental health difficultiesTo explore individual experiences of participating in the pilot randomised, controlled trialUKCancerTo investigate the factors contributing to poor recruitment to the EaStER trial "Early Stage glottic cancer: Endoscopic excision or Radiotherapy" feasibility study.UKFemoroacetabular impingement syndromeTo understand the recruitment process so that any difficulties	UKCancerTo provide in-depth, explanatory information to inform the main trialThree patient focus groups (each comprising three patients) and 23 interviews with clinical staff were conducted.NorwayFecal incontinenceTo improve the quality of the planned trialOne focus group interviews.UKMental health difficultiesTo explore individual experiences of participating in the pilot randomised, controlled trial13 participantsUKCancerTo investigate the factors contributing to poor recruitment to the EaStER trial "Early Stage glottic cancer: Endoscopic excision or Radiotherapy" feasibility study.Surgeons and nurse recruitersUKFemoroacetabular impingement syndromeTo understand the recruitment process so that any difficulties12 consultations with 60 patients were recorded	UKCancerTo provide in-depth, explanatory information to inform the main trialThree patient focus groups (each comprising three patients) and 23 interviews with clinical staff were conducted.Focus groups and semi-structured interviewsNorwayFecal incontinenceTo improve the quality of the planned trialOne focus group interview (n = 7) and 4 individual interviews.Focus groups and 

Page 59 of 106

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		identified and changes put in place.		n-2021-0555	
UK	Moderate to severe fatigue	To test the proof of concept and inform the design of an effectiveness trial.	19 participants	Semi-structured telephome interviews.	Content analysis
UK	Depression	To inform the design of a full-scale trial	Nine psychological wellbeing practitioners and 15 participants	Semi-structured interviews	Thematic analysis
UK	Intermittent Exotropia X	To inform the design and conduct of a future full randomised controlled trial (RCT).	parents and treatment orthoptists	Semi-sguctured interviews	Thematic analysis
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 recruitionent consultations	Thematic analysis
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 224 by guest. Protected by copyright.	Framework approach
	UK UK UK	Image: Image of the synthesis of the synthesynthesis of the synthesynthesis of the synthesis of the synthesis o	UKModerate to severe fatigueidentified and changes put in place.UKModerate to severe fatigueTo test the proof of concept and inform the design of an effectiveness trial.UKDepressionTo inform the design of a full-scale trialUKIntermittent Exotropia XTo inform the design and conduct of a future full randomised controlled trial (RCT).UKChronic fatigue syndromeTo explore the feasibility and acceptability of the recruitment, randomization and interventions.UKObesityTo elicit men's experiences of participation in the	UKModerate to severe fatigueidentified and changes put in place.19 participantsUKModerate to severe fatigueTo test the proof of concept and inform the design of an effectiveness trial.19 participantsUKDepressionTo inform the design of a full-scale trialNine psychological wellbeing practitioners and 15 participantsUKIntermittent Exotropia XTo inform the design and conduct of a future full randomised controlled trial (RCT).parents and treatment orthoptistsUKChronic fatigue syndromeTo explore the feasibility and acceptability of the recruitment, randomization and interventions.13 mothers and 12 children on three occasionsUKObesityTo 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	UKModerate to severe fatigueidentified and changes put in place.19 participantsSemi-sguctured telephage interviews.UKModerate to severe fatigueTo test the proof of concept and inform the design of an effectiveness trial.19 participantsSemi-sguctured telephage interviews.UKDepressionTo inform the design of a full-scale trialNine psychological wellbeing practitioners and 15 participantsSemi-sfuctured interviewsUKIntermittent Exotropia XTo inform the design and conduct of a future full randomised controlled trial (RCT).parents and treatment orthoptistsSemi-sfuctured interviewsUKChronic fatigue syndromeTo explore the recruitment, randomization and intervientors.13 mothers and 12 children on three occasionsIn-depth interviews and audio- recordings of recruitagent consultationsUKObesityTo elicit men's experiences of participation in the prilot trial.Four focus groups total of 26 men sampled purposively from a list ofFocus groups total of 26 men sampled purposively from a list of

			BMJ Open		1136/bmjopen	Page 60 of 106
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	Individ al, group interviews face-to- face and telephone interviews bmj.com/ 9 April 19, 20	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

Page 61 of 106

					1136/bmjopen-2	
			chemotherapy treatments as part of ASPECTS (Aspirin and Esomeprazole Chemoprevention in Barrett's metaplasia) trial.		-2021-055521 on 18 April 2022. Dov	
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 recruition 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 iffterviews 2024 by guest. Protected by copyright.	Thematic analysis

Page 6	52 of 106
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			BMJ Open		1136/bm	Page 62 of 106
					1136/bmjopen-2021-0555	
			breast symptoms in older women		21-05552	
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	<ul> <li>14 parents (across intervention and control groups)</li> <li>7 telephone interviews with women who were randomised to the intervention group but who did not attend any sessions</li> </ul>	Semi-structured interviews and focus groups A II 2022 2. Downloaded from htt	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-stppuctured interviews 19, 2024 by guest. Protected by copyright	Thematic analysis
					copyright.	

Page	63	of	106
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Page 63 of 10	06			BMJ Open		. 1136/bmjopen-202 Semi-stro	
1 2 3 K						2012	
5 Ki 5 6 7 8 9 10 11 12 13	endrick 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 21 on 18 April 2022. Dowr	Thematic analysis
14       15     N       16     17       18     19       20     21       21     22       23     24       25     26       27     28	Лyall 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-statuctured telephote interviews from http://bmjopen.bmj.com/ on April 19, 2024 by	Framework approach
29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45			For peer review only -	http://bmjopen.bmj.com/sit	te/about/guidelines.xhtml	pril 19, 2024 by guest. Protected by copyright.	
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		BMJ Open	1136/bmjopen-2021-0555521
S5: Bari	riers to recruitment		-055521 c
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)	<ul> <li>Some participants struggled to understand the concept or need for randomisation.</li> <li>Despite explaining random allocation, some participants were still uncertain whether they would be selected based on some personal or illness characteristics.</li> </ul>	<ul> <li>Randomisation will be explained to participants in the following way:</li> <li>'To try and make sure both groups are the same, each perso put into a group at random. This is the fairest way of decidi who gets the test and means everyone will have a 50/50 ch of being put in either group'.</li> </ul>	n <del>g</del>
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.	<ul> <li>Attention to be focused on training trialists who are involved in recruitment to complicated trials, both in te of communication processes and on the assimilation of complex trial pathways.</li> </ul>	<u>o</u>
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.	<ul> <li>It was necessary to emphasize that recruiters must be genuinely uncertain about the best treatment, believer patient to be suitable for all three treatments, and be confident in these beliefs.</li> <li>Recruiters were encouraged to elicit patients' lay views then discuss differences with ProtecT study information explain that randomisation offered a way of resolving t dilemma of treatment choice.</li> </ul>	t by guest. adotect

Pag	e 65 of 106		BMJ Open	.1136/bmjopen	
1 2 3 4 5 6 7	Paramasivan 2011 (Transitional cell	<ul> <li>The complexity of the trial design led to confusion among some patients and recruiters about the timing of</li> </ul>	<ul> <li>The randomization period was simplified and clarified that patients could be randomized at any time before three cycles of chemotherapy rather than during the</li> </ul>	-2021-055521en	• Yes
8 9 10 11	carcinoma of the bladder)	randomization.	second cycle.	18 April 2022	
12 13 14 15 16 17 18 19 20 21 22 23 24	McEachan 2016 (Childhood obesity)	<ul> <li>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.</li> <li>Some control group women interviewed expressed disappointment at being allocated to the control group.</li> </ul>	No changes reported to address this barrier	Downloaded from http://bmjopen.bmj	• No
25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47		For peer review only	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	.com/ on April 19, 2024 by guest. Protected by copyright.	

			BMJ Open	.1136/bmjopen	Page 66 of 1
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25	Kendrick 2017 (Depression)	<ul> <li>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.</li> <li>It was apparent that several of the standard care patients had not adequately understood management allocation prior to agreeing to participate in the trial.</li> <li>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.</li> </ul>	<ul> <li>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.</li> <li>The study team needs to spend more time at participractices training them in the recruitment process.</li> <li>Patients should be supported to take the necessary rensure understanding of patient information sheets signing consent, especially with regard to clinical equand that they will not necessarily benefit from partice</li> </ul>	-2021-055521 on the partia April 2022 Point of the partia April 2022 Point of the p	Unclear
26 27 28 29 30 31 32 33 34	Citation	Findings associated with code: clinical equipoise	Changes planned before the full trial	on April 19, 2024 by g	Were the proposed changes clearly linked to coded data?
35 36 37 38 39 40 41 42 43 44 45 46		For peer review only	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	Jest. Protected by copyright.	

Paç	je 67 of 106		BMJ Open	.1136/bmjopen
1 2 3 4 5 6 7 8 9 10 11 12	Paramasivan 2017 (Complex obesity)	<ul> <li>Recruiters found it difficult to maintain equipoise.</li> <li>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)</li> </ul>	• Feedback sessions used to make recruiters aware of instances where they inadvertently used loaded terminology.	njopen-2021-055521 on 18 April 2022.
13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42	Griffin 2016 (hip impingement)	<ul> <li>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.</li> <li>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).</li> <li>Some surgeons favoured surgery as the optimal treatment for FAI (n = 2), which is the case for the two</li> </ul>	Providing frequent and comprehensive training to recruiters.	Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected by copyright
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		BMJ Open	.1136/bmjope	Page 68 of 1
1 2			7	
3 4 5 6 7 8 9 10	physiotherapists who were not in equipoise. Concerns that discussing uncertainty with patients could be detrimental to creating trust in their relationship.		2021-055521 on 18 April 20	
11       Ritchie 2015         13       (Cancer)         14       15         16       17         18       19	<ul> <li>Interviews with clinical staff revealed device preferences for certain subgroups of patients.</li> </ul>	Recruiters should gently challenge and acknowle own bias in device preference.	edge the Yes Downloaded from htt	
<ul> <li>Hamilton 2013</li> <li>(head and neck</li> <li>cancer)</li> <li>24</li> <li>25</li> <li>26</li> <li>27</li> </ul>	• 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.	<ul> <li>Principal investigators and recruiters need to thin critically about the concept of scientific equipoise that should underpin the RCT.</li> </ul>	e and how	
27 28 29 30 31 32 33 34 35 36 37 38	• 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.	0 7 J	en.bmj.com/ on April 19, 2024 by guest. Protected by copyright.	
39 40 41	While the EaStER protocol identified locoregional recurrence as the primary		id by copy	
42 43 44 45	For peer review only	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	right.	

Page	69	of	1	06
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Page 69 of 106		BMJ Open	.1136/br
1 2			1136/bmjopen-20
3 4 5 6 7 8 9 10 11	outcome and voice quality posttreatment as the secondary outcome, some recruiting staff felt that this main research question had already been answered.		21-055521 on
Pentecost 2015         13       (Depression)         14       15         16	<ul> <li>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.</li> <li>Difficulties in psychological wellbeing practitioners' (PWPs) adapting to recruitment procedures.</li> </ul>	Finding ways of enabling PWPs to engage with study procedures is recommended.	18 April 2022. Downloaded from http://bmjopen.bmj.com/ on Ap
<ul> <li>29 Clarke 2015</li> <li>30 (childhood</li> <li>31 intermittent</li> <li>33 exotropia)</li> <li>34</li> <li>35</li> <li>36</li> </ul>	• 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.	<ul> <li>Trial team suggested separation of the role of the trea clinician from the main recruiter to the trial. This prove extremely beneficial in aiding the process of recruitme and should be be considered in a future study.</li> </ul>	ed <sub>N</sub>
<ul> <li>37</li> <li>38</li> <li>39</li> <li>40</li> <li>41</li> </ul>	• Apparent inconsistency between lack of personal equipoise over the value of invasive urodynamic testing on the one	<ul> <li>No changes were suggested (the majority of responde regarded the basic research question as being importa</li> </ul>	nted ind by copy
42 43 44 45 46	For peer review only	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	ig ht.

			BMJ Open	.1136/br	Pa	ge 70 of <sup>-</sup>
1 2 3 4 5 6 7	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	(70%), and most would be prepared to randomise into a definitive RCT to address this (60%).	1136/bmjopen-2025 patien patien		
8 9 10 11 12 13 14 15	Crawley 2013 (children with chronic fatigue syndrome)	<ul> <li>Discussion of the interventions tended to be weighted towards the Lightning Process rather than the specialist medical care during recruitment consultations.</li> </ul>	No specific change reported to address this issue.	n 18 April 2022. Downloaded fro		
16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34	Moynihan 2012 (bladder cancer)	<ul> <li>An explanation of equipoise was usually perceived to be absent in the information process.</li> <li>The need to believe in expert physicians and an inability to accept medical uncertainty is documented.</li> <li>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</li> </ul>	<ul> <li>Attention to be focused on training trialists who a involved in recruitment to complicated trials, both of communication processes and on the assimilati complex trial pathways to avoid a palpable breakd communication.</li> </ul>	m http://bmjonen.bmj.com/ on April 19, 2024 by o own international own international own international own international own international own international own	Unclear	
35 36 37 38 39 40 41 42 43 44 45 46		For peer review on	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	guest. Protected by copyright.		

Pag	ge 71 of 106	BMJ Open 1136/bmjoper
1 2 3 4 5 6 7 8 9 10 11 12	Audrey 2011 (Cancer)	<ul> <li>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</li> <li>Recruiters were asked to change the order in which the reatments were presented (active monitoring, surgery, and radiotherapy) and to describe their respective advantages and disadvantages in equivalent detail.</li> <li>Issues of randomization and clinical equipoise were clarified for both patients and recruiters.</li> </ul>
13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28	Paramasivan 2011 (Prostate cancer)	<ul> <li>waiting.</li> <li>Centers sometimes appeared to take on a 'collective' preference - one that represented the views of most staff in the center.</li> <li>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.</li> </ul>
29 30 31 32 33 34 35 36 37 38 39 40 41 42 43	Palmer 2016 (joint hypermobility syndrome)	<ul> <li>Physiotherapists anticipated that it may be difficult to 'persuade' patients that clinical equipoise existed and felt that this was an issue related to recruitment.</li> <li>Training and monitoring of trial personnel to ensure notifons of equipoise are delivered and reinforced consistently is that this was an issue related to recruitment.</li> </ul>
44 45 46 47		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

		BMJ Open	1136/bmjopen	Page 7
			njopen-20	
Citation	Findings associated with code: Patient treatment preferences	Changes planned before the full trial	1-055521 on	Were the proposed changes clearly linked to coded data?
Paramasivan 2017 (complex obesity)	Patients tended to decline study participation, often choosing bypass surgery.	<ul> <li>Do not indicate patient preference anywhere on the n</li> <li>Move beyond initial probing questions in relation to preferences toward rectifying any erroneous views.</li> <li>Request patients who appear to have a preference or decision about trial participation to 'keep an open min until they had heard all the relevant information.</li> </ul>	Aprient atie022.	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 question and raise concerns.	from	Yes
Hilton 2015 (stress urinary incontinence)	<ul> <li>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.</li> </ul>	No specific changes planned to address this barrier.	com/ on April 19, 2024 by	
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	<ul> <li>Principal investigators and recruiters must try to elicit understand patient views and preferences.</li> <li>The need to gently challenge preferences that are base inaccurate information.</li> </ul>	st. Protected by	Yes
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Pag	e 73 of 106		BMJ Open	.1136/bn
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23	Clarke 2015 (childhood intermittent exotropia)	<ul> <li>surgery, because it was perceived as more convenient.</li> <li>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.</li> <li>Recruitment was hampered by strong parental preferences.</li> </ul>	<ul> <li>The need for training recruiters to enable them to exp the need for randomisation and the rationale for the l patients.</li> <li>To account for parental preferences, a future trial will incorporate a preference arm or accept that recruitme will inevitably be restricted to those parents who are prepared to consider surgery as a treatment.</li> </ul>	C521 on 18 April 2022. Downloaded from Yes
24 25 26 27 28 29 30 31 32 33 34 35 36 37	Audrey 2011 (Cancer)	<ul> <li>Patients often expressed lay views that cancer should be removed or came with media information that was biased in favor of radical treatments.</li> </ul>	No specific changes planned to address this barrier.	m/ on April 19, 2024 by g
37 38 39 40 41 42 43 44 45 46		For peer review only	r - http://bmjopen.bmj.com/site/about/guidelines.xhtml	uest. Protected by copyright.

			BMJ Open	.1136/bmjopen	Page 74 of
1 2				njopen-20	
3 4 5 6 7 8 9 10	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.	-2021-055521 on 18 April 2022.	
11 12 13 14 15 16 17 18 19		<ul> <li>Some control group women interviewed expressed disappointment at being allocated to the control group.</li> </ul>	No specific changes planned to address this barrier	Downloaded from htt	
20 21 22 23 24 25 26 27 28	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	p://bmjopen.bmj.com/ on Ap	
29 30 31 32 33 34	Citation	Findings associated with code: Issues related to the control group	Changes planned before the full trial	oril 19, 2024 by gu	Were the proposed changes clearly linked to coded data?
35 36 37 38 39 40 41	Nair 2014 (lung cancer)	<ul> <li>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.</li> </ul>	Changes made to the study design or Participant Inform Leaflet (PIL)	eo. Protected by copyright	Yes
41 42 43 44 45 46		For peer review only	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	pyright.	

Pag	e 75 of 106	BMJ Open	
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28	Audrey 2011 (cancer)	BMU Open       BMU Open         • 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.       • The control group will be changed to non-test group, which is what participants were most comfortable with".         • Some people who understood the need for a control group, found it hard to appreciate the need for this in a screening trial.       • 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'.       • Tissues identified by the qualitative research led to changes in the study information, randomisation, terminology used and presentation of the non-radical arm.       Yes	
29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

		BMJ Open	.1136/b	Page 76 o
1 2			mjopen-2	
Kendrick 2017         (depression)         (diamondation of the second stress of the second st	<ul> <li>One standard care patient pointed out that he could not grasp an understanding of the purpose of the control arm.</li> <li>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.</li> <li>Some patients felt that they would not have the best treatment if they were randomized to standard care.</li> </ul>	<ul> <li>Patients should be supported to take the necessary ensure understanding of patient information sheets signing consent, especially with regard to clinical eq and that they will not necessarily benefit from parti</li> <li>A lack of skills in introducing research could be addr through more training in a smaller group of practice</li> </ul>	s befoge juipolse cipation. a resse	Yes
<ul> <li>Palmer 2016</li> <li>(joint</li> <li>hypermobility</li> <li>syndrome)</li> <li>30</li> </ul>	<ul> <li>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.</li> </ul>	<ul> <li>Patients and health professionals offered a number suggestions for augmenting the content of the cont including providing ongoing support through group meetings, gym membership and the provision of ge not targeted, exercises, so the two arms were perce more equitable.</li> </ul>	rol arm, neralg	Yes
31         Citation           32         33           34	Findings associated with code: Communicating study information and associated terminology	Changes planned before the full trial	, 2024 by	Were the proposed changes clearly linked to coded data?
<ul> <li>Griffin 2016 (hip</li> <li>impingement)</li> <li>impingement</li> </ul>	<ul> <li>Graphic descriptions of surgery that may have put patients off randomisation.</li> </ul>	• Providing frequent and comprehensive training to recruiters.	st. Protected by	Unclear
41 42 43 44 45 46	For peer review onl	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	copyright.	

Paç	je 77 of 106	BMJ Open BMJ open	
1 2		njopen-20	
3 4 5 6 7 8 9 10 11 12 13		<ul> <li>Presenting trial information in an order that is confusing for patients.</li> <li>Surgeons going beyond their protocol brief, to explain the trial rather than referring patients on to the trial recruiter for this information.</li> </ul>	
14 15 16 17 18 19 20	Aventin 2016 (Sexual health)	<ul> <li>The baseline questionnaire was too long and some did not feel comfortable answering questions relating to sexuality.</li> <li>At an individual level, researchers should ensure that date collection documentation is clear to parents and pupils, a perhaps involving steering group members in ensuring clarity.</li> </ul>	Yes
21 22 23 24 25 26 27	Crawley 2013 (chronic fatigue syndrome)	<ul> <li>Patient information sheets were perceived as long, difficult to understand, repetitive in places and not visually appealing to 12 to 18-year olds.</li> <li>Consider using different patient information sheets for children aged 12 to 14 years than those used for older teenagers.</li> </ul>	Yes
28 29 30 31 32 33 34 35 36 37 38 39 40 41	Moynihan 2012 (transitional cell carcinoma of the bladder)	<ul> <li>Patients displayed what may be perceived as 'poor understanding' of trial procedures and concepts. Patients' accounts suggested that information giving was often suboptimal and/or understanding unverified.</li> <li>An explanation of equipoise was usually perceived to be absent in the information process.</li> </ul>	Unclear
42 43 44 45		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

			BMJ Open	.1136/bmjopen	Page 78 of 7
1 2					
3 4 5 6 7		<ul> <li>Patients across the sample failed to understand the 'language' of trial procedures.</li> <li>Research overload, information</li> </ul>		2021-055521 on 18	
8 9 10 11		overload and a perceived lack of information affected decision making.		8 April 2022.	
12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46	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.	2. Downloaded from h	
	Audrey 2011 (cancer)	<ul> <li>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'.</li> </ul>	<ul> <li>Issues identified by the qualitative research led to chain the study information, randomisation, terminology and presentation of the non-radical arm.</li> <li>Recruiters were asked to change the order in which t treatments were presented (active monitoring, surge radiotherapy) and to describe their respective advant and disadvantages in equivalent detail.</li> <li>Recruiters were asked to replace 'trial' with 'study'.</li> </ul>	r usgo open.bmj he mj ry, gnd	Yes
	Paramasivan 2011 (transitional cell carcinoma of the bladder)	<ul> <li>Recruiters and investigators agreed that the SPARE trial was difficult to explain.</li> <li>Recruiters indicated that they found the quantity of information problematic as well as its complexity.</li> </ul>	<ul> <li>The construction of a simpler version of the study flow which was then issued to recruiters so that they could provide a clearer articulation of the trial.</li> <li>The consent for chemotherapy was separated from the consent for SPARE in response to recruiters indicating</li> </ul>	guest. Protected	Yes
		For peer review on	ly - http://bmjopen.bmj.com/site/about/guidelines.xhtml	copyright.	

Page 79 of 106		BMJ Open	. 1136/br
1			njopen-200
3 4 5 6 7 8 9 10 11 12		<ul> <li>patients were given too much information about various aspects of the trial at the same time.</li> <li>The recruitment study team drafted a new, shorter and clearer PIS which removed the 'loaded' terminology, explained the simplified study outline and included the inflowchart.</li> </ul>	055521 on 18
13         14       Ellis 2016 (lung         15       cancer)         16	<ul> <li>For some participants, the questionnaire items probed areas that they had not thought about or had chosen not to think about.</li> <li>Carers also expressed some discontent with the questionnaires and this was seen as a potential barrier to recruitment.</li> </ul>	The number of questionnaires to be used in the subsequence trial will be decreased.	ownt Yes Deaded from http://bmjopen.bn
25 <b>Citation</b> 26 27 28	Findings associated with code: issues around the eligibility criteria	Changes planned before the full trial	Were the proposed changes clearly linked to coded data?
<ul> <li>Hilton 2015</li> <li>(stress urinary</li> <li>incontinence)</li> <li>33</li> <li>34</li> <li>35</li> <li>36</li> </ul>	<ul> <li>Interpretation of eligibility criteria differed between centers (Authors' judgement).</li> </ul>	screening training exercises might be considered for a future definitive trial to ensure	TI 19, 2024 by guest. P
<ul> <li>Bhattacharya</li> <li>2011 (older</li> <li>population</li> <li>unintentionally</li> </ul>	• 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.	Protected by copyright.
42 43 44 45 46	For peer review onl	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

Page	80	of	106
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1 2				njopen-2(	
3 4 5 6	non-adherent to medication)	proposed resulted in over one-third of patients being ineligible for study participation		021-055521 c	
7 8 9 10 11 12 13	Hamilton 2013 (head and neck cancer)	<ul> <li>Surgeons applied the inclusion/exclusion criteria variably, thereby reducing the available number of eligible patients and creating differences between centers.</li> </ul>	<ul> <li>Issues related to inclusion/ exclusion criteria, may rec close examination and regular meetings to discuss an resolve evolving issues.</li> </ul>	00	Yes
14 15 16 17 18 19 20 21 22	Clarke 2015 (childhood intermittent exotropia)	<ul> <li>Difficulty in confirming eligibility at the initial screening visit</li> <li>Subsequent blockage of appointment slots by children who needed rescreening for eligibility, contributed to a failure to recruit to target.</li> </ul>	<ul> <li>A future trial will consider a limit on the upper age at participants would be included.</li> </ul>	h whaded from http://bmjop	Yes
23 24 25 26 27	Paramasivan 2011 (transitional cell carcinoma of the bladder)	<ul> <li>Some recruiters thought there was leeway for interpretation of the inclusion/exclusion criteria in partnership with the main trial team.</li> </ul>	<ul> <li>No changes planned to address this issue (The possible relaxing certain inclusion criteria was discussed with the TMG but it was decided that these could not be change without invalidating the aims of the RCT).</li> </ul>	he	
28 29 30 31 32 33 34 35 36 37 38 39	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.	<ul> <li>No changes planned to address this barrier (eligibility criteria will remain the same for the subsequent trial</li> </ul>	April 19, 2024 by guest. Protected	
40 41 42 43 44 45 46 47		For peer review only	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	by copyright.	

Page 81 of 106		BMJ Open	.1136/bm
Citation Griffin 2016 (hip	<ul> <li>Findings associated with code: Practical barriers</li> <li>Difficulty in implementing procedures</li> </ul>	<ul> <li>Changes planned before the full trial</li> <li>Regular visits to the centers by the PI and other TGM</li> </ul>	Uppen-20     Were the proposed changes       1-055     clearly linked to coded       data?     on       1     Yes
8       Griffin 2016 (nip         9       impingement)         10       11         12       13         13       14         15       16         16       17         18       19         20       21         21       22         23       24         25       26         27       28         29       30	due to the multicenter nature of the pilot.	<ul> <li>Regular visits to the centers by the Prand other rown members to keep momentum</li> <li>Delivery of a slick and easy-to-implement recruitment process to be the least disruptive to routine clinical practice.</li> <li>Providing frequent and comprehensive training to recruiters.</li> <li>Modifying the support to teams in other centers accord to their research experience.</li> <li>Setting recruitment targets and engendering a healthy competition between centers.</li> <li>Follow up with messages and regular newsletters abou need to recruit.</li> <li>Contacts between research and clinical departments at recruitment opportunities should be encouraged.</li> </ul>	8 April 2022. Downloaded from the principal state of the principal s
31Hamlet 201732(young people33with appearance-34altering35conditions)3737	<ul> <li>Barriers of the primary care environment (time-limited consultations, high workload, competing studies)</li> </ul>	No specific changes to address these barriers.	, 2024 by guest. Protei
<ul> <li>Aventin 2016</li> <li>(Sexual health)</li> <li>41</li> </ul>	<ul> <li>Perceived lack of time for potential study participants to take part.</li> </ul>	• Environmental facilitators of recruitment: approaching schools attending RSE training days, highlighting the innovative nature of the intervention, flexibility in term	eter Yes by
43 44 45	For peer review onl	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	<u>,</u>

			BMJ Open	Page 82 of 1 Bonjoper
1 2				njopen-20
3 4 5 6 7 8 9 10		<ul> <li>Involvement in another research projects.</li> </ul>	how and when the research was conducted in individua schools, the provision of support to schools by facilitation 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.	og N N B
11 12 13 14 15 16 17	Gabbay 2017 (Debt Counselling for Depression)	<ul> <li>Delayed practice recruitment due to higher administrative issues.</li> <li>Staffing and workload Complexity of primary care services</li> </ul>	• 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.	022. Downloaded f
17 18 19 20 21 22 23 24 25 26 27	Lawton 2017 (postpartum haemorrhage)	Staff reluctance to forgo written consent procedures	<ul> <li>Staff who are inexperienced in using alternatives to prospective written consent may benefit from training a support to increase their confidence and willingness to alternative consent approaches. This training and suppor could focus on raising staff awareness and understandin ethical review processes and of how, and why, they are legally protected when alternatives to prospective writte consent are used.</li> </ul>	pe use of ng of
28 29 30 31 32	Trevelyan 2016 (phantom limb syndrome)	<ul> <li>Failure to identify suitable participants due to units not operating in full capacity.</li> </ul>	<ul> <li>A future trial would need to ensure that trial centers allocated adequate time and personnel.</li> <li>Applying multicentered approach to recruitment.</li> </ul>	April 19, 2024
33 34 35 36 37 38 39 40 41	Blekken 2015 (fecal incontinence)	<ul> <li>Staff discontinuity</li> <li>Insufficient time</li> <li>Large care staff</li> <li>sub-optimal use of skill-mix</li> </ul>	<ul> <li>For the main study, the plan is to include personal meet with the director of health and social affairs and the car managers of the NHs.</li> <li>One of the RNs from the pilot study will also be invited share her experience and to answer questions about participating.</li> </ul>	guest. Protested by
42 43 44 45 46 47		For peer review only	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	copyright.

Pag	ge 83 of 106		BMJ Open 36/pr	
1 2			BMJ Open 36/bmjopen-20	
3 4 5 6 7 8 9 10 11 12		•	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 cluster will improve study feasibility by increasing the number of potential clusters, which impacts power more than increasing individuals enrolled.	3
13 14 15 16 17	Pentecost 2015 (depression)	<ul> <li>Staff attrition: randomised participants' not seeing study psychological wellbeing practitioners.</li> </ul>	Finding ways of enabling PWPs to engage with study procedures is recommended.	Unclear
18 19 20 21 22 23 24 25	Clarke 2015 (childhood intermittent exotropia)	<ul> <li>There was a lag in recruitment due to the delay in the subsequent appointment for the recruitment clinic.</li> </ul>	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
26 27 28 29 30 31 32 33 34	Marshman 2012 (dental caries)	<ul> <li>Shortage in radiographs and its impact on the number of eligible participants.</li> <li>Time constraints and busy schedule.</li> </ul>	Practitioners should be advised that patients will required 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
35 36 37 38 39	Ellis 2016 (lung cancer)	<ul> <li>Inconvenient time frame between providing consent and receiving the first intervention.</li> </ul>		Yes
40 41 42 43 44 45 46		For peer review only - h	http://bmjopen.bmj.com/site/about/guidelines.xhtml	

			BMJ Open 300	Page 84 of 1
1 2			BMJ Open 360 bmjopen 20	
3 4 5 6 7 8 9 10 11 12 13 14	Latter 2018 (cancer patients at the end of life)	<ul> <li>Organisational change, team staffing levels, nurse workloads and variable flow of palliative care referrals.</li> <li>Nurses' unfamiliarity with recruitment.</li> <li>Incompatibility of recruitment procedures with nursing.</li> </ul>	No specific changes planned to address these barriers.     No specific changes planned to addr	
14 15 16 17 18	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?
19 20 21 22 23 24 25 26 27 28 29	Paramasivan 2011 (transitional cell carcinoma of the bladder)	<ul> <li>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.</li> </ul>	<ul> <li>Clinical centers were asked to identify two Lead Recruited (LRs) per site whose responsibilities would be to act as the focus for SPARE recruitment activity.</li> </ul>	
30 31 32 33 34	Latter 2018 (cancer patients at the end of life)	<ul> <li>Recruiting fewer dyads than anticipated affected nurses' engagement and the priority they gave to the study.</li> </ul>	No specific changes reported     Solution	
35 36 37 38 39 40	Citation	Findings associated with code: Beliefs and expectations about trial participation	Changes planned before the full trial Protected by copyright	Were the proposed changes clearly linked to coded data?
41 42 43 44 45 46 47		For peer review only	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

Page 85 of 106	BMJ Open BMJ Open
123Hamlet 20174(young people5with appearand6with appearand7altering8conditions)91011121314	<ul> <li>A 'conspiracy of silence': Beliefs that young people would prefer not to discuss appearance-related concerns with their GP.</li> <li>Participants seemed hesitant approaching the topic directly.</li> <li>Participants seemed hesitant approaching the topic directly.</li> <li>Yes</li> <li>Yes</li> <li>Yes</li> <li>Participants seemed hesitant approaching the topic directly.</li> </ul>
15       Van Den Berg         16       2017 (chest pained)         17       2017 (chest pained)         18       19         20       2017 (chest pained)         21       2017 (chest pained)         22       23         23       24         25       26         27       28         29       29	<ul> <li>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.</li> <li>Concerns about being experimented on: some participants felt being generally sceptical of clinical research and initially felt anxious about participation.</li> <li>Waive verbal consent for initial trial procedures that do not feel ready to commit they can provide appropriate written informed consent.</li> <li>The need to explore shared decision making to cater for wide spectrum of perspectives.</li> </ul>
30 31Trevelyan 201632(phantom limb33 34 35syndrome)	Intensity of Phantom Limb Pain (PLP)     Consider lowering or excluding the severity of PLP.     Yes
36       Ritchie 2015         37       (Cancer)         38	Patient self-preservation (the need to retain control of choice of device or treatment schedules).     Recruiters should gently challenge patients'     Provide their own bias in device preference.     Yes     Yes
43 44 45 46	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

			BMJ Open	.1136/bmjope	Page 86 of 1
1 2 3	Hamilton 2013	• Low boliefs: The encology	No specific shapped planned to address this barrier	n-20	
4 5 6 7 8	(head and neck cancer)	<ul> <li>Lay beliefs: The oncology centre/hospital where radiotherapy was performed had a negative image and was seen as a 'place to die'.</li> </ul>	<ul> <li>No specific changes planned to address this barrier.</li> </ul>	21-055521 on 18 A	
9 10 11 12 13 14 15 16 17 18 19	Nair 2014 (cancer)	<ul> <li>Participants felt stigmatized (because of their smoking status) by some of the language used in the PILs.</li> <li>The perception held by some participants that the trial is designed to encourage people to stop smoking.</li> </ul>	<ul> <li>"We removed all mention of providing smoking cess information and advice from the Patient information leaflets".</li> <li>'Lung cancer can happen to anyone, including the yo old and people who do not smoke, but the risk is hig those over 50 and those who have smoked.'</li> </ul>	2022. Downd	Yes
20 21 22 23 24 25 26 27 28 29	Moynihan 2012(transitional cell carcinoma of the bladder)	<ul> <li>The patients' sense of alienation was evident. Feelings of isolation, loss of control and powerlessness underwrote involvement in the trial process.</li> </ul>	<ul> <li>Attention to be focused on training trialists who are involved in recruitment to complicated trials, both i of communication processes and on the assimilation complex trial pathways.</li> <li>It is suggested that health professionals consider far a context in which patients feel fully included in the enterprise.</li> </ul>	n terens n of en.bmj.com cilitationg	Unclear
30 31 32 33 34 35 36 37	Ellis 2016 (lung cancer)	<ul> <li>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.</li> </ul>	<ul> <li>No specific changes planned to address this barrier.</li> </ul>	19, 2024 by guest. Prote	
38 39 40 41 42 43 44 45 46 47		For peer review only	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	cted by copyright.	

Paç	e 87 of 106		BMJ Open BMJ Open	
1 2			njopen-200	
3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	Kendrick 2017(depression)	<ul> <li>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.</li> <li>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.</li> </ul>	<ul> <li>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.</li> <li>April 2022. Downloaded from http://www.loaded.com/limit/2022.</li> </ul>	Yes
21 22 23 24 25 26 27 28 29 30 31	Latter 2018(cancer patients at the end of life)	<ul> <li>Nurses 'protecting' patients and carers from additional burden or distress.</li> <li>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.</li> </ul>	No specific changes reported to address these barriers.     No specific changes reported to address these barriers.     Planned changes before the full trial	
32 33 34 35 26	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?
36 37 38 39 40 41	Paramasivan 2017(complex obesity)	<ul> <li>Well-established routines for clinical service provision led to the trial being presented to patients as an 'add-on'</li> </ul>	<ul> <li>Mention the study in the opening statements of the surgecal consultations.</li> <li>Express enthusiasm for the study.</li> </ul>	Yes
42 43 44 45		For peer review only	۲- http://bmjopen.bmj.com/site/about/guidelines.xhtml	

		BMJ Open	.1136/b	Page 88 of 7
1 2 3 4 5 6 7 Griffin 2016 (hip	<ul> <li>extra rather than an integral part of existing clinical services.</li> <li>Teams experienced issues such as</li> </ul>	<ul> <li>Delivery of a slick and easy-to-implement recruitment</li> </ul>	njopen-2021-0555521 o Unclear	
7       impingement)         9       10         10       11         12       13         13       14         15       16         17       18         19       20         21       22         23       24         25       26         27       28         29       30	<ul> <li>remembering to approach patients at each possible opportunity, or the need not to discuss surgery before diagnosis was confirmed.</li> <li>Some research associates expressed their concern about talking to patients about the audio recording of the consultation.</li> </ul>	<ul> <li>Derivery of a slick and easy-to-implement recruitment process to be the least disruptive to routine clinical practice.</li> <li>Providing frequent and comprehensive training to recruiters.</li> </ul>	on 18 April 2022. Downloaded from http://bmjopen.bmj.com/ on April 19, 2	
31 32Paramasivan332011(transitional34cell carcinoma of35the bladder)363738394041	• 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	<ul> <li>Clinical centers were asked to identify two Lead Recru (LRs) per site whose responsibilities would be to act a focus for SPARE recruitment activity.</li> <li>The LRs were also advised to see if they could arrange specific 'recruitment appointment' about 7-10 days at the chemotherapy discussion, with the aim of providi</li> </ul>	e a Protectul freetectul ing dull	
42 43 44 45 46	For peer review onl	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	copyright.	

Pag	je 89 of 106		BMJ Open BMJ Open	
1 2 3 4 5 6 7 8 9 10		(surgery or oncology, or local /regional) centres that might be involved.	<ul> <li>information about the trial and obtaining consent for participation.</li> <li>It was also recommended that trial participants should be referred to the respective specialists after randomization rather than before to ensure consistency of information Provide Note Note Note Note Note Note Note Not</li></ul>	
11 12 13 14 15 16 17 18	Ritchie 2015 (Cancer)	<ul> <li>Potential delays from referral to treatment.</li> <li>Additional service provision and increased workload.</li> </ul>	<ul> <li>The remit of the funded role of trial Champion has been D developed to encompass not only recruitment and randomisation but also coordination and facilitation of device insertion appointments and communication.</li> </ul>	Unclear
19 20 21 22	Citation	Findings associated with code: Participation burden	Changes planned before the full trial	Were the proposed changes clearly linked to coded data?
23 24 25 26 27	Lawton 2017 (postpartum haemorrhage)	• The burden of completing and signing consent form.	No specific changes planned to address this issue	
28 29 30 31 32 33 34 35 36 37 38 39	Clarke 2015 (childhood intermittent exotropia)	<ul> <li>For parents and clinicians, the initial screening appointment presented a challenge, in that it had to encompass many points within a limited time.</li> <li>The initial two visits, for screening and recruitment, often gave insufficient time for parents to fully consider participation in the trial.</li> </ul>	<ul> <li>The use of research nurses in all centers should be considered in a future study.</li> <li>Separation of the role of the treating clinician from the main recruiter to the trial.</li> </ul>	
40 41 42 43 44 45 46 47		For peer review only	by copyright. y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

			BMJ Open	.1136/bmjope	Page 90 of 1
1 2				n-20	
3 4 5 7 8 9 10 11 12 13	Nair 2014 (cancer)	<ul> <li>The main obstacle to participation appeared to be the need for flexible appointments.</li> <li>work commitments among some of the younger participants were seen as a potential barrier.</li> </ul>	<ul> <li>Those expressing interest in the study are sent the full F and at least 24 hours after anticipated receipt are phone to discuss the study, answer questions, undertake a preliminary eligibility assessment and to arrange a recruitment visit at a time suitable to the patient.</li> <li>Appointment reminders by phone, text message or emains</li> </ul>	0 <del>58</del> 521 on 18 Apr	ear
14 15 16 17 18 19 20 21 22 23	Moynihan 2012 (transitional cell carcinoma of the bladder)	<ul> <li>Patients spontaneously indicated the need to 'work' their way around NHS waiting times and hospital administration.</li> <li>Patients often criticized their need to 'work' against 'bad administration', sometimes affecting trial decisions.</li> </ul>	<ul> <li>It is suggested that health professionals consider facilita a context in which patients feel fully included in the tria enterprise.</li> </ul>	0 -	ear
23 24 25 26 27	Citation	Findings associated with code: Confidence about approaching patients	Changes planned before the full trial	Wer	e the proposed changes ly linked to coded ?
28 29 30 31 32 33 34 35 36 37 38 39	Griffin 2016 (hip impingement)	<ul> <li>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.</li> <li>Long periods between recruitment clinics represented a challenge for research associates to maintain</li> </ul>	<ul> <li>Modifying the support to teams in other centers accord to their research experience.</li> </ul>	April 19,	ear
40 41 42 43 44 45 46 47		For peer review onl	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	- by copyright.	

Page 91	of	106
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Pag	ge 91 of 106		BMJ Open BMJ Open	
1 2			BMJ Open 36/bmjo pen-2021-0555	
3 4 5		confidence and knowledge about the UK FASHION trial.	21-0555 552	
6 7 8 9 10 11 12 13	Hamlet 2017 (young people with appearance- altering conditions)	Participants seemed hesitant     approaching the topic directly.	<ul> <li>Training, with a particular focus on how to talk to young people who might be experiencing appearance concernst could facilitate doctor-patient communication about the psychosocial challenges of living with a condition or injury that alters appearance and, in turn, patient disclosure.</li> </ul>	
14 15 16 17 18 19 20 21			2. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by gue	
22 23 24 25 26 27			njopen.bmj.com/ on	
28 29 30 31 32 33 34			April 19, 2024 by gu	
35 36 37 38 39 40			guest. Protected by copyright.	
41 42 43 44 45 46 47		For peer review onl	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

## 1136/bmjopen-2021-05 Were the proposed changes Citation Findings associated with code: Altruism and Changes planned before the full clearly dinked to coded data? trial personal gain 8 April 2022. Downloaded from http://bmjopen.bmj.cbm/ on April 19, 2024 by guest. Protected by copyright Hamlet 2017 (young Participants reported a personal interest No changes reported • people with in the topic, which increased its appearance-altering pertinence and served as a motivator for conditions) recruitment. Van Den Berg 2017 Participation seemed motivated by No changes reported ٠ (Chest pain) 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. Bhattacharya 2011 Patients wanted to take part to help No changes reported • (older people others, to help themselves, to give unintentionally nonpayback to the NHS. adherent to medication) Notley 2015 Participants expressed keenness to be No changes reported • ٠ (psychological involved in research, for altruistic reasons. difficulties) Hilton 2015 (stress Altruistic factors motivated participation. No changes reported ٠ urinary incontinence)

## S6: Facilitators for recruitment

			1136/bmjopen-2021
Citation	Findings associated with code: Communicating study information	Changes planned before the full trial	Were the proposed changes clearly inked to coded data?
Aventin 2016 (sexual health)	<ul> <li>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.</li> <li>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.</li> </ul>	No changes reported	1 18 April 2022. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by
Hilton 2015 (stress urinary incontinence)	<ul> <li>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.</li> <li>Good understanding of the study</li> </ul>	<ul> <li>No changes reported</li> </ul>	guest. Protected by
		en.bmj.com/site/about/guidelines.xhtml	d by copyright.

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Van Den Berg 2017 (Chest pain)	<ul> <li>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</li> </ul>	No changes reported	1136/bmjopen-2021-055521 on 18 April 2022. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by Yes
Notley 2015 (psychological difficulties)	<ul> <li>11 participants displayed a sound understanding of the randomization process.</li> <li>There was a thorough understanding of the rationale for the processes or measures used.</li> </ul>	No changes reported	wnloaded from http://bmjop
Realpe 2016 (hip impingement)	<ul> <li>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): <ul> <li>Step 1: explain what the condition is to the patient</li> <li>Step 2: reassure the patient that they will receive best treatment</li> <li>Step 3; explain that there is uncertainty about which treatment is the best</li> <li>Step 4; explain the purpose of the study</li> </ul> </li> </ul>	• 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.	en.bmj.com/ on April 19, 2024 by guest. Protected by copyright.

Page	95	of	1	06
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Page 9	95 of 106	BN	/J Open	.1136/b
1 2				njopen-20
3 4 5 6 7 8 9 10 11	Hilton 2015 (stress urinary incontinence)	<ul> <li>Step 5; give the patient a balanced view about the advantages and disadvantages of each treatment being compared.</li> <li>Step 6; explain the study procedures.</li> <li>Supplementary information from trial and clinic staff was seen as important.</li> </ul>	No changes reported	1136/bmjopen-2021-055521 on 18 April 2022
12 13 14 15 16 17 18 19 20	Crawley 2013 (chronic fatigue syndrome)	<ul> <li>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.</li> </ul>	No changes reported	2. Downloaded from http:/
20 21 22 23	Citation	Findings associated with code: Patients' social networks and positive experience of research	Changes planned before the full trial	
24 25 26 27	Van Den Berg 2017 (chest pain)	Participants positive experience was     sufficient to recommend participation in     clinical research to others.	No changes reported	bmjopen.bmj.com/ on
28 29 30 31 32 33 34 35 36 37 38 39	Thompson 2016 (haemodialysis patients)	<ul> <li>Patients' social networks in the unit were an effective means of disseminating information.</li> <li>Hearing other participants discuss their participation in the trial were effective means of promoting participation in the study.</li> </ul>	No changes reported	April 19, 2024 by guest. Protected by copyright.
40 41 42 43 44 45 46 47		For peer review only - http://bmjop	en.bmj.com/site/about/guidelines.xhtml	sy copyright.

## 1136/bmjopen-2021-05 S7: Barriers to retention Citation Findings associated with: Burden of follow-up Changes planned before the full trial Were the proposed changes clearly linked to questionnaires coded data? Gabbay 2017 With regard to feasibility and acceptability The study failed to reach its recruitment (Depression) of the outcome measures, it was apparent target and was terminated early during the that the number of outcome measures internal pilot phase, and, therefore, it did Downloaded fro (and their form and content) was not progress to main trial. 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. Hilton 2015 Repeating questionnaires at 6 months The need to complete and return Yes • (stress urinary when many women had few, if any, questionnaires even if there are few incontinence) symptoms to report was sometimes felt to symptoms was emphasized. be burdensome and irrelevant; this is in Modify questionnaires to allow 'short-April 19, 202. keeping with the number of blank followcutting' of irrelevant areas to reduce up questionnaires returned. respondent burden. A further possibility is to link questionnaire completion at follow-up to the face-to-face clinic review. Crawley 2013 The number of questionnaires used at Measures to improve outcome data collection Unclear ₫● (chronic fatigue follow-up was considered a burden by the using a variety of strategies, including telephone syndrome) opyright

e 97 of 106		BMJ Open	1136/hmiopon-20
	<ul> <li>majority of children and parents interviewed and observed.</li> <li>Parents felt the timing of questionnaires did not allow time for change, as they were too close together.</li> </ul>	follow-up, would need to be implemented in a full study.	0.000
Gray 2013 (male obesity)	Focus group participants found difficulties with some of the wording in the questionnaires.	assisting men with questionnaire completion if required (e.g., if participants have literacy	ti → Yes Download
McEachan 2016 (infant obesity)	Some of the measurement tools were found to be burdensome to complete.	<ul> <li>Maintaining regular contact with participants throughout follow-up.</li> <li>A future trial should ensure that a range of communication channels are used to maximise retention.</li> <li>Strike a balance between collecting valid and reliable data and overly burdening participants, which may lead to missing data, withdrawal or trial attrition.</li> </ul>	• Yes
Tsianakas 2016 (recurrent or metastatic cancer)	<ul> <li>All outcome measures were judged appropriate except the Scottish Physical Activity Questionnaire (SPAQ). Eight participants reported it was repetitive and difficult to complete.</li> </ul>	duration and frequency of physical activity in any future study are recommended.	1• Yes
Ellis 2016 (lung cancer)	<ul> <li>Patients and carers expressed some discontent with the questionnaires and this was seen as a potential barrier to retention.</li> </ul>	The number of questionnaires to be used in the subsequent trial will be decreased.	Po Yes
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		BMJ Open	1136/bmjopen
Kendrick 2017 (depression)	<ul> <li>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.</li> <li>Two patients pointed out that they thought that the patient questionnaire was intrusive.</li> </ul>	<ul> <li>No specific changes reported to address these barriers.</li> </ul>	pen-20 <u>21-055521 on 18 April 2022. Downlo</u> s
Myall 2015 (cancer-related fatigue)	<ul> <li>Few participants found the questionnaires at 3-time points burdensome.</li> <li>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.</li> <li>Several participants considered the psychological aspect of cancer was missing and should be included in the questionnaires.</li> <li>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.</li> </ul>	• 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.	ded from http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected by

Page 99 of 106		BMJ Open	.1136/bmjopen
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3 4 5 <b>Citation</b> 6 7 8	Findings associated with: Practical barriers	Changes planned before the full trial	Were the proposed changes clearly linked to
9 10 11 (infant obesity) 12 13 14 15 16	<ul> <li>One issue for both participants and facilitators was setting up the groups in a convenient location.</li> <li>Some participants reported making journeys that required considerable effort</li> </ul>	<ul> <li>No specific changes reported to address these barriers.</li> </ul>	April 2022. Downloade
17       Kendrick 2017         18       (depression)         19       20         20       21         22       23         24       24	• 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.	<ul> <li>Patients should be reassured that participation in the trial should cause the patient the least amount of inconvenience, especially in terms of travel necessities.</li> </ul>	a ToUnclear B <u>Pttp://bppjopen bmjopen bmj.</u>
25         26         27         28         29         30         31         32         33         34         35         36         37         38         39         40         41         42         43		ny Ny	com/ on April 19, 2024 by guest. Protected by copyright.

		ВМЈ Ор	en		1136/bmjopen-2021-05	Page 100 of 1
S8: CERQual Evidence	Profile_ Recruitm	ent barriers			2021-0	
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 t evidence	5521 on <b>2</b> 8 April 2022.	Explanation of CERQual assessment
<ul> <li>1- Changes planned before the full trial to address issues with randomisation</li> <li>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.</li> </ul>	(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	Dowhloaded from http://bmjopen.bmj.com/ on April 19, 2024 by	6 studies with moderate concerns about adequacy and coherence. No or very minor concerns about methodological limitations and relevance.
<ul> <li>2- Changes planned before the full trial to address issues with clinical equipoise:</li> <li>Changes included feedback sessions to make recruiters aware of instances where they inadvertently used loaded terminology, providing frequent training to recruiters and to</li> </ul>	(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)		April 19, 2024 by guest. Protected by copyright.	12 studies with moderate concerns about coherence. No or minor concerns about methodological limitations, adequacy and relevance.

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of 106		BMJ Op	pen		136/bm	
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present treatment options in a balanced way.					1136/bmjopen-2021-055521 on 18 April	
<ul> <li>3- Changes planned before the full trial to address issues with patient treatment preferences:</li> <li>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.</li> </ul>	(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	2022. Downloaded from http://bmjopen.bmj.com	9 studies with moderate concerns about adequacy an coherence. No or minor concerns about methodological limitations and relevance.
<ul> <li>Changes planned before the full trial to address issues related to the control group:</li> <li>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</li> </ul>	(3,6,16,19)	No or very minor concerns about adequacy	No or very minor concerns about coherence	High confider	on April 19, 2024 by guest. Protected by copyright.	4 studies with no or very minor concerns about methodological limitations, coherence, adequacy and relevance.

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				-	omiopen-2	
renamed 'active monitoring' and suggestions for augmenting the content of the control arm so the two arms were perceived as more equitable.	~0r.			High confidence	36/bmiopen-2021-055521 on 18 April 2022. Download	
Changes planned before the full trial to address issues around the eligibility criteria:	(12,13,17,18,20,21)	No or very minor concerns about adequacy	No or very minor concerns about coherence	High confidence	ed from http:	6 studies with no or very minor concerns about methodological limitations,
<ul> <li>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.</li> </ul>			Lien of	VL.	m http://bmiopen.bmi.com/ on April 19. 2024	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)	confidence	by quest. Protected by convright.	12 studies with moderate concerns about adequacy and coherence. No or very minor concerns about methodological limitations and relevance.

3 of 106		ВМЈ Ор	en	136/bn	
				njopen-z	
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	(12,15,19,30)	Moderate concerns about adequacy	Moderate concerns about coherence (one	Moderate confidence	
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.		(one study reported no changes to address these barriers)	study with well- grounded changes and 3 studies with unclearly-linked changes)	Moderate Compared to an and the confidence moderate confidence moderate to an and the compared to an	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 High confidence by guest. Protected by copyright.	8 studies with minor concerns about adequacy and coherence. No or very minor concerns about methodological limitations and relevance.

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				njopen-20	
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.	<i>K</i> on			2021-055521 on 18 April 2022. Dowr	
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	(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)	.1136/bmjopen-2021-055521 on 18 April 2022. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by High confidence	10 studies with moderate concerns about adequacy. Minor or very minor concerns about methodological limitations, coherence and relevance.
participant and removing all mention of providing smoking cessation information and advice from the Patient information leaflets" to avoid smoking stigma.				guest. Prote	
				cted by copyright	

Page 105 of 106			BMJ Op	.1136/bm	
1 2					jopen-20
3	Changes planned before the full	(7-9,18)	No or very concerns	Minor concerns about	High confidence
4 5	trial to address barriers related to		about adequacy	coherence (3 studies	055
6	Integration of the trial into			with well-grounded	521
7	clinical practice:			changes and one study	On On

	(, ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	No of very concerns			i studies with no of finitor
trial to address barriers related to		about adequacy	coherence (3 studies	555	concerns about
Integration of the trial into			with well-grounded	21 0	methodological limitations,
clinical practice:			changes and one study	on 1	coherence, adequacy and
Changes reported were the need			with unclearly linked	8 A	relevance.
to mention the study in the			changes)	pril	
opening statements of the surgical				202	
consultations, express enthusiasm				N.	
for the study, delivery of a slick				Dow	
and easy-to-implement				nloa	
recruitment process to be the				adec	
least disruptive to routine clinical				d fro	
practice, ensure that trial				m T	
participants will be referred to the				nttp:	
respective specialists after				//bm	
randomization rather than before				ŋjop	
to ensure consistency of				en.t	
information, and providing				, Din Alexandre Ale	
frequent training to recruiters.				055521 on 18 April 2022. Downloaded from http://bmjopen.bmj.com/	
Changes planned before the full	(8,22)	No or very concerns	No or very concerns	High confidence by cc	2 studies with no or very
trial to address barriers related to	(-//	about adequacy	about coherence	pril	minor concerns about
Confidence about approaching		,		19,	methodological limitations,
patients:				20)	coherence, adequacy and
				24 b	relevance.
Modifying the support to teams in				J Si Si	
other centers according to their				Juest	
research experience and the need				קי	
for training to educate primary				otec	
care staff to broach the topic of a				ted	
visible difference confidently,				b d	
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4 studies with no or minor

	BMJ Open					113 36) Page 106 of 1	
					njopen-2(		
both within and outside the					021-		
parameters of research.					1136/bmjopen-2021-055521 on 18 April 2022.		
Changes planned before the full	(4,29)	Moderate concerns	Moderate concerns	Moderate	18 April 2	2 studies with moderate	
trial to address barriers related to	(1)=3)	about adequacy	about coherence (only	confidence	2022	concerns about adequacy and	
assiduousness and commitment		(one study reported		connucince		coherence. No or very minor	
of recruiters:		no changes to	grounded changes)		owr	concerns about	
		address these	8		lload	methodological limitations	
Clinical centers were asked to		barriers)			ded	and relevance.	
identify two Lead Recruiters (LRs)					fron		
per site whose responsibilities					n ht		
would be to act as the focus for					tp://		
SPARE recruitment activity.					Downloaded from http://bmjcpen.bmj.com/ on April 19, 2024 by		
Changes planned before the full	(11,19)	Minor concerns	Moderate concerns	Moderate	per	2 studies with moderate	
trial to address issues around the		about adequacy	about coherence (one	confidence	ı.bm	concerns about coherence.	
invitation to participate:			study with well-		nj. co	No or very minor concerns	
Changes included sending postal			grounded changes)		m/	about methodological	
invitation letter with a summary					∧ nc	limitations, adequacy, and	
of the main points at the front of				5	vpril	relevance.	
the PIL; and, where necessary or					19,		
appropriate invitation during					202		
consultation with GP/Practice					.4 b		
Nurse, placing posters in GP							
waiting rooms and finding ways of					lest.		
enabling psychological wellbeing					Pro		
practioners' to engage with study					otect		
procedures.					ted t		
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of 106		BMJ O	pen	.1136/bmjopen-2021-055521 CERQual	
S9: CERQual Evidence Profi	le_ Retention	barriers		oen-2021-0	
Summary of review finding	Studies contributing to the review finding.	Adequacy	coherence	CERQual 52 assessment of on 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 2022. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by	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

Journal:	BMJ Open
Manuscript ID	bmjopen-2021-055521.R1
Article Type:	Original research
Date Submitted by the Author:	15-Mar-2022
Complete List of Authors:	Elfeky, Adel; University of Warwick, Warwick Medical School; University of Aberdeen, Health Services Research Unit Treweek, Shaun; University of Aberdeen, Health Services Research Unit Hannes, Karin; KU Leuven, Research Group SoMeTHin'K, Faculty of Social Sciences Bruhn, Hanne; University of Aberdeen, Health Services Research Unit Fraser, Cynthia; University of Aberdeen, Health Services Research Unit Gillies, Katie; University of Aberdeen, Health Services Research Unit
<b>Primary Subject Heading</b> :	Health services research
Secondary Subject Heading:	Qualitative research
Keywords:	QUALITATIVE RESEARCH, Clinical trials < THERAPEUTICS, STATISTICS & RESEARCH METHODS





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1	Using qualitative methods in pilot and feasibility trials to
2	inform recruitment and retention processes in full-scale
3	randomised trials: a qualitative evidence synthesis
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10	
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**BMJ** Open

# 12 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 21 data extraction form that captured study aims, design, methodological approach, and main 22 findings, including barriers and facilitators to recruitment and or retention. The synthesis was 23 undertaken using Thomas and Harden's thematic synthesis method and reported following the 24 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. 

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33 **Conclusions** Many trial teams do pre-trial gualitative work with the aim of improving recruitment 34 and retention in future full-scale trials. Just over half of all reports of such work do not clearly 35 show how their findings will change the recruitment and retention strategy of the future trial. The

36 scope of pre-trial work needs to expand beyond looking for problems and also look for what

- 37 might help and spend more time on retention.
- 38 Strengths and limitations of this study
  - 39 Our comprehensive search strategy optimises the likelihood that we have identified relevant 40 studies published in the time period in principal journals.
- 41 Although we did not apply a quality assessment checklist to individual included studies to 42 consider the relationship between quality and maximising the value of pre-trial qualitative 43 research, the systematic methodology and the use of GRADE-CERQual assessment of 44 confidence in the findings is a strength of the review.
- 45 The review was based on what was written in published research and this may not reflect 46 the breadth of qualitative research that is undertaken in practice.
- 47 Most of the included studies were UK-based, that means it is uncertain whether and to what 48 extent the findings apply to the trial environment outside the UK.

# 53 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 

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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 gualitative 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 gualitative data to inform the design and feasibility of a larger trial also highlighted that gualitative 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%).

96 The aim of this qualitative evidence synthesis (QES) was to explore how pre-trial qualitative
97 research with trial participants, recruiters, clinicians, chief investigators and trial managers was
98 used to inform recruitment and retention processes in full-scale randomised trials.

99 Understanding how existing studies have employed qualitative methods at the pre-trial stage to100 inform recruitment and retention in future full-scale trials has the potential to identify how the

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3 4	101	value of pre-trial work could be maximised and highlight key aspects for others to focus on when		
5 6 7	102	considering this type of work.		
8 9 10	103	Methods		
11 12	104	This systematic evidence synthesis is reported in accordance with the Enhancing Transparency		
13 14 15	105	in Reporting the Synthesis of Qualitative Research (ENTREQ) statement (23). The protocol was		
16 17	106	developed but was considered outside of scope by PROSPERO as it does not address health		
17 18 19 20	107	outcomes.		
21 22 23	108	Search strategy		
24 25	109	Searches were conducted on key electronic databases from inception to 4 March 2018:		
26 27 28	110	Dissertation Abstracts International, CINAHL, Embase, MEDLINE, Sociological Abstracts,		
29 30	111	Psycinfo, SSCI (Social Science Citation Index), the Cochrane Library and Health Technology		
31 32	112	Assessment. There were no language, date or geographic restrictions. The MEDLINE search		
32 33 34 35 36 37 38 39	113	strategy is included in supplementary document 1.		
	114	Different search strategies were used alongside electronic databases as using multiple search		
	115	methods is more likely to locate relevant qualitative studies than relying solely on bibliographic		
40 41	116	databases (24). Methods applied included following up reference lists, hand searching and		
42 43 44 45	117	contacting experts or authors.		
46 47 48	118	Inclusion/Exclusion criteria		
49 50 51	119	Types of studies		
52 53	120	We included all primary qualitative studies embedded in health-related feasibility or pilot studies.		
54 55	121	We also included studies using mixed methods if a clearly identifiable qualitative component		
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59 60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml		

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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

125 poor recruitment were also included.

## 126 Participants

127 All studies focusing on the perceptions and experiences of trial participants (e.g., patients,

128 carers, or parents) who took part in a healthcare related pilot or feasibility RCT were included.

129 We also included studies reporting on the perceptions of stakeholders directly or indirectly

130 involved in recruiting or retaining participants to RCTs (including chief investigators, trial

131 managers, clinicians, research nurses, funders and research ethics committees).

## 132 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.

## 137 Evaluation

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

## 140 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 gualitative 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.

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## 7 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

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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 guotes 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 gualitative findings were linked to any proposed changes to the recruitment and retention plan of action for subsequent full-scale trials.

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## 184 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.

95 For CERQuaL assessment, we had no concerns regarding methodological limitations and 96 relevance for the body of data contributing to each review finding. Our goal was not to judge 97 whether some absolute standard of methodological quality had been achieved, but rather to 98 indicate how and if findings from the gualitative research were transformed into an action plan to 99 inform recruitment or retention processes for the full-scale trial. Considering that, a specific 0 methodological quality checklist was deemed unnecessary as high or low scores would not 1 affect our confidence in how and if qualitative findings informed the design of a subsequent full-)2 scale trial. For the sake of brevity these two components were not included in the CERQual 3 evidence profile.

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## 204 Patient and public involvement statement

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

## **Results**

208 Thirty-five studies (connected to 31 feasibility studies) met the pre-specified inclusion criteria

209 and were included in this QES. For some feasibility studies, there was more than one paper

210 reporting findings from qualitative investigations. We included all relevant studies for

211 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.

## 214 Characteristics of the included studies

All the included studies were published in English (19, 28-61) and were conducted in three highincome 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.

Page 13 of 111

2		
2 3 4	224	The setting of the feasibility studies in which the qualitative research was embedded included a
5 6	225	range of clinical contexts such as; cancer (n=11), mental health (n=5), obesity (n=3), sexual and
7 8	226	reproductive health (n=3), chronic fatigue (n=2), musculoskeletal conditions (n=2), pain (n=2),
9 10	227	incontinence (n=2), tooth decay (n=1), childhood intermittent exotropia (n=1), renal disease
11 12	228	(n=1), non-adherence to medications (n=1) and appearance-related distress (n=1). As
13 14	229	expected, the clinical context differed as did the interventions under investigation; two studies
15 16	230	(28, 38) were Clinical Trials of an Investigational Medicinal Product (CTIMP) and 29 were non-
17 18 19	231	CTIMP studies. These interventions were also broadly categorised as: surgical (n = 6) and non-
20 21	232	surgical (n=25).
22 23	000	
24	233	All the included studies were embedded in pilot or feasibility trials to inform design aspects in
25 26	234	preparation for a subsequent full-scale trial. The main data collection and analysis methods
27 28	235	used were interviews (n = 31; 88%) and thematic analysis (n = 25; 71%). Audio recording of
29 30	236	recruitment consultations and non-participant observations of consultations were used in six of
31 32	237	the included studies (31, 45, 46, 50, 54, 55).
33 34		
35 36	238	Findings
37 38	000	
38 39	239	Twelve themes were identified as recruitment barriers and three as recruitment facilitators,
38 39 40 41	239 240	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
38 39 40 41 42 43		
38 39 40 41 42 43 44 45	240	whereas only two themes were identified as barriers for retention and none as retention
38 39 40 41 42 43 44 45 46 47	240 241	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
38 39 40 41 42 43 44 45 46 47 48 49	240 241 242	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
38 39 40 41 42 43 44 45 46 47 48 49 50 51	240 241 242 243	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
38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53	240 241 242 243 244	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
38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55	240 241 242 243 244	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
38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57	240 241 242 243 244	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
38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56	240 241 242 243 244	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).

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3 4	246	The findings that led to the identification of the barriers and facilitators highlighted in Table 1 and
5 6	247	their link to the proposed changes for the full-scale trial are presented below in more detail.
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Table 1 Summary of findings for themes linked to recruitment and retention barriers and
 facilitators.

	Barriers	Facilitators
Recruitment	<ol> <li>Lack of clarity or understanding of randomisation</li> </ol>	<ol> <li>Personal gain and makin difference</li> </ol>
-	2- Lack of clinical equipoise	2- Communicating study information
-	3- Strong patient treatment preferences	<ol> <li>Social networks and experience of research</li> </ol>
-	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	2
	10- Mismatch between the trial protocol and clinical care pathways	0
-	11- Participation burden	
	12- Lack of confidence in approaching study participants	
Retention	1- Burden of follow-up questionnaires	None identified
	2- Practical barriers	

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# 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.

## 257 Participant level factors

1. Lack of clarity or understanding of randomisation

260 Six studies (19, 52, 54, 55, 57, 60) outlined the influence of randomisation as a major barrier to

261 recruitment. Trial participants believed the concept of randomisation was often not clear or

262 perceived haphazardly and some struggled to understand the need for randomisation (19, 52).

263 Despite explaining random allocation, some participants were still uncertain whether they would

be selected based on some personal or illness characteristics (19, 60).

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

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

268 The changes planned before the full trial to deal with issues around clarity of the randomisation

269 process were clearly linked to coded data in three of the six studies (19, 54, 55). To clarify the

270 concept of randomisation, one study reported that randomisation will be explained to

271 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,

274 randomisation period was simplified and clarified and recruiters were encouraged to elicit

Page 17 of 111

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75 patients' lay views and explain that randomisation offered a way of resolving the dilemma of 76 treatment choice (54, 55).

77 Two studies reported changes that were not explicitly linked to the qualitative findings (52, 60). 78 In one study, authors suggested that the focus would be on training trialists who are involved in 79 recruitment to complicated trials, both in terms of communication processes and on the 80 assimilation of complex trial pathways (52). To resolve misunderstanding about the process of 281 random allocation, one study reported that the study team needs to spend more time at 82 participating practices training them in the recruitment process; patients should be supported to 83 take the necessary time to ensure understanding of patient information sheets before signing 84 consent (60). In one study, no changes to address the lack of understanding of randomisation 85 were reported (57).

86 2. Strong patient treatment preferences

87 Patient treatment preferences was a theme in nine studies (29, 31, 32, 35, 45, 49, 54, 55, 57). 88 Recruitment was hampered by strong preferences with patients often wanting the intervention 89 and then expressing disappointment at being allocated to the control group (29, 31, 32, 35, 49, 90 54, 57).

291 Recruiters' perception of unequal treatment processes was also common, and they believed 92 that many patients opted for one treatment because it was perceived as more convenient (45). 93 In two studies (45, 54), recruiters assumed that patients came with media information that was 94 biased in favour of the intervention (radical treatment) and often expressed lay views that 95 cancer should be surgically removed.

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trial

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"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

03 The changes proposed before the full trial to address patient treatment preferences were clearly 04 linked to gualitative data in four studies (31, 32, 45, 49). Changes reported were: recruiters were 05 asked to move beyond initial probing questions in relation to patient preferences toward 06 rectifying any erroneous views and to ask patients who appear to have a preference to 'keep an 07 open mind' until they had heard all the relevant information (31), the need to gently challenge 80 preferences that are based on inaccurate information and training recruiters to enable them to 09 explain the need for randomisation and the rationale for the RCT to patients (45) and the 10 incorporation of a preference arm in a future trial to account for parental preferences (49). 11 In five studies, no specific changes were reported to account for strong patient treatment 12 preferences (29, 35, 54, 55, 57).

### 313 **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

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3 4	320	caused difficulties for both patients and recruiters with the potential for interpretation as 'no
5 6	321	treatment' (54).
7 8	322	
9 10	323	"Participant: Aye. If I was one of the 50% when they said, "Right, we're gonna take a
11 12	324	sample from you and test it", then yeh, but if I was one of the 50% that didn't get picked
13 14 15	325	(the control group), then no. I would rather not know, actually. No." (Patient) (19)
16 17 18 19	326	Link between control group findings and changes proposed for the full-scale trial
20 21	327	The changes proposed before the full trial to address the issues related to the control group
22 23	328	were clearly linked to qualitative data in all four studies (19, 29, 54). The changes reported
24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40	329	were: modification of the Participant Information Leaflet (PIL) where the control group will be
	330	changed to non-test group, which is what participants were most comfortable with (19), giving
	331	participants the necessary time to ensure understanding of patient information sheets before
	332	signing consent, especially with regard to clinical equipoise and that they will not necessarily
	333	benefit from participation (60) and augmenting the content of the control arm so that the trial
	334	arms could be perceived as more equitable (29).
	335 336	4. Participation burden
40 41 42	337	The burden imposed by participation in the trial was a prominent theme in four studies (19, 38,
43 44	338	49, 52). The experience of completing and signing a consent form at the time of enrolment was
45 46	339	burdensome in one study (38). In two studies, limited appointment time for the initial screening
47 48	340	and the need for flexible appointments presented a challenge for participants to fully consider
49 50	341	participation in the trial (19, 49). In the study by Moynihan (2012), patients commented on how
51 52	342	poor administration and the need to 'work' their way around NHS waiting times prevented them
53 54 55	343	from being fully included in the trial enterprise (52).
56 57		18

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2 3 4	344	"Well, your appointments would have to be flexible, because people are still working.
5	345	Not myself, I'm retired, but there are always people working who might not be able to get
7 8	346	time off work" (Patient) (19)
9 10 11 12	347	Link between participation burden findings and changes proposed for the full-scale trial
13 14	348	The changes proposed before the full trial to account for participation burden were not clearly
15 16	349	linked to qualitative data in three studies (19, 49, 52). The changes proposed included
17 18	350	facilitating a context in which patients feel fully included in the trial enterprise (52), separation of
19 20	351	the role of the treating clinician from the main recruiter to the trial (49) and providing a phone
21 22 23	352	call to potential participants to discuss the study after anticipated receipt of the full PIL (19).
23 24 25	050	In one study, as exactly a character way presented to address this harrian (20)
26 27	353	In one study, no specific changes were reported to address this barrier (38).
28 29	354	5. Beliefs and expectations about trial participation
30 31	355 356	Pre-existing beliefs and expectations amongst study participants hindered recruitment efforts in
32 33	357	ten studies (19, 30, 33, 36, 39, 42, 45, 52, 59, 60).
34 35	358	Participants' beliefs that undermined involvement in the trial process were: feelings of anxiety
36 37	359	about a poor medical outcome and scepticism about being experimented on (36, 60), negative
38 39 40	360	image about the hospital 'a place to die' (45), social desirability perception that the trial was
40 41 42	361	designed to encourage people to stop smoking (19, 60), feelings of isolation and powerlessness
43 44	362	(52) and a sense of denial (participants tended to deny their symptoms and therefore were
45 46	363	ineligible) (59). In other cases, nurses believed they needed to protect patients from additional
47 48	364	burden (which implicitly they believed the trial would cause) and this was cited as a main
49 50	365	recruitment barrier (30).
51 52	366	
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368	"You've got to explain everything and they don't want to go to X hospital because they think
369	once they go to-that's where the oncology centre is -so they think when they go there, they
370	die, because that's where you go to die' (Recruiter).(45)
371	Link between beliefs and expectations findings and changes proposed for the full-scale
372	trial
373	The changes proposed before the full trial to address pre-existing beliefs and expectations were
374	clearly linked to qualitative data in six studies (19, 33, 36, 39, 42, 60). The changes proposed
375	included asking recruiters to gently challenge patients' preconceptions (42) and to wait until the
376	patient's condition is more settled before providing appropriate written informed consent (36).
377	One study reported changes which were not explicitly linked to coded data (52). In three
378	studies, no specific changes were planned to address these issues (30, 45, 59).
379	
380	Clinician/recruiter factors
381	6. Lack of clinical equipoise
382	Twelve studies outlined the influence of lack of clinical equipoise as a major barrier to
383	recruitment (29, 31, 32, 35, 42, 45, 48-50, 52, 54, 55). Recruiters and clinical staff found it
384	difficult to maintain equipoise as interviews revealed treatment preferences for certain
385	subgroups of patients and this affected not only the number of individuals approached and
386	invited but also the number of randomised participants (31, 35, 42, 45, 48). In many cases the
387	explanation of the lack of evidence underlying the effectiveness and timing of intervention
388	served to undermine the participant's confidence in the treating clinician, and by extension, the
389	trial (32, 49).
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	<ul> <li>369</li> <li>370</li> <li>371</li> <li>372</li> <li>373</li> <li>374</li> <li>375</li> <li>376</li> <li>377</li> <li>378</li> <li>379</li> <li>380</li> <li>381</li> <li>382</li> <li>383</li> <li>384</li> <li>385</li> <li>386</li> <li>387</li> <li>388</li> </ul>

Page 22 of 111

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1 2		
2 3 4	390	Audio recording of recruitment consultations revealed that the terminology used by recruiters
5 6 7 8	391	created unbalanced presentations of treatment options for which one treatment was presented
	392	at greater length and more favourably than the other and this was a strong indicator for the lack
9 10	393	of trial equipoise (31, 32, 45, 50, 54, 55).
11 12 13 14	394	
	395	"I share the concerns and doubts that many of the patients do, i.e. that it won't work and
15 16	396	it's difficult to sell a treatment when you yourself don't really believe it's going to make
17 18 19	397	any difference" (Principal investigator) (32)
20 21 22 23 24	398	Link between clinical equipoise findings and changes proposed for the full-scale trial
	000	
25	399	Changes planned before the full trial to maintain clinical equipoise were explicitly linked to
26 27	400	qualitative data in six studies (29, 31, 42, 45, 49, 54). Changes reported were: Feedback
28 29	401	sessions to be used to make recruiters aware of instances where they inadvertently used
30 31	402	loaded terminology (31), asking recruiters to gently challenge and acknowledge their own bias
32 33	403	in device preference (42), highlighting the need for principal investigators and recruiters to think
34 35	404	more critically about the concept of scientific equipoise and how that should underpin the RCT
36 37 28	405	(45), separation of the role of the treating clinician from the main recruiter to the trial (49),
38 39 40	406	changing the order in which the treatments were presented and to describe their respective
40 41 42	407	advantages and disadvantages in equivalent detail (54), training and monitoring of trial
43 44	408	personnel to ensure notions of equipoise are delivered and reinforced consistently (29).
45 46 47	409	Three studies suggested changes to maintain clinical equipoise but were not clearly linked to
48 49	410	qualitative data (32, 48, 52). These changes involved providing frequent and comprehensive
50 51	411	training to recruiters (36,39) and finding ways of enabling practitioners to engage with study
52 53	412	procedures (41). In three studies, no specific changes to maintain clinical equipoise were
54 55 56	413	reported (35, 50, 55).
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### 7. Communicating study information and associated terminology

415 Presentation of trial information was a major barrier to recruitment and this was evident in eight 416 studies (32, 34, 50, 52-55, 59). In many cases, patients failed to understand the language of trial 417 procedures or interpreted trial and clinical terminology guite differently than as intended by 418 practitioners (for example, 'trial' was interpreted as 'try and see') (31, 52, 54). In other cases, 419 recruiters and investigators agreed that the trial was difficult to explain and indicated that they 420 found the quantity and content of trial information problematic (31, 53). There were also cases 421 where study documentation was perceived as long, difficult to understand or repetitive in places 422 and this affected decision making (34, 50). In the study by Griffin (2016), graphic description of 423 surgery was thought to have put patients off randomisation and surgeons tended to go beyond 424 their protocol brief, to explain the trial rather than referring patients on to the trial recruiter for 425 this information (32).

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

## 429 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).

1 2		
2 3 4	437	Two studies suggested changes to improve trial presentation but were not clearly linked to
5 6	438	qualitative data (32, 52). These changes involved providing frequent and comprehensive
7 8	439	training to recruiters on the assimilation of complex trial pathways (32, 52). In one study, no
9 10	440	specific changes were reported to address this barrier (53).
11 12 13 14	441 442	8. Issues around the eligibility criteria
15 16 17	443	Another recurring theme that hampered recruitment efforts was the complexity trial staff faced in
17 18 19	444	applying the eligibility criteria, which appeared in six studies (35, 41, 45, 49, 55, 59). In some
20 21	445	cases, interpretation of the eligibility criteria differed between centres; there was less clarity over
22 23	446	the minimum age for recruiting participants to the study and recruiters thought there was leeway
24 25	447	for interpretation of the inclusion/exclusion criteria in partnership with the trial team (35, 41, 45,
26 27	448	55). In other cases, highly restrictive eligibility criteria and the difficulty to confirm eligibility for
28 29 30	449	the trial at the initial screening visits hindered recruitment efforts (49, 59).
31 32	450	"I personally don't have a problem (with applying the eligibility criteria), but that's
33 34	451	because I deal with trials all the time (), but I think with some of my colleagues, both
35 36 27	452	juniors within oncology and colleagues in surgery are not as familiar with trials, maybe
37 38 39 40	453	have a little more difficulty in interpretation" (Recruiter). (55)
40 41 42 43	454	Link between eligibility findings and changes proposed for the full-scale trial
43 44 45	455	The changes proposed before the full trial to address the problems related the complexity of
46 47	456	applying the eligibility criteria were clearly linked to qualitative data in four studies (35, 41, 45,
48 49	457	49). The changes reported were: running screening training exercises to ensure similar
50 51	458	screening standards and practices and an 'assumed eligibility' approach in all centres (35),
52 53 54	459	close examination and regular meetings to discuss and resolve evolving issues (45) and
55 56 57		23
58 59		
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1 2		
2 3 4	460	considering a limit on the upper age at which participants would be included (49). Two studies
5 6	461	reported no changes to address this issue (55, 59).
7 8 9 10	462 463	9. Commitment to the trial
11 12	464	Variable staff commitment to the trial was a major barrier to recruitment in two studies (30, 55).
13 14	465	Recruiters believed that some trial members were very committed to the trial but others were
15 16	466	less dedicated or even antagonistic to it, and this contributed to the development of strong
17 18	467	patient treatment preferences to one arm or the other (55). In other cases, recruitment of fewer
19 20 21	468	than anticipated dyads affected nurses' commitment and the priority given to the trial (30).
22		
23 24	469	"when we were doing the training it's just right there. And then it slips to tenth place.
25 26	470	And if you haven't recruited, it's twentieth place because you're doing this, this and this"
27 28	471	(Recruiter) (30).
29 30 31 32	472	Link between staff commitment findings and changes proposed for the full-scale trial
33 34	473	The changes proposed before the full trial to address variable commitment by both participants
35 36	474	and staff were clearly linked to qualitative data in one study (55) where clinical centres were
37 38	475	asked to identify two Lead Recruiters (LRs) per site whose responsibilities would be to act as
39 40	476	the focus for trial recruitment activity. The remaining study reported no changes to account for
41 42	477	this barrier (30).
43 44		
45 46 47	478 479	10. Lack of confidence in approaching study participants
48 49	480	Lack of confidence in approaching study participants or the topic of interest hindered
50 51	481	recruitment in two studies (32, 33). In one study (32), time lag between recruitment clinics posed
52 53	482	a challenge for research staff to preserve confidence and knowledge about the study. Research
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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).

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

488 Link between 'lack of confidence in approaching participants' findings and changes
489 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.

498 Contextual/situational factors

## **11. Practical barriers**

500 Practical barriers to recruitment was a major recurring theme in twelve studies (30, 32-34, 37-

50139, 43, 48, 49, 53, 59). Commonly cited barriers were: difficulty in implementing procedures

502 owing to the multi-centre nature of the pilot (32), barriers of the primary care environment (33,

503 37) (time-limited consultations, high workload and competing studies), widespread reluctance in

1 2		
2 3 4	504	practice to forgo written consent procedures at the time of trial enrolment (62), staffing issues
5 6	505	(staff attrition, insufficient time, sub-optimal use of skill-mix) (30, 39, 43, 48) and delay in
7 8 9	506	recruitment appointments (49).
10 11	507	"I then had a full caseload, so I wasn't taking on any new patients for quite a long time.
12 13	508	[] We've had the consultants doing first visits and I would follow on afterwards
14 15 16	509	because we've been so short staffed' (Recruiter) (30)
17 18 19	510	Link between practical barriers findings and changes proposed for the full-scale trial
20 21 22	511	The changes proposed before the full trial to address practical barriers were clearly linked to
22 23 24	512	qualitative data in five studies (34, 38, 39, 53, 59). The proposed changes included allowing
25 26	513	flexibility in terms of how and when the research was conducted (34), ensuring that future trial
27 28	514	centres are allocated adequate time and personnel (39), advising practitioners that patients will
29 30 31	515	require longer appointments than normal for involvement in the trial (53).
32 33	516	Four studies reported changes to address this barrier but these were not clearly linked to
34 35	517	qualitative data (32, 43, 48, 49). In three studies, no changes to address practical barriers were
36 37 38	518	reported (30, 33, 37).
39 40 41 42	519 520	12. Mismatch between the trial protocol and clinical care pathways
42 43 44	521	Integrating the trial into clinical practice was considered a particular challenge hindering
45 46	522	recruitment in four studies (31, 32, 42, 55). In some cases, the trial was presented as an 'add-
47 48	523	on' rather than an integral part of existing clinical services (31, 32). In other cases, the pathway
49 50	524	that potential participants had to follow from diagnosis to being recruited to the trial proved
51 52 53 54	525	extremely complex (55).
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"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). N.C.

#### 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).

1 2		
3 4	549	"I know that's sort of a I´ thing to say, but it's true, I mean I'm not try', for sympathy,
5 6	550	but I have had a terrible time, and I don't want other people to have it like, if you know, if
7 8	551	I have children I wouldn't want them to have go through that I went through, and um, in
9 10	552	generally I just, you know, want to take part in it for other people"(Patient) (44)
11 12 13 14 15 16 17 18 19	553	Link between altruism findings and changes proposed for the full-scale trial
	554	No changes were reported in the five studies to take advantage of the conditional altruism
	555	expressed by participants and its potential impact on recruitment before the full-scale trial starts.
20 21	556	2 Communicating study information
21 22 23	557	2. Communicating study information
24 25	558	Providing clear and informative study information to potential participants was an important
26 27	559	facilitator for recruitment in six studies (34-36, 44, 46, 50). In many cases, providing clear and
28 29	560	informative study information and ensuring study participants had a thorough understanding of
30 31	561	the study were important factors to facilitate a decision about taking part (34-36, 44, 50)
32 33	562	(34,47,50,61,62). In the study by Realpe, a logical sequence for information sharing (six step
34 35	563	recruitment model) emerged after analysis of recruitment consultations and this seemed to
36 37 38	564	facilitate recruitment (46).
39 40	565	"So everything was really well explained you know, so yeah I mean I can't fault it really,
40 41 42	566	no I was well impressed with it all" (Patient) (35)
43 44	567	Link between information communication findings and changes proposed for the full-
45 46	568	scale trial
47 48		
49 50	569	The changes planned before the full-scale to take advantage of providing clear study
51 52	570	information were reported in only one study (46). The study proposed a six-step recruitment
53 54 55	571	model (specifying: explain the condition, reassure patients about receiving treatment, establish
56 57		20
58 59		28
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3 4	572	uncertainty, explain the study purpose, give a balanced view of treatments, and explain study
5 6	573	procedures) to train and support recruiters in the large number of new centers in the full-scale
7 8 9	574	trial.
10 11	575	3. Social networks and experience of research
12 13	576	Patients' social networks and positive experience of research helped to promote study
14 15	577	participation in two studies (36, 40).
16 17	578	"So, I think because a lot of them are friends here, so they talk, and, you know, if you're
18 19 20	579	doing that, "What do you think about it?" So, they ask each otherCause a lot of things
20 21 22	580	happen that way here, cause they listen to what other patients talk to nurses about, then
23 24 25	581	they think, "Oh, okay, I'll try that, too" (patient) (40)
25 26 27	582	Link between networks and experiences findings and changes proposed for the full-scale
28 29 30	583	trial
31 32	584	No changes were reported in the two studies that identified social networks as influential for
33 34 35	585	recruitment before the full-scale trial starts.
36 37 38	586	
39 40 41 42	587	Barriers to retention
43 44	588	Two retention barriers were identified. Supplementary document 6 outlines the findings
45 46 47	589	associated with each theme and their link to the proposed changes for the full-scale trial.
48 49 50	590 591	1. Burden of follow-up questionnaires
51 52	592	Nine studies outlined that the burden of follow-up questionnaires was a major barrier to
53 54 55	593	retention (35, 37, 47, 50, 51, 57-60). Across a variety of contexts, questionnaire structure was
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Page 31 of 111

1 2		
2 3 4	594	perceived to be burdensome and this encompassed many forms: forced choice responses of
5 6	595	questionnaires which did not capture the reality of patients' experiences (37), lack of clarity and
7 8	596	difficulties with some of the wording in the questionnaires (51, 60), repetitive and difficult-to-
9 10	597	complete questionnaires (47, 58). In two studies, the timing of questionnaires was perceived to
11 12	598	be burdensome and irrelevant because it did not allow time for change when many patients had
13 14	599	few, if any symptoms to report (35, 50).
15 16 17	600	"I didn't understand a lot of the questions so she [researcher] was having to interpret
17 18 19	601	them and that probably it probably went longer than what it should have done"
20 21	602	(patient) (37)
22 23	603	Link between questionnaire burden findings and changes proposed for the full-scale trial
24 25	005	Link between questionnalle burden multigs and changes proposed for the full-scale that
26 27	604	The changes proposed before the full trial to address the burden of follow-up questionnaires
28 29	605	were clearly linked to qualitative data in five studies (35, 51, 57-59). The changes reported
30 31	606	involved modifying questionnaires to allow 'short-cutting' of irrelevant areas to reduce
32 33	607	respondent burden (35), reducing the number of questionnaires in the subsequent trial (59) and
34 35 36	608	training fieldworkers in assisting participants with questionnaire completion if required (51).
37 38	609	In two studies, changes reported were not clearly linked to coded data (47, 50). These involved
39 40 41	610	identifying measures to improve outcome data collection using a variety of strategies. Two
41 42 43	611	studies reported no changes to address this barrier (37, 60).
44 45	612	2. Practical barriers
46 47	613	Practical issues appeared to hinder participant retention in two studies (57, 60). Some
48 49	614	participants reported that making journeys to the site required considerable effort (57, 60). A
50 51	615	small minority of patients found the process of getting a chest X-ray difficult. Some
52 53		enter minority of patiente found the proceed of getting a cheet A ray amount come
54 55		
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3 4	616	participants had to pay for the parking costs and using public transport seemed to be too
5 6 7	617	problematic (60).
8 9 10	618	Link between practical barriers findings and changes proposed for the full-scale trial
11 12	619	One study reported changes to account for practical barriers but were not clearly linked to
13 14	620	qualitative data (60). The study reported that patients should be reassured that participation in
15 16	621	the trial should cause them the least amount of inconvenience. In one study, no changes to
17 18 19	622	address practical barriers were reported (57).
20 21 22 23	623	Facilitators for retention
24 25	624	There were no facilitators for retention reported in the included studies.
26 27 28	625	
29 30 31 32	626	GRADE-CERQual assessment
33 34	627	The CERQual Evidence profile is presented in supplementary documents 7 and 8 which
35 36	628	highlights each review finding along with its CERQual assessment.
37 38 39 40	629	Discussion
41 42 43	630	Embedded qualitative investigations to illuminate barriers to recruitment and retention prior to a
44 45	631	full-scale trial have increased in the last decade (20, 63). This systematic qualitative evidence
46 47	632	synthesis was based on findings from 35 studies. The review provides important insights on
48 49	633	how the findings of qualitative research methods at the pre-trial stage were used to inform
50 51	634	changes to the recruitment and retention plan of future full-scale trials.
52 53 54 55	635	
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Page 33 of 111

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636 The systematic synthesis identified an assortment of recruitment barriers (n=12) but only 637 identified two barriers to retention. There were only three facilitators for recruitment, and there 638 were no facilitators for retention. The findings of included studies tended to focus more on the 639 challenges to recruitment and retention rather than the facilitators. Perhaps researchers are 640 instinctively more interested in what is not working well (the barriers) and trying to make 641 changes to remove those barriers. However, it is also important for researchers to take 642 advantage of what facilitated recruitment and retention at the pre-trial stage and to ensure 'what 643 worked well' stays working well in the full-scale trial and that should be reflected in the reporting. 644 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 645 646 is hard to believe that there are no facilitators for retention in the included studies; perhaps 647 researchers were not looking for, or reporting, this.

648 The focus on recruitment may have meant that retention was overlooked, something that is in 649 line with findings from a qualitative interview study with stakeholders from five trials (64). The 650 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 651 652 retention practices and a wider recognition of the importance of retention from funding 653 organisations. A recent evidence synthesis of gualitative studies identified only 11 studies that 654 had explored any aspect of trial retention with participants who had not completed the trial until 655 the end (65). While it may be hard to re-engage with former participants to understand why trials 656 fail to retain them, the lack of knowledge about this issue is striking. To date, very few 657 interventions have been shown to improve retention in RCTs, with only moderate certainty 658 evidence available for the use of monetary incentives with a prompts or reminder to improve 659 responses to postal questionnaires (10). Yet, none of the retention interventions to date has 660 been informed by evidence on the perspectives of participants and/or former participants from a

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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: guestionnaire 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 gualitative 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

Page 35 of 111

#### **BMJ** Open

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686 could take to improve recruitment. The qualitative analysis of recruitment consultations 687 highlighted communication practices that helped the multicentre pilot UK FASHION trial to 886 achieve a 70% recruitment rate, although it had been assumed at the outset that it would be 688 extremely difficult (46). On the other hand, retention was rarely discussed during clinical trial 690 consultations. An embedded mixed-methods with a purposive sample of audio-recorded trial 691 consultations obtained from four sites of a large multicenter UK-based surgical RCT revealed 92 that there was no discussion of retention across 79% of consultations. If retention was 693 discussed, it only made up 3% (at best) of the consultation content (68).

694 The changes reported in the included studies to address recruitment barriers mainly aimed to 695 clarify the concept of randomisation to study participants, maintain clinical equipoise, challenge 696 patient treatment preferences and ensure clarity around the eligibility criteria. The changes 697 reported to address retention barriers centered around identifying ways to ease the burden of 698 follow-up questionnaires. However, in many cases, the link between the changes proposed for 699 the full-scale trial and the pre-trial qualitative findings was not explicit. This was the case in '00 nearly 50% of the included studies, meaning that capitalising on the value of pre-trial qualitative '01 research when reporting these studies was not clear despite findings suggesting there was a '02 problem that needed to be addressed. This might be because of limited article word count in '03 papers reporting the results of the qualitative work alongside the pilot trial results, where very '04 little space was allocated to the qualitative component and its impact was usually reported '05 rather than demonstrated. It could also, of course, be because the proposed changes were not '06 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

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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.

# 717 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.

729 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

Page 37 of 111

#### **BMJ** Open

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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).

739 There are however limitations. The review was based on what was written in published research 740 and this may not reflect the breadth of qualitative research that is undertaken in practice. Every 741 effort was made to contact corresponding authors to obtain a full account of qualitative data 742 where information was lacking in the published report, or when researchers reported that a 743 stand-alone article based on gualitative research will be published separately but was not yet 744 available. However, not all authors provided these data, in which case it means the synthesis 745 was limited to the findings and quotes published in the qualitative reports. Of the 35 included 746 studies, 33 were UK based (the other two were conducted in Canada and Norway) and this 747 resonates with the fact that both recruitment and retention are among the top three 748 methodological research priorities in the UK (71). It does, however, mean it is uncertain whether 749 and to what extent the findings apply to the trial environment outside the UK. The geographical 750 spread of studies included in our QES is in line with the Cochrane review on factors that impact 751 on recruitment to randomised trials (72). Of the 29 studies included in the review, 16 studies 752 were conducted in the UK, six in other European countries (Austria n = 1, Denmark n = 1, 753 Germany n = 2, Sweden n = 1, the Netherlands n = 1); three in the USA; and one each in 754 Australia, Canada, New Zealand and Tanzania.

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## 755 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 gualitative research will be used to optimise their recruitment and retention approaches in the full-scale trial. This gualitative 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 gualitative 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.

776 This evidence synthesis provides some pointers for how researchers can improve their
 777 approach to pre-trial qualitative work. Below we have suggested two summary
 <sup>4</sup> 778 recommendations that may help to maximise the value of undertaking this type of work:

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### 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.

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

787 In some cases, there was a clear link between qualitative findings and a particular
788 change being made to the recruitment or retention plan for the full-scale trial. In others,
789 there was no explicit link between findings and changes, or the lack of changes. For
790 these the influence of pre-trial qualitative work on the recruitment or retention plans for
791 the full-scale trial remained unclear, either because of poor reporting or because there
792 was no link. Researchers should provide a clear statement of their findings and the
101 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.

# 800 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.

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

**Funding** This research received no specific grant from any funding agency in the public,

812 commercial or not-for-profit sectors.

**Competing interests** None declared.

**Patient consent** Not required.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data sharing statement** All data relevant to the study are included in the article or uploaded as

817 supplementary information.

- 818 Ethics approval Not applicable

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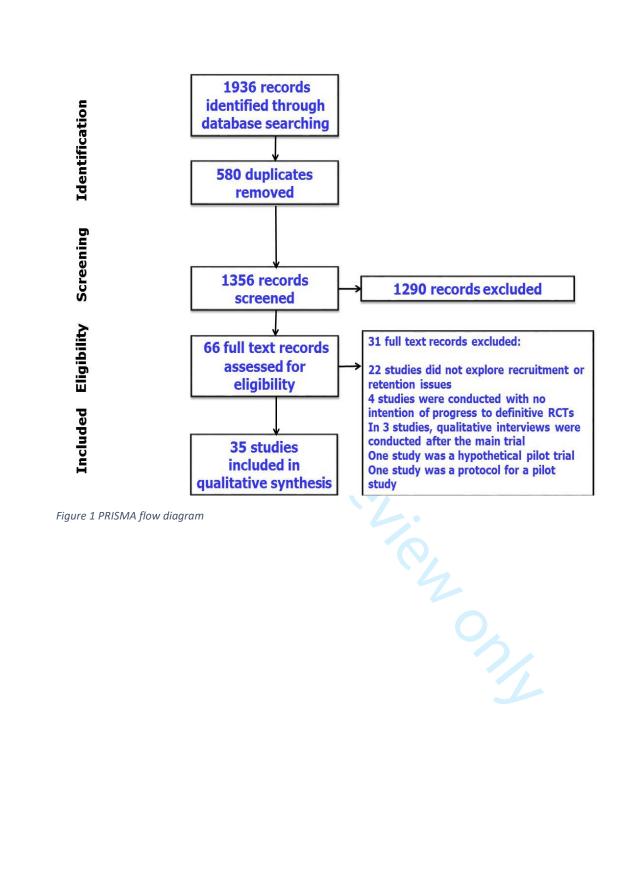
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28 29 30 31 32	1053	Figure legends/caption Figure 1- PRISMA flow diagram
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## MEDLINE MULTI-FILE SEARCH STRATEGY

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:

- qualitative research/ (89507)
- qualitative research.tw,kw. (33140)
- (qualitative adj3 method\$).tw. (52706)
- (qualitative method? or qualitative methodology).kw. (2407)
- (qualitative adj3 stud\$).tw. (94525)
- qualitative study.kw. (2277)
- focus groups/ use ppez (25522)
- focus group?.tw,kw. (80757)
- grounded theory/ (5381)
- grounded theory.tw,kw. (20998)
- narrative analys?s.tw,kw. (2073)
- process evaluation.tw,kw. (5813)
- mixed method?.tw,kw. (27752)
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- (in depth adj4 interview\$).tw. (40998)
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- qualitative interview\$.tw. (17258)
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24	(interview\$ and audio recorded).tw. (4755)
25	qualitative case stud\$.tw. (1950)
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34	qualitativ\$ analys\$.tw. (32509)
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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)
	Patient Selection/ (145510)

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- 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)
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- 73 limit 72 to English language (832) MEDLINE 422 EMBASE 351
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# S4: Characteristics of included studies.

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S4:	Character	ristics of included	d studies.		-2021-05	
Study ID	Country	Clinical area	Study aim/ objective	Participants	Method og data collectiong	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-strugtured interviews 2002 2022 2022 2022 2022 2022 2022 20	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 elephone interviews with six patients who declined to take patt 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-fage semi- structured qualitative interviews	Framework approach
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1 2						njopen-20	
3 4 5 7 8 9 10 11 12	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 recording of recruitment consultations and non- participare observations of consultations	Thematic analysis using constant comparative methods
13 14 15 16 17 18 19 20 21 22 23 24 25	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-fage In-depth interviews oaded from http://bmjopen.bmj.com	Constant comparison and case study approaches
26 27 28 29 30 31 32 33 34 35 36 37	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
38 39 40 41 42 43 44 45 46 47			For pee	r review only - http://bmjopen.bm	j.com/site/about/guidelines.xhtr	cted by copyright.	

exual health tress urinary ncontinence	To determine the facilitators and barriers to recruitment and retention to a school- based sexual-health cluster randomised trial 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	Principals, vice-principals, teachers, pupils and parents recruited to the study 29 women who had participated in the pilot study.	Semi-structured interviewSand focus groups Semi-structured interviewS2 Semi-structured interviewS2 Downloaded	Thematic analysis Framework analysis
tress urinary	and barriers to recruitment and retention to a school- based sexual-health cluster randomised trial 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	teachers, pupils and parents recruited to the study 29 women who had participated in the pilot	interview groups Semi-structured interview	
	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	participated in the pilot	interview	Framework analysis
	urodynamic testing prior to surgery for stress urinary incontinence in women (INVESTIGATE-I)		Downloaded from http://bmjopen.t	
ardiac 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-strugtured interviews (two interviews were undertaken face to face and eght by telephone.	Framework analysis
epression and ebt	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-strugstured interviews of tec tec tec tec tec tec tec tec tec tec	Thematic analysis
)e	pression and bt	rdiac chest pain rdiac 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 epression and bt To explore participants' experience of involvement in the trial (Debt Counselling for Depression in Primary Care: an adaptive randomised	rdiac 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 Ppression and bt To explore participants' experience of involvement in the trial (Debt Counselling for Depression in Primary Care: an adaptive randomised 10 participants 10 participants 10 participants 10 participants 10 participants 23 patients, 7 GPs and 4 CAB (Citizens Advice Bureau) advisors who participated in the trial	rdiac chest pain rdiac 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 Ppression and bt To explore participants' experience of involvement in the trial (Debt Counselling for Depression in Primary Care: an adaptive

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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.		1136/bmjopen-2021-055521 on 18 April 2022. Downloaded fr	
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://bmjopen.bmj.com/ 9	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-strugtured interviews, 2024 by guest. Protect	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-struetured	Thematic analysis
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Page 55 of 111			BMJ Ope	en	1136/bm	
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			evaluating the efficacy of cycling and resistance exercise each performed during the haemodialysis treatment on QoL		1136/bmjopen-2021-055521 on 18 Ap	
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 gro222. Downloaded from http://bmjopen.bmj	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 Fil 19, 2024 by guest. P	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 grogps and semi-strugtured interviews	Thematic analysis
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Page 56	of 1	11
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3 4 5 6				care staff concerning nursing home patients' fecal incontinence		1136/bmjopen-2021-055521	
7 8 9 10 11 12 13	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 qualitativessemi- structure interviews	Thematic analysis
14 15 16 17 18 19 20 21 22	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-strugtured interviews focus groups and audio- recordings of recruitment encounters	Thematic analysis
23 24 25 26 27 28 29 30 31 32 33 34 35	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-recoding of recruitment consultations on April 19, 2024 by guess	Thematic analysis and focused conversation analysis.
36 37 38 39 40 41 42	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 by copy right	Content analysis
42 43 44 45 46 47			For pee	er review only - http://bmjopen.bm	j.com/site/about/guidelines.xhtr	-	

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			enhance self-efficacy to manage cancer-related fatigue)		1136/bmjopen-2021-055521 o	
Pentecost 2015 0 1 2 3 4 5 6	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-strugtured interview I NO NO NO NO NO NO NO NO NO NO NO NO NO	Thematic analysis
	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-strugtured interviews bmjopen.bmj.c	Thematic analysis
26 Crawley 2013 27 28 29 30 31 32 33 34 55	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 Precordings of recruit consultations	Thematic analysis
Gray 2013 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 fected by copyright	Framework approach
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		I	delivered through professional football clubs.	of different ages and baseline BMIs	1-05552	
	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 18 April 2022. Downloaded	Thematic analysis
Moynihan l 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 http://bmjopen.bmj.open.bmj.open.bmj.o	Thematic analysis
Marshman U 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 interview Sface-to- face and Relephone interview & VO24 by guest. Protect	Framework approach
Audrey 2011 l	UK	Localized prostate cancer	The purpose of ASPECTS (Aspirin and Esomeprazole	45 patients	In-depth interviews and audio op yrecording of	Framework approach

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1 2						.1136/bmjopen-202 recruitme <del>fi</del> t	
3 4 5 6 7 8 9 10 11 12 13 14			<i>R</i> o	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 221 on 18 April 2022. Down	
15 16 17 18 19 20 21 22 23 24 25	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 discussion between potential CT participants and recruitment staff In-depth interviews with Trial Management Group	Simple counts, cross tabulations and content analysis
26 27 28 29 30 31 32 33 34 35 36 37 38	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 ril 19, 2024 by guest. Protected by copyright.	Thematic analysis
39 40 41 42 43 44 45 46 47			For pee	er review only - http://bmjopen.bm	j.com/site/about/guidelines.xhti		

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1 2						mjopen-20	
3 4 5 6 7 8 9 10 11 12 13	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	<ul> <li>14 parents (across intervention and control groups)</li> <li>7 telephone interviews with women who were randomised to the intervention group but who did not attend any sessions</li> </ul>	Semi-structured interview groups 18 April 2022 Dog	Thematic analysis
14 15 16 17 18 19	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-strug telephoneinterviews	Thematic analysis
20 21 22 23 24 25 26 27 28 29 30	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 open.bmj.com/ on April 19	Thematic analysis
31 32 33 34 35 36 37 38 39	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-strugtured interviewg guest Protected	Thematic analysis
<ul> <li>39</li> <li>40</li> <li>41</li> <li>42</li> <li>43</li> <li>44</li> <li>45</li> <li>46</li> <li>47</li> </ul>			For pee	r review only - http://bmjopen.bm	j.com/site/about/guidelines.xhtr	by copyright. nl	

Pa	ge 61 of 111			BMJ Ope	n	.1136/b	
1 2						1136/bmjopen-20	
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 4 35 36 37 38 38 38 38 38 38 38 38 38 38	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 21 on 18 April 2022. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by guest.	Framework approach
39 40 41 42 43 44 45 46 47			For pee	r review only - http://bmjopen.bm	j.com/site/about/guidelines.xhtr	Protected by copyright.	

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

				<del>0</del>
	Barriers (number of studies contributing to the	Were there any	Facilitators	Were there any changes planned for
	review finding)	changes		Be full-scale trial based on pre-trial
		planned for the		qualitative data? (Yes, Unclear, No)
		full-scale trial		Dow
		based on pre-		nloa
		trial qualitative		adec
		data? Yes,		l fro
		Unclear, No		m hi
		(the number of		ttp://
		studies		l bringing and an
		contributing to		op pe
		the review		n br
		finding)		Downloaded from http://bmjopen.bmj.com
-	1- Lack of clarity or understanding of randomisation	N/ (0/0)	1- Altruism and personal	on k
Recruitment	(n=6/35 <sup>1</sup> )	Yes (3/6)	gain (n=5/35 <sup>1</sup> )	-go changes reported ⊒.
				19,
		Unclear (n=2/6)		202
				4 by
			-	gu
		No (n=1/6)		est.
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<sup>1</sup> There were 35 in	ncluded studies in total.			руп
				ght.

Page 63	of	1	1	1
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		BMJ Open		a haniopen-2
2-	Lack of clinical equipoise (n=12/35)	Yes (n=5/12)	2- Communicating study information (n=7/35)	6/bm 
		Unclear (n=4/12 (33%)		2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
		No (n=3/12)		
3-	Strong patient treatment preferences (n=9/35)	Yes (n=4/9 (44%)	<ul> <li>3- Social networks and experience of research (n=2/35)</li> </ul>	to (n=6/7)
		No (n=5/9)	-	
4-	Issues related to the control group (n=4/35)	Yes (n=4/4)	24	bri for April 19 2024 by quest Protected by convright
5-	Communicating study information and associated terminology (n= 8/35)	Yes (n=5/8)		
		Unclear (n=2/8)		
		No (n=1/8)		

		BMJ Open	6/bmjopen-2021
6-	Issues around the eligibility criteria (n=6/35)	Yes (n=4/6)	.055521 on
		No (n=2/6)	18 April 2
7-	Practical barriers (n=12/35)	Yes (n=5/12)	D22. Down
		Unclear (n=4/12)	lloaded from ht
	-64	No (n=3/12)	tp://bmjop
8-	Commitment of staff and participants to the trial (n= 2/35)	Yes (n=1/2)	6/bmjopen-2021-Q55521 on 18 April 2022. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by guest.
9-	Beliefs and expectations (n= 10/35)	Yes (n=6/10)	xiil 19, 2024
		Unclear (n=1/10)	by guest. Pr
		No (n=3/10)	Protected by copyright.
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			6/bmjopen-2021-055521
	<ul><li>10- Mismatch between the trial protocol and clinical care pathways (n= 4/35)</li></ul>	Yes (n=2/4)	55521 or
		Unclear (n=2/4)	on 18 April 2022.
	11- Participation burden (n= 4/35)	Unclear (n=3/4)	
		No (n=1/4)	None identified
	12- Lack of confidence in approaching study participants (n= 2/35)	Yes (n=1/2)	om http://b
		Unclear (n=1/2)	- mjopenbr
Retention	1- Burden of follow-up questionnaires (n= 9/35 <sup>1</sup> )	Yes (n=5/9)	None identified
		Unclear (n=2/9)	April 19,
		No (n=2/9)	- 2024 by g
	2- Practical barriers (n= 2/35)	Unclear (n=1/2)	- uest. Prot
		No (n=1/2)	Protected by copyright.
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# ss: Barriers to recruitment

Build open       Build open         Stady ID (clinical area)       1. Findings associated with code: Lack of clarity or understanding of randomisation       Changes planned before the full trial       Despite explaining random allocation, some participants struggled to understand the concept or need for randomisation.       • Randomisation will be explained to participants in the following way:         To try and make sure both groups are the same, each person is some participants were still uncertain whether they would be selected based on some personal or illness characteristics.       • Attention to be focused on training trialists who are involved in recruitment to complicated trials, both in teroffs of complex trial pathways.         Moynihan 2012 (Transitional (TCC) of the bladder)       • Often randomisation was perceived haphazardly as patients strove to make some of their involvement in the trial process while questioning scientific principles.       • Attention to be focused on training trialists who are similation of the bladder)       • It was necessary to emphasize that recruiters must be work of the bladder of trial pathways.	
Study ID (clinical area)1. Findings associated with code: Lack of clarity or understanding of randomisationChanges planned before the full trialNair 2014 (Lung Cancer)• Some participants struggled to understand the concept or need for randomisation.• Randomisation will be explained to participants in the following way:• 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:• 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 terps of communication processes and on the assimilation of complex trial pathways.• Audrey 2011• Patients and recruiters had difficulty• It was necessary to emphasize that recruiters must be	
<ul> <li>Nair 2014 (Lung Cancer)</li> <li>Some participants struggled to understand the concept or need for randomisation.</li> <li>Despite explaining random allocation, some participants were still uncertain whether they would be selected based on some personal or illness characteristics.</li> <li>Moynihan 2012 (Transitional Cell Carcinoma (TCC) of the bladder)</li> <li>Often randomisation was perceived haphazardly as patients strove to make sense of their involvement in the trial process while questioning scientific principles.</li> <li>Audrey 2011</li> <li>Patients and recruiters had difficulty</li> <li>It was necessary to emphasize that recruiters must be</li> </ul>	Were the proposed changes clearly linked to coded data?
<ul> <li>Moynihan 2012 (Transitional Cell Carcinoma (TCC) of the bladder)</li> <li>Often randomisation was perceived haphazardly as patients strove to make sense of their involvement in the trial process while questioning scientific principles.</li> <li>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 principles.</li> <li>Audrey 2011</li> <li>Patients and recruiters had difficulty</li> <li>It was necessary to emphasize that recruiters must be</li> </ul>	Yes
Audrey 2011 • Patients and recruiters had difficulty • It was necessary to emphasize that recruiters must be	Unclear
4       (Prostate cancer)       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       genuinely uncertain about the best treatment, believe the patient to be suitable for all three treatments, and be confident in these beliefs.         8       •       Recruiters were encouraged to elicit patients' lay views and then discuss differences with ProtecT study information, of the discuss	• Yes

Page 68	3 of 111
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			BMJ Open	.1136/bi	Page 68 of 1
1 2 3		information that was often biased in	explain that randomisation offered a way of resolving	1136/bmjopen-2021	
4 5		favor of radical treatments.	explain that randomisation offered a way of resolving dilemma of treatment choice.	55	
6 7 8 9 10 11 12 13	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 that patients could be randomized at any time before three cycles of chemotherapy rather than during the second cycle.	n <b>4</b> 8 April 2022.	• Yes
14 15 16 17 18 19 20 21 22 23 24 25	McEachan 2016 (Childhood obesity)	<ul> <li>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.</li> <li>Some control group women interviewed expressed disappointment at being allocated to the control group.</li> </ul>	No changes reported to address this barrier	Oownloaded from http://bmjopen.bmj.co	> No
26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47		For peer review onl	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	m/ on April 19, 2024 by guest. Protected by copyright.	

Page 69 of 111		BMJ Open BMJ open	
1         2         3       Kendrick 2017         4       (Depression)         6         7         8         9         10         11         12         13         14         15         16         17         18         19         20         21         22         23         24         25         26	<ul> <li>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.</li> <li>It was apparent that several of the standard care patients had not adequately understood management allocation prior to agreeing to participate in the trial.</li> <li>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.</li> </ul>	<ul> <li>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.</li> <li>The study team needs to spend more time at participating practices training them in the recruitment process.</li> <li>Patients should be supported to take the necessary time consure understanding of patient information sheets before signing consent, especially with regard to clinical equipose and that they will not necessarily benefit from participation.</li> </ul>	Unclear
<ul> <li>27</li> <li>28</li> <li>29</li> <li>30</li> <li>21</li> </ul>	Findings associated with code: Strong patient treatment preferences	Changes planned before the full trial April 19, N	Were the proposed changes clearly linked to coded data?
31         32       Paramasivan         33       2017 (complex         34       obesity)         35       36         37       38         39       40	Patients tended to decline study participation, often choosing bypass surgery.	<ul> <li>Do not indicate patient preference anywhere on the notes.</li> <li>Move beyond initial probing questions in relation to patient preferences toward rectifying any erroneous views.</li> <li>Request patients who appear to have a preference or decision about trial participation to 'keep an open mind'e until they had heard all the relevant information.</li> </ul>	Yes
41 42 43 44 45	For peer review only	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	·]

Page 70 of 111

			BMJ Open	.1136/br	Page 70 of
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	Griffin 2016 (hip impingement) Hilton 2015 (stress urinary incontinence)	<ul> <li>Concerns about patient reactions and preferences at the start of the trial.</li> <li>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 central group.</li> </ul>	<ul> <li>The patient should have the opportunity to talk to a researcher for longer and should be able to ask quest and raise concerns.</li> <li>No specific changes planned to address this barrier.</li> </ul>	1136/bmjopen-2021-055521 on 18 April 2022. Downloaded from	Yes
17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38	Hamilton 2013 (head and neck cancer)	<ul> <li>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.</li> <li>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.</li> </ul>	<ul> <li>Principal investigators and recruiters must try to elicit understand patient views and preferences.</li> <li>The need to gently challenge preferences that are bas inaccurate information.</li> <li>The need for training recruiters to enable them to exp the need for randomisation and the rationale for the patients.</li> </ul>	http://demjopen.com/gon sedmj.com/gon	Yes
39 40 41 42 43 44 45 46		For peer review on	ly - http://bmjopen.bmj.com/site/about/guidelines.xhtml	by copyright.	

Pag	ge 71 of 111		BMJ Open	.1136/bn	
1 2				36/bmjopen-20	
3 4 5 6 7 8	Clarke 2015 (childhood intermittent exotropia)	<ul> <li>Recruitment was hampered by strong parental preferences.</li> </ul>	<ul> <li>To account for parental preferences, a future trial will incorporate a preference arm or accept that recruitme will inevitably be restricted to those parents who are prepared to consider surgery as a treatment.</li> </ul>	055521 on 18	Yes
9 10 11 12 13 14	Audrey 2011 (Cancer)	<ul> <li>Patients often expressed lay views that cancer should be removed or came with media information that was biased in favor of radical treatments.</li> </ul>	<ul> <li>No specific changes planned to address this barrier.</li> </ul>	April 2022. Downl	
15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37	Paramasivan 2011 (transitional cell carcinoma of the bladder)	<ul> <li>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.</li> </ul>	No specific changes planned to address this barrier.	paded from http://bmjope	
	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	n.bmj.com/ on A	
	Palmer 2016 (joint hypermobility syndrome)	<ul> <li>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.</li> </ul>	<ul> <li>No specific changes planned to address this barrier</li> </ul>	pril 19, 2024 by guest. Prote	
38 39 40 41 42	Study ID (clinical area)	Findings associated with code: Issues related to the control group	Changes planned before the full trial	ected by copyright	Were the proposed changes clearly linked to coded data?
43 44 45 46		For peer review only	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	ght.	

			BMJ Open	.1136/b	Page 72 of
$\begin{array}{c}1\\2\\3\\4\\5\\6\\7\\8\\9\\10\\11\\2\\3\\14\\15\\16\\17\\18\\9\\20\\21\\22\\34\\25\\26\\7\\28\\9\\30\\31\\32\\33\\4\\5\\36\\37\\38\\9\\0\\41\\42\\43\\44\\5\\46\\7\end{array}$	Nair 2014 (lung cancer)	<ul> <li>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.</li> <li>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.</li> <li>some people who understood the need for a control group, found it hard to appreciate the need for this in a screening trial.</li> </ul>	<ul> <li>Changes made to the study design or Participant Infor Leaflet (PIL)</li> <li>The control group will be changed to non-test grout is what participants were most comfortable with".</li> <li>'Whenever a new test is developed, we need to fin works. We do this by having a group of people who the test and a group of people who do not. Both gr need to be similar so that we can compare what has the people in each group.'</li> <li>'If you are in the non-test group, the information yous will be really important in helping us find out if the lung cancer blood test works, by comparing what he to both groups.</li> </ul>	p, whether it backgroups by the second secon	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'.	<ul> <li>Issues identified by the qualitative research led to a in the study information, randomisation, terminolo and presentation of the non-radical arm.</li> <li>The non-radical arm was renamed 'active monitorin additional emphasis placed on the regular scrutiny tests and the availability of radical intervention if re or requested. As a result of these changes, recruitin were able to express confidence in this treatment or the section.</li> </ul>	gy used S Agy ng' with of PS as equires	Yes
		For peer review on	ıly - http://bmjopen.bmj.com/site/about/guidelines.xhtml	st. Protected by copyright.	

Pag	ge 73 of 111		BMJ Open BMJ open	
1 2 3			n-202	
4 5 6 7	Kendrick 2017 (depression)	<ul> <li>One standard care patient pointed out that he could not grasp an understanding of the purpose of the control arm.</li> </ul>	<ul> <li>Patients should be supported to take the necessary time to ensure understanding of patient information sheets before signing consent, especially with regard to clinical equipolitie and that they will not necessarily benefit from participation.</li> </ul>	Yes
8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39		<ul> <li>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.</li> <li>Some patients felt that they would not have the best treatment if they were randomised to standard care.</li> </ul>	<ul> <li>A lack of skills in introducing research could be addressed in through more training in a smaller group of practices.</li> <li>Downloaded from http://bmjop</li> </ul>	
	Palmer 2016 (joint hypermobility syndrome)	<ul> <li>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.</li> </ul>	<ul> <li>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 generals not targeted, exercises, so the two arms were perceived as more equitable.</li> </ul>	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     Totop     Totop	
40 41 42 43 44 45 46		For peer review only	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	
47				

Page 74	of 1	11
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		BMJ Open 33	Page 74 o
Clarke 2015 (childhood intermittent exotropia)	<ul> <li>For parents and clinicians, the initial screening appointment presented a challenge, in that it had to encompass many points within a limited time.</li> <li>The initial two visits, for screening and recruitment, often gave insufficient time for parents to fully consider participation in the trial.</li> </ul>	<ul> <li>BMJ Open</li> <li>The use of research nurses in all centers should be considered in a future study.</li> <li>Separation of the role of the treating clinician from the main recruiter to the trial.</li> </ul>	Unclear
4         5         16         (cancer)         7         8         9         20         21         22         23         24	<ul> <li>The main obstacle to participation appeared to be the need for flexible appointments.</li> <li>work commitments among some of the younger participants were seen as a potential barrier.</li> </ul>	<ul> <li>Those expressing interest in the study are sent the full PE and at least 24 hours after anticipated receipt are phone to discuss the study, answer questions, undertake a preliminary eligibility assessment and to arrange a recruitment visit at a time suitable to the patient.</li> <li>Appointment reminders by phone, text message or emails of the patient of the pat</li></ul>	Unclear
Moynihan 2012 (transitional cell carcinoma of the bladder) bladder)	<ul> <li>Patients spontaneously indicated the need to 'work' their way around NHS waiting times and hospital administration.</li> <li>Patients often criticized their need to 'work' against 'bad administration', sometimes affecting trial decisions.</li> </ul>	<ul> <li>It is suggested that health professionals consider facilitation a context in which patients feel fully included in the trial enterprise.</li> </ul>	
<ul> <li>Study ID (clinical</li> <li>area)</li> <li>area</li> </ul>	Findings associated with code: Beliefs and expectations about trial participation	Changes planned before the full trial	Were the proposed changes
Hamlet 2017 (young people	• A 'conspiracy of silence': Beliefs that young people would prefer not to	<ul> <li>This study highlights the potential need for training to generative educate primary care staff to broach the topic of a visible generative educate primary care staff to broach the topic of a visible generative educate primary care staff to broach the topic of a visible generative educate primary care staff to broach the topic of a visible generative educate primary care staff to broach the topic of a visible generative educate primary care staff to broach the topic of a visible generative educate primary care staff to broach the topic of a visible generative educate primary care staff to broach the topic of a visible generative educate primary care staff to broach the topic of a visible generative educate primary care staff to broach the topic of a visible generative educate primary care staff to broach the topic of a visible generative educate primary care staff to broach the topic of a visible generative educate primary care staff to broach the topic of a visible generative educate primary care staff to broach the topic of a visible generative educate primary care staff to broach the topic of a visible generative educate primary care staff to broach the topic of a visible generative educate primary care staff to broach the topic of a visible generative educate primary care staff to broach the topic educate primary educate primary care staff to broach the topic educate primary educate</li></ul>	Yes
12 13 14 15 16	For peer review only	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

Paç	ge 75 of 111	BMJ Open 66/bm
1 2 3 4 5 6 7 8 9 10 11	with appearance- altering conditions)	discuss appearance-related concerns with their GP.       difference confidently, both within and outside the parameters of research. Training, with a particular focusion how to talk to young people who might be experiencing appearance concerns, could facilitate doctor-patient appearance and, in A turn, patient disclosure.
12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39	Van Den Berg 2017 (chest pain)	<ul> <li>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.</li> <li>Concerns about being experimented on: some participants felt being generally sceptical of clinical research and initially felt anxious about participation.</li> <li>Waive verbal consent for initial trial procedures that do got affect the participant.</li> <li>Waive verbal consent for initial trial procedures that do got affect the participant.</li> <li>Waiting until the patient's condition is more settled and they can provide appropriate written informed consent.</li> <li>The need to explore shared decision making to cater for wide spectrum of perspectives.</li> </ul>
	Trevelyan 2016 (phantom limb syndrome)	<ul> <li>Intensity of Phantom Limb Pain (PLP) was a major barrier.</li> <li>Consider lowering or excluding the severity of PLP.</li> <li>Yes</li> <li>Non-the severity of PLP.</li> <li>Non-the severity o</li></ul>
	Ritchie 2015 (Cancer)	<ul> <li>Patient self-preservation (the need to retain control of choice of device or treatment schedules).</li> <li>Recruiters should gently challenge patients' gently challe</li></ul>
40 41 42 43 44 45		by copyright For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

			BMJ Open	.1136/bmjopen	Page 76 of <sup>-</sup>
1 2					
3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19	Hamilton 2013 (head and neck cancer)	<ul> <li>Lay beliefs: The oncology centre/hospital where radiotherapy was performed had a negative image and was seen as a 'place to die'.</li> </ul>	<ul> <li>No specific changes planned to address this barrier.</li> </ul>	-2021-055521 on 18 A	
	Nair 2014 (cancer)	<ul> <li>Participants felt stigmatized (because of their smoking status) by some of the language used in the PILs.</li> <li>The perception held by some participants that the trial is designed to encourage people to stop smoking.</li> </ul>	<ul> <li>"We removed all mention of providing smoking cessation information and advice from the Patient information leaflets".</li> <li>'Lung cancer can happen to anyone, including the your old and people who do not smoke, but the risk is higher those over 50 and those who have smoked.'</li> </ul>	2022. Dowald	Yes
20 21 22 23 24 25 26 27 28 29	Moynihan 2012(transitional cell carcinoma of the bladder)	<ul> <li>The patients' sense of alienation was evident. Feelings of isolation, loss of control and powerlessness underwrote involvement in the trial process.</li> </ul>	<ul> <li>Attention to be focused on training trialists who are involved in recruitment to complicated trials, both in the of communication processes and on the assimilation of complex trial pathways.</li> <li>It is suggested that health professionals consider faciling a context in which patients feel fully included in the trienterprise.</li> </ul>	of m.bmj.cong	Unclear
30 31 32 33 34 35 36 37	Ellis 2016 (lung cancer)	<ul> <li>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.</li> </ul>	<ul> <li>No specific changes planned to address this barrier.</li> </ul>	19, 2024 by guest. Prote	
38 39 40 41 42 43 44		Ear poor roview and	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	cted by copyright.	
45 46 47		For peer review on	y - http://bmjopen.bmj.com/site/about/guidelines.xntml		

Page 77 of 111	BMJ Open
1 2 3 <b>Kendrick</b>	BMJ Open       BMJ Open         • One participant expressed anxiety       • Patients should be assured that the aim of the study is not yet.       Yes
5     2017(depression)       6     7       8     9       10     11       12     13       14     15       16     17       18     19       20	<ul> <li>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.</li> <li>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.</li> </ul>
21 22 23 24Latter 2018 (cancer patients at the end of life)25 26 	<ul> <li>Nurses 'protecting' patients and carers from additional burden or distress.</li> <li>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.</li> <li>No specific changes reported to address these barriers.</li> </ul>
32 33 34 35 36 37 38 39 40 41 42 43 44 45 46	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Page /8 of 111	age 78 of 1	11	
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		BMJ Open	.1136/bmjopen-2	Page 78
Clinician/recru	uiter factors		021-055	
Study ID (clinical area)	Findings associated with code: clinical equipoise	Changes planned before the full trial	521 on 18 April 2022.	Were the proposed changes clearly linked to coded data?
Paramasivan 2017 (Complex obesity)	<ul> <li>Recruiters found it difficult to maintain equipoise.</li> <li>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)</li> </ul>	<ul> <li>Feedback sessions used to make recruiters aware of instances where they inadvertently used loaded terminology.</li> </ul>	Downloaded from http://bmjope	Yes
Griffin 2016 (hip impingement)	<ul> <li>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.</li> <li>Unbalanced presentations of treatment options for which surgery has been presented at greater length and more favourably than either choosing conservative care or</li> </ul>	Providing frequent and comprehensive training to recruiters.	an.bmj.com/ on April 19, 2024 by guest. Protected by copyright.	Unclear
	For peer review onl	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	rright.	

Page 79 of 111	BMJ Open	.1136/br
1 2		njopen-20
3 4 5 6 7 8 9	<ul> <li>participating in the RCT (surgeons tend to talk most about what they are most familiar with).</li> <li>Some surgeons favoured surgery as</li> </ul>	1136/bmjopen-2021-055521 on 18 Ap
10 11 12 13 14 15 16 17 18 19	<ul> <li>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.</li> </ul>	April 2022. Downloaded from htt
Normalization       Ritchie 2015         21       (Cancer)         22       23         24       25         26       27	<ul> <li>Interviews with clinical staff revealed device preferences for certain subgroups of patients.</li> <li>Recruiters should own bias in device</li> </ul>	gently challenge and acknowledge the
<ul> <li>28 Hamilton 2013</li> <li>29 (head and neck cancer)</li> <li>31</li> <li>32</li> <li>33</li> <li>34</li> <li>35</li> <li>36</li> <li>37</li> <li>38</li> <li>39</li> </ul>	<ul> <li>whether patients with disease critically about the involving the anterior commissure or those with cancer in situ would have better outcomes with a particular modality.</li> <li>The language describing the treatment processes for the two options was not equivalent: toddling home' and 'nice</li> </ul>	024 by guest.
40 41 42 43 44	and simple' for laser surgery compared with 'a bit more labour intensive,' 'a	Protected by copyright.

				BMJ Open	.1136/br	Page 80 o
1 2					njopen-20	
3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 3 24 25 26 27 28 29 30 13 22 33 34 35 36	Pentecost 2015 (Depression)	•	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. 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.	.1136/bmjopen-2021-055521 on 18 April 2022. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by guest. F	Unclear
37 38 39 40 41 42 43	L	<u> </u>			uest. Protected by copyright.	1]
44 45			For peer review only	/ - http://bmjopen.bmj.com/site/about/guidelines.xhtml	•	

Paç	e 81 of 111	BMJ Open 36
1 2		BMJ Open 36/bmjopen-20
3 4 5 6 7 8 9 10	Clarke 2015 (childhood intermittent exotropia)	<ul> <li>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.</li> <li>Trial team suggested separation of the role of the treating clinician from the main recruiter to the trial. This proved of the treating clinician from the main recruiter to the trial. This proved of the treating clinician from the main recruiter to the trial. This proved of the treating clinician from the main recruiter to the trial.</li> <li>Trial team suggested separation of the role of the treating clinician from the main recruiter to the trial. This proved of the treating clinician, and by extension, the trial.</li> </ul>
11 12 13 14 15 16 17 18 19 20 21	Hilton 2015 (stress urinary incontinence in women)	<ul> <li>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.</li> <li>No changes were suggested (the majority of respondents regarded the basic research question as being importants into a definitive RCT to address this (60%).</li> </ul>
21 22 23 24 25 26 27 28 29	Crawley 2013 (children with chronic fatigue syndrome)	<ul> <li>Discussion of the interventions tended to be weighted towards the Lightning Process rather than the specialist medical care during recruitment consultations.</li> <li>No specific change reported to address this issue.</li> <li>No specific change reported to address this issue.</li> <li>No specific change reported to address this issue.</li> </ul>
30 31 32 33 34 35 36 37 38 39 40 41	Moynihan 2012 (bladder cancer)	<ul> <li>An explanation of equipoise was usually perceived to be absent in the information process.</li> <li>The need to believe in expert physicians and an inability to accept medical uncertainty is documented.</li> <li>Physicians find the concept of equipoise difficult, both because of</li> </ul>
41 42 43 44		For poor roviou only, http://bmionon.hmi.com/cito/about/quidalings.yhtml

		BMJ Open	.1136/bmj	Page 82 of
1         2         3         4         5         6         7         8         9         Audrey 2011         10         (Cancer)         11         12         13         14         15         16         17         18         19         20         Paramasivan         2011 (Prostate         cancer)         24         25         26         27         28         29         30         31         32         33         34         35	<ul> <li>personal preference, and the difficulties of explaining the uncertainty prevailing in any form of randomization</li> <li>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.</li> <li>Centers sometimes appeared to take on a 'collective' preference - one that represented the views of most staff in the center.</li> <li>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.</li> </ul>	<ul> <li>Recruiters were asked to change the order in which treatments were presented (active monitoring, surg radiotherapy) and to describe their respective advarant disadvantages in equivalent detail.</li> <li>Issues of randomization and clinical equipoise were for both patients and recruiters.</li> <li>No specific changes planned to address these barriers</li> </ul>	ery, clarited ntage: Downed clarited	Yes
36 37 38 39 40 41 42 43 44 45 46	For peer review only	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	. Protected by copyright.	

Pag	ge 83 of 111		BMJ Open 60 BMJ Op	
1 2 3 4 5 6 7 8 9 10	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.	<ul> <li>Training and monitoring of trial personnel to ensure notions of equipoise are delivered and reinforced consistently is the improve recruitment rates to a future RCT.</li> <li>93</li> <li>84</li> <li>91</li> <li>85</li> <li>93</li> <li>94</li> <li>94</li> <li>95</li> <li>95</li> <li>96</li> <li>97</li> <li>97</li> <li>98</li> <li>97</li> <li>98</li> <li>97</li> <li>99</li> <li>91</li> <li>91</li> <li>91</li> <li>91</li> <li>92</li> </ul>	5 Unclear
11 12 13 14 15	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?
15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30	Griffin 2016 (hip impingement)	<ul> <li>Graphic descriptions of surgery that may have put patients off randomisation.</li> <li>Presenting trial information in an order that is confusing for patients.</li> <li>Surgeons going beyond their protocol brief, to explain the trial rather than referring patients on to the trial recruiter for this information.</li> </ul>	Providing frequent and comprehensive training to recruiters.	Unclear
31 32 33 34 35 36 37 38 39 40 41 42	Aventin 2016 (Sexual health)	<ul> <li>The baseline questionnaire was too long and some did not feel comfortable answering questions relating to sexuality.</li> </ul>	<ul> <li>At an individual level, researchers should ensure that data collection documentation is clear to parents and pupils, <sup>4</sup> by great perhaps involving steering group members in ensuring clarity.</li> <li>Protected by copyright</li> </ul>	Yes
43 44 45 46 47		For peer review only	과 - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

		BMJ Open	.1136/bmjope	Page 84 of
Crawley 2013 (chronic fatigue syndrome)	<ul> <li>Patient information sheets were perceived as long, difficult to understand, repetitive in places and not visually appealing to 12 to 18-year olds.</li> </ul>	<ul> <li>Consider using different patient information sheets f children aged 12 to 14 years than those used for olde teenagers.</li> </ul>	ror 1-055521 on 18	
0Moynihan 20121(transitional cell2carcinoma of the4bladder)5-6-7-8-9-0-1-2-3-4-5-6-7-8-9-0-1-1-	<ul> <li>Patients displayed what may be perceived as 'poor understanding' of trial procedures and concepts. Patients' accounts suggested that information giving was often suboptimal and/or understanding unverified.</li> <li>An explanation of equipoise was usually perceived to be absent in the information process.</li> <li>Patients across the sample failed to understand the 'language' of trial procedures.</li> <li>Research overload, information overload and a perceived lack of information affected decision making.</li> </ul>	<ul> <li>Attention to be focused on training trialists who are involved in recruitment to complicated trials, both in of communication processes and on the assimilation complex trial pathways.</li> <li>No specific changes planned to address this barrier.</li> </ul>	April 2005 of Downloaded from http://bmjopen.bmj.com/ on April 19, 202	
Marshman 2012 (dental caries) (dental caries)	<ul> <li>Finding an appropriate form of words to explain aspects of the trial to parents and children was difficult for some dentists.</li> </ul>	No specific changes planned to address this barrier.	st. Protected	
5 2 3 4 5 6	For peer review onl	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	by copyright.	

Pag	ge 85 of 111	BMJ Open 136/bmjope
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	Audrey 2011 (cancer) Paramasivan	<ul> <li>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'.</li> <li>Recruiters were presented (active monitoring, surgery, and radiotherapy) and to describe their respective advantages and disadvantages in equivalent detail.</li> <li>Recruiters were asked to replace 'trial' with 'study'.</li> <li>Recruiters and investigators agreed</li> <li>The construction of a simpler version of the study flowctpart</li> </ul>
18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33	2011 (transitional cell carcinoma of the bladder)	<ul> <li>Recruiters and investigators agreed that the SPARE trial was difficult to explain.</li> <li>Recruiters indicated that they found the quantity of information problematic as well as its complexity.</li> <li>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.</li> <li>The recruitment study team drafted a new, shorter and 9 clearer PIS which removed the 'loaded' terminology, explained the simplified study outline and included the new flowchart.</li> </ul>
34 35 36 37 38 39 40	Ellis 2016 (lung cancer)	<ul> <li>For some participants, the questionnaire items probed areas that they had not thought about or had chosen not to think about.</li> <li>The number of questionnaires to be used in the subsequent trial will be decreased.</li> </ul>
41 42 43 44 45 46 47		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Page	86	of	1	1	1	
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1 2		_	pen-20 20	
3 4 5 6 7 8		<ul> <li>Carers also expressed some discontent with the questionnaires, and this was seen as a potential barrier to recruitment.</li> </ul>	BMJ Open 2021-055521 on 18	
9 10 11 12	Study ID (clinical area)	Findings associated with code: issues around the eligibility criteria	Changes planned before the full trial April 2022.	Were the proposed changes clearly linked to coded data?
12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42	Hilton 2015 (stress urinary incontinence)	<ul> <li>Interpretation of eligibility criteria differed between centers (Authors' judgement).</li> </ul>	<ul> <li>Ensure clarity over inclusion/exclusion criteria Running screening training exercises might be considered for a future definitive trial to ensure</li> <li>similar screening standards and practices and an 'assumed eligibility' approach in all centers.</li> </ul>	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)	<ul> <li>Surgeons applied the inclusion/exclusion criteria variably, thereby reducing the available number of eligible patients and creating differences between centers.</li> </ul>	<ul> <li>Issues related to inclusion/ exclusion criteria, may require close examination and regular meetings to discuss and resolve evolving issues.</li> </ul>	Yes
	Clarke 2015 (childhood intermittent exotropia)	Difficulty in confirming eligibility at the initial screening visit	<ul> <li>A future trial will consider a limit on the upper age at wheth participants would be included.</li> <li>by copy</li> <li>copy</li> <li>copy</li></ul>	n Yes
42 43 44 45 46		For peer review only	पु - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

Pag	e 87 of 111		BMJ Open	.1136/br	
1 2				njopen-20	
3 4 5 6 7 8		• Subsequent blockage of appointment slots by children who needed rescreening for eligibility, contributed to a failure to recruit to target.		21-055521 on 18	
9 10 11 12 13	Paramasivan 2011 (transitional cell carcinoma of the bladder)	<ul> <li>Some recruiters thought there was leeway for interpretation of the inclusion/exclusion criteria in partnership with the main trial team.</li> </ul>	<ul> <li>No changes planned to address this issue (The possibility 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).</li> </ul>	ril 20 <u>22</u> . Dow	
14 15 16 17 18 19 20 21 22 23 24	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.	<ul> <li>No changes planned to address this barrier (eligibility criteria will remain the same for the subsequent trial</li> </ul>	hloaded from http://bmjopen.bmj.	
25 26 27 28 29	Study ID (clinical area)	Findings associated with code: commitment to the trial	Changes planned before the full trial	com/ on April	Were the proposed changes clearly linked to coded data?
29 30 31 32 33 34 35 36 37 38 39 40	Paramasivan 2011 (transitional cell carcinoma of the bladder)	<ul> <li>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.</li> </ul>		2월24 by guest. Protected by	Yes
41 42 43 44 45 46		For peer review onl	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	/ copyright.	

			BMJ Open	.1136/b	Page 88 of 1
1 2 3				1136/bmjopen-202	
5 4 5 6 7 8	Latter 2018 (cancer patients at the end of life)	<ul> <li>Recruiting fewer dyads than anticipated affected nurses' engagement and the priority they gave to the study.</li> </ul>	<ul> <li>No specific changes reported</li> </ul>	21-055521 on 18	
9 10 11 12	Citation	Findings associated with code: Lack of confidence in approaching study participants	Changes planned before the full trial	April 2022.	Were the proposed changes clearly linked to coded data?
13 14 15 16 17 18 19 20 21 22 23 24 25 26 27	Griffin 2016 (hip impingement)	<ul> <li>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.</li> <li>Long periods between recruitment clinics represented a challenge for research associates to maintain confidence and knowledge about the UK FASHION trial.</li> </ul>	<ul> <li>Providing frequent and comprehensive training to recruiters.</li> <li>Modifying the support to teams in other centers acco to their research experience.</li> </ul>	Downloadeerrom http://bmjopen.bmj.com/ or	Unclear
28 29 30 31 32 33 34 35 36 37 38 39	Hamlet 2017 (young people with appearance- altering conditions)	<ul> <li>Participants seemed hesitant approaching the topic directly.</li> </ul>	<ul> <li>Training, with a particular focus on how to talk to you people who might be experiencing appearance conce could facilitate doctor-patient communication about psychosocial challenges of living with a condition or ir that alters appearance and, in turn, patient disclosure</li> </ul>	rns <u>,</u> the ju	Yes
40 41 42 43 44 45 46 47		For peer review only	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	y copyright.	

Pag	ge 89 of 111		BMJ Open	. 1136/bmjopen-20
1 2 3 4 5 6	Contextual/sit	uational factors		en-2021-055521
7 8 9 10	Study ID (clinical area)	Findings associated with code: Practical barriers		on 18 April 2
111 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34	Griffin 2016 (hip impingement)	<ul> <li>Difficulty in implementing procedures due to the multicenter nature of the pilot.</li> </ul>	<ul> <li>Regular visits to the centers by the PI and other TGM members to keep momentum</li> <li>Delivery of a slick and easy-to-implement recruitment process to be the least disruptive to routine clinical practice.</li> <li>Providing frequent and comprehensive training to recruiters.</li> <li>Modifying the support to teams in other centers according to their research experience.</li> <li>Setting recruitment targets and engendering a healthy competition between centers.</li> <li>Follow up with messages and regular newsletters about need to recruit.</li> <li>Contacts between research and clinical departments about recruitment opportunities should be encouraged.</li> </ul>	Yes Yes P22. Downloaded from http://bmjo P21. Downloaded from http://bmjo P22. Downloaded from http://bmjo P22. Downloaded from http://bmjo P22. Downloaded from http://bmjo P22. Downloaded from http://bmjo P23. Downloaded from http://bmjo P24. Downloaded from http://bmjo P25. Downloaded from http://bmjo P26. Downloaded from http://bmjo P27. Downloaded from http://bmjo P28. Downloaded from http://b
35 36 37 38 39 40 41	Hamlet 2017 (young people with appearance- altering conditions)	<ul> <li>Barriers of the primary care environment (time-limited consultations, high workload, competing studies)</li> </ul>	No specific changes to address these barriers.	uest. Protected by copyright
42 43 44 45 46 47		For peer review onl	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	right.

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1 2				mjopen-20	
<ul> <li>Aventin 2</li> <li>(Sexual he</li> <li>6</li> <li>7</li> <li>8</li> <li>9</li> <li>10</li> <li>11</li> <li>12</li> <li>13</li> <li>14</li> </ul>		<ul> <li>Perceived lack of time for potential study participants to take part.</li> <li>Involvement in another research projects.</li> </ul>	<ul> <li>Environmental facilitators of recruitment: approach schools attending RSE training days, highlighting the innovative nature of the intervention, flexibility in te how and when the research was conducted in indivi schools, the provision of support to schools by facilit the project by dedicated researchers, providing a cle outline of the roles and responsibilities of the schoo research team) from the outset and facilitating discu on the benefits and perceived barriers to taking part</li> </ul>	erms bf dual tatio Pri l (an Statio A Dri l (an Statio C	Yes
15         Gabbay 20           16         (Debt Could           17         for Depress           18         19           20         10	unselling	<ul> <li>Delayed practice recruitment due to higher administrative issues.</li> <li>Staffing and workload Complexity of primary care services</li> </ul>	• The study failed to reach its recruitment target and terminated early during the internal pilot phase, and therefore, it did not progress to main trial.	-	
21 Lawton 20 22 (postpartu 23 haemorrh 25 26 27 28 29 30	um	Staff reluctance to forgo written consent procedures	<ul> <li>Staff who are inexperienced in using alternatives to prospective written consent may benefit from traini support to increase their confidence and willingness alternative consent approaches. This training and su could focus on raising staff awareness and understa ethical review processes and of how, and why, they legally protected when alternatives to prospective w consent are used.</li> </ul>	ing and to use uppott nding of are A vritten 19	Yes
313233(phantom343536	n limb	• Failure to identify suitable participants due to units not operating in full capacity.	<ul> <li>A future trial would need to ensure that trial centers allocated adequate time and personnel.</li> <li>Applying multicentered approach to recruitment.</li> </ul>	2024 by guest. I	Yes
<ul> <li>36</li> <li>37 Blekken 2</li> <li>38 (fecal</li> <li>39 incontine</li> <li>40</li> </ul>		<ul><li>Staff discontinuity</li><li>Insufficient time</li></ul>	• For the main study, the plan is to include personal m with the director of health and social affairs and the managers of the NHs.	care d by	Unclear
41 42 43 44 45		For peer review onl	- http://bmjopen.bmj.com/site/about/guidelines.xhtml	oopyright.	

Pag	e 91 of 111		BMJ Open	.1136/bmjopen
1 2				njopen-20
3 4 5 7 8 9 10 11 12 13 14 15 16 17		<ul> <li>Large care staff</li> <li>sub-optimal use of skill-mix</li> </ul>	<ul> <li>One of the RNs from the pilot study will also be invited t share her experience and to answer questions about participating.</li> <li>The economic compensation and the recommendation releasing the responsible RNs from daily work.</li> <li>Recruitment of a local opinion leader and using the unit cluster will improve study feasibility by increasing the number of potential clusters, which impacts power mor than increasing individuals enrolled.</li> </ul>	a 255521 on #8 April 2822. Downloaded fro
18 19 20 21	Pentecost 2015 (depression)	<ul> <li>Staff attrition: randomised participants' not seeing study psychological wellbeing practitioners.</li> </ul>	<ul> <li>Finding ways of enabling PWPs to engage with study procedures is recommended.</li> </ul>	H Unclear
22 23 24 25 26 27 28 29	Clarke 2015 (childhood intermittent exotropia)	• There was a lag in recruitment due to the delay in the subsequent appointment for the recruitment clinic.	<ul> <li>The use of research nurses in all centers should be considered in a future study.</li> <li>Separation of the role of the treating clinician from the main recruiter to the trial.</li> </ul>	Unclear Unclear
30 31 32 33 34 35 36 37 38	Marshman 2012 (dental caries)	<ul> <li>Shortage in radiographs and its impact on the number of eligible participants.</li> <li>Time constraints and busy schedule.</li> </ul>	<ul> <li>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.</li> <li>The recommendation for recruitment of whole practices with participation of all members of the practice team rather than individual practitioners.</li> </ul>	φ 2024 by gue
<ul> <li>39</li> <li>40</li> <li>41</li> <li>42</li> <li>43</li> <li>44</li> <li>45</li> <li>46</li> <li>47</li> </ul>		For peer review onl	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	d by copyright.

Page	92	of	1	1	1	
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			BMJ Open	.1136/bmjopen	Page 92 of
1 2 3 4 5 6 7	Ellis 2016 (lung cancer)	<ul> <li>Inconvenient time frame between providing consent and receiving the first intervention.</li> </ul>	• The timeframe between consent and delivery of the first RDSI session has been expanded to 2 weeks.	-20	Yes
8 9 10 11 12 13 14 15 16 17 18	Latter 2018 (cancer patients at the end of life)	<ul> <li>Organisational change, team staffing levels, nurse workloads and variable flow of palliative care referrals.</li> <li>Nurses' unfamiliarity with recruitment.</li> <li>Incompatibility of recruitment procedures with nursing.</li> </ul>	• No specific changes planned to address these barriers.	18 April 2022. Downloaded from h	
19 20 21 22 23 24 25	Study ID (clinical area)	Findings associated with code: Mismatch between the trial protocol and clinical care pathways	Planned changes before the full trial	http://bmiopen.bmi.c	Were the proposed changes clearly linked to coded data?
26 27 28 29 30 31 32	Paramasivan 2017(complex obesity)	<ul> <li>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.</li> </ul>	Express enthusiasm for the study.	a 012/00 April 19, 2024	Yes
33 34 35 36 37 38 39 40	Griffin 2016 (hip impingement)	<ul> <li>Teams experienced issues such as remembering to approach patients at each possible opportunity, or the need not to discuss surgery before diagnosis was confirmed.</li> <li>Some research associates expressed</li> </ul>	process to be the least disruptive to routine clinical practice.	4 by quest. Protected by copyright	Unclear
41 42 43 44 45	<u> </u>	their concern about talking to patients For peer review only	y - http://bmjopen.bmj.com/site/about/guidelines.xhtml	opyright.	

Page 93 of 111	BMJ Open 60
<ul> <li>about the audio recording consultation.</li> <li>Various sites expressed constraints being referred for instead of 'treatment'. Source a conservative approar therefore, patients tend the physiotherapy first before surgeon appointment. Real they would find it difficult these patients or to feel convolution would agree to take part i</li> <li>Paramasivan 2011(transitional cell carcinoma of the bladder)</li> <li>The pathway that potentian participants followed from of bladder cancer to being the SPARE trial proved ext difficult because of the numpeople who might come in with the patient during the sometimes the different con (surgery or oncology, or low /regional) centres that might involved.</li> </ul>	ncern about f'surgery' me centres ch and, og of or arriving at a rruiters said to approach onfident they in the trial. Il trial a diagnosis recruited to remely mber of to contact eir visits and inical cal N 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 tull information about the trial and obtaining consent for participation. N 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 tull information about the trial and obtaining consent for participation.
36 37 38Ritchie 2015 (Cancer)• Potential delays from refe treatment.39 40 41-	<ul> <li>The remit of the funded role of trial Champion has been of the developed to encompass not only recruitment and randomisation but also coordination and facilitation of device insertion appointments and communication.</li> </ul>
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		BMJ Open	.1136/bm	Page 94 of 11	1
1 2			njopen-20		
3 4 5	Additional service provision and increased workload.		.1136/bmjopen-2021-05552		
6 <sup>L</sup> 7 8			21 on 18	11	
9 10 11 12 13 14 15 16 17		er review only	April 2022. Downloaded fro		
18 19 20 21 22 23			m http://bmjopen.bi		
24 25 26 27 28 29 30			nj.com/ on April 19		
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## S6: Facilitators for recruitment

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S6: Facilitato	rs for recruitment		1-2021-0
Citation	Findings associated with code: Altruism and personal gain	Changes planned before the full trial	Were the proposed changes clearly मुंगked 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.	<ul> <li>No changes reported</li> </ul>	18 April 2022. Downloa
Van Den Berg 2017 (Chest pain)	<ul> <li>Participation seemed motivated by altruism and the expectation that their participation may benefit both them and their families.</li> <li>Participants also perceived that the research may bring direct personal benefits.</li> </ul>	No changes reported	April 2022. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by
Bhattacharya 2011 (older people unintentionally non- adherent to medication)	<ul> <li>Patients wanted to take part to help others, to help themselves, to give payback to the NHS.</li> </ul>	No changes reported	om/ on April 19, 202
Notley 2015 (psychological difficulties)	<ul> <li>Participants expressed keenness to be involved in research, for altruistic reasons.</li> </ul>	<ul> <li>No changes reported</li> </ul>	A by guest. Protected by copyright.
Hilton 2015 (stress urinary incontinence)	Altruistic factors motivated participation.	<ul> <li>No changes reported</li> </ul>	ted by cop

	BMJ Open		1136/bmjopen-2021-05
Citation	Findings associated with code: Communicating study information	Changes planned before the full trial	Were tहिंe proposed changes clearly डुंगked to coded data?
Aventin 2016 (sexual health)	<ul> <li>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.</li> <li>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.</li> </ul>	No changes reported	18 April 2022. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by
Hilton 2015 (stress urinary incontinence)	<ul> <li>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.</li> <li>Good understanding of the study</li> </ul>	No changes reported	24 by guest. Protected by copyright.

97 of 111	BM	IJ Open	.1136/bmjo
			1136/bmjopen-2021-055521
Van Den Berg 2017 (Chest pain)	<ul> <li>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</li> </ul>	<ul> <li>No changes reported</li> </ul>	5521 on 18 April 2022. Dow
Notley 2015 (psychological difficulties)	<ul> <li>11 participants displayed a sound understanding of the randomization process.</li> <li>There was a thorough understanding of the rationale for the processes or measures used.</li> </ul>	No changes reported	vnloaded from http://bmjope
Realpe 2016 (hip impingement)	<ul> <li>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): <ul> <li>Step 1: explain what the condition is to the patient</li> <li>Step 2: reassure the patient that they will receive best treatment</li> <li>Step 3; explain that there is uncertainty about which treatment is the best</li> <li>Step 4; explain the purpose of the study</li> </ul> </li> </ul>	• 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 Yes
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	<ul> <li>Step 5; give the patient a balanced view about the advantages and disadvantages of each treatment being compared.</li> <li>Step 6; explain the study procedures.</li> </ul>		1136/bmjopen-2021-055521 on 18 ,
Hilton 2015 (stress urinary incontinence)	• Supplementary information from trial and clinic staff was seen as important.	<ul> <li>No changes reported</li> </ul>	April 2022
Crawley 2013 (chronic fatigue syndrome)	<ul> <li>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.</li> </ul>	<ul> <li>No changes reported</li> </ul>	. Downloaded from http://bmjopen.bmj.com/ on
Citation	Findings associated with code: Patients' social networks and positive experience of research	Changes planned before the full trial	/bmjoper
Van Den Berg 2017 (chest pain)	<ul> <li>Participants positive experience was sufficient to recommend participation in clinical research to others.</li> </ul>	<ul> <li>No changes reported</li> </ul>	1.bmj.com/ on
Thompson 2016 (haemodialysis patients)	<ul> <li>Patients' social networks in the unit were an effective means of disseminating information.</li> <li>Hearing other participants discuss their participation in the trial were effective means of promoting participation in the</li> </ul>	No changes reported	April 19, 2024 by guest. Protected by copyright.

99 of 111		BMJ Open	1136/bmiopen-2021
S7: Barr	iers to retention		n-2021-05
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)	<ul> <li>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.</li> </ul>	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.	April 2022. Downloaded from http://bmione
Hilton 2015 (stress urinary incontinence)	<ul> <li>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.</li> </ul>	<ul> <li>The need to complete and return questionnaires even if there are few symptoms was emphasized.</li> <li>Modify questionnaires to allow 'short-cutting' of irrelevant areas to reduce respondent burden.</li> <li>A further possibility is to link questionnaire completion at follow-up to the face-to-face clinic review.</li> </ul>	• Yes
Crawley 2013 (chronic fatigue syndrome)	• The number of questionnaires used at follow-up was considered a burden by the	<ul> <li>Measures to improve outcome data collection using a variety of strategies, including telephone</li> </ul>	Diffee Unclear Unclear

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	majority of children and parents interviewed and observed.	follow-up, would need to be implemented in a full study.	njopen-20 <u> 21-055</u>
	• Parents felt the timing of questionnaires did not allow time for change, as they were too close together.		5 <u>21 on 18 April</u>
Gray 2013 (male obesity)	<ul> <li>Focus group participants found difficulties with some of the wording in the questionnaires.</li> </ul>	<ul> <li>Fieldworkers should be given full training in assisting men with questionnaire completion if required (e.g., if participants have literacy problems).</li> </ul>	• Yes 022 Download
McEachan 2016 (infant obesity)	<ul> <li>Some of the measurement tools were found to be burdensome to complete.</li> </ul>	<ul> <li>Maintaining regular contact with participants throughout follow-up.</li> <li>A future trial should ensure that a range of communication channels are used to maximise retention.</li> <li>Strike a balance between collecting valid and reliable data and overly burdening participants, which may lead to missing data, withdrawal or trial attrition.</li> </ul>	ed from http://bmjopen.bmj.com/ on Apr
Tsianakas 2016 (recurrent or metastatic cancer)	<ul> <li>All outcome measures were judged appropriate except the Scottish Physical Activity Questionnaire (SPAQ). Eight participants reported it was repetitive and difficult to complete.</li> </ul>	<ul> <li>Alternative methods for measuring the intensity, duration and frequency of physical activity in any future study are recommended.</li> </ul>	H • Yes 9, <u>2024 by <del>guest.</del></u>
Ellis 2016 (lung cancer)	<ul> <li>Patients and carers expressed some discontent with the questionnaires and this was seen as a potential barrier to retention.</li> </ul>	• The number of questionnaires to be used in the subsequent trial will be decreased.	P• Yes

1 of 111		BMJ Open	136/bmjopen-
Kendrick 2017 (depression)	<ul> <li>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.</li> <li>Two patients pointed out that they thought that the patient questionnaire was intrusive.</li> </ul>	<ul> <li>No specific changes reported to address these barriers.</li> </ul>	open-20 <u>21-055521 on 18 April 2022. Down</u> l
Myall 2015 (cancer-related fatigue)	<ul> <li>Few participants found the questionnaires at 3-time points burdensome.</li> <li>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.</li> <li>Several participants considered the psychological aspect of cancer was missing and should be included in the questionnaires.</li> <li>Questionnaires requested the same information more than once. For some this was a source of anxiety and revealed</li> </ul>	• 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.	Inclear Unclear from http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protection

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Citation	Findings associated with: Practical barriers	Changes planned before the full trial	Were the proposed Changes clearly linked to
McEachan 2016 (infant obesity)	<ul> <li>One issue for both participants and facilitators was setting up the groups in a convenient location.</li> <li>Some participants reported making journeys that required considerable effort</li> </ul>	<ul> <li>No specific changes reported to address these barriers.</li> </ul>	April 2022. Downloaded
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.	GUnclear
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S8: CERQual Evidence	Profile_ Recruitm	ent barriers		-2021-05	
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 on confidence in the evidence ovidence	Explanation of CERQual assessment
1- Changes planned before the full trial to address issues with randomisation	(1-6)	Minor concerns about adequacy (one study reported	Moderate concerns about coherence (3 studies with well-	Moderate on the second	6 studies with moderate concerns about adequacy an coherence. No or very minor
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.		no changes to address this barrier)	grounded changes relevance, two studies with unclear fit)	from http://bmjopen.bmj.com/ on Ap	concerns about methodological limitations and relevance.
<ul> <li>2- Changes planned before the full trial to address issues with clinical equipoise:</li> <li>Changes included feedback sessions to make recruiters aware of instances where they inadvertently used loaded terminology, providing frequent training to recruiters and to</li> </ul>	(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 Protected by	12 studies with moderate concerns about coherence. No or minor concerns about methodological limitations, adequacy and relevance.

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present treatment options in a balanced way.				1-2021-055521 on 18 Ap	
<ul> <li>3- Changes planned before the full trial to address issues with patient treatment preferences:</li> <li>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.</li> </ul>	(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)	1136/bmjopen-2021-055521 on 18 April 2022. Downloaded from http://bmjopen.bmj.com/ Moderate confidence	9 studies with moderate concerns about adequacy and coherence. No or minor concerns about methodological limitations and relevance.
<ul> <li>Changes planned before the full trial to address issues related to the control group:</li> <li>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</li> </ul>	(3,6,16,19)	No or very minor concerns about adequacy	No or very minor concerns about coherence	High confidence April 19, 2024 by guest. Protected by copyright.	4 studies with no or very minor concerns about methodological limitations, coherence, adequacy and relevance.

age 105 of 111		ВМЈ Ор	en	1136/br	
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renamed 'active monitoring' and suggestions for augmenting the content of the control arm so the two arms were perceived as more equitable.	~07 ×			)21-055521 on 18 April 2022. Downloade	
<ul> <li>Changes planned before the full trial to address issues around the eligibility criteria:</li> <li>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.</li> </ul>	(12,13,17,18,20,21)	No or very minor concerns about adequacy	No or very minor concerns about coherence	.1136/bmjopen-2021-055521 on 18 April 2022. Downloaded & om http://bmjopen.bmj.com/ on April 19, 2024 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 by guest. confidence Protected by copyright.	12 studies with moderate concerns about adequacy and coherence. No or very minor

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process to be the least disruptive to routine clinical practice,					pen-2021-055	
providing frequent and comprehensive training to recruiters and to ensure that trial centres allocated adequate time and personnel.					1136/bmjopen-2021-055521 on 18 April 2022	
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	. Downloaded from http://bmjopen.bmj.com/ on	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 confiden	Agril 19, 2024 by guest. Protected by copyright.	8 studies with minor concerns about adequacy and coherence. No or very minor concerns about methodological limitations and relevance.

Page	107	of	11	1	
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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.				136/bmjopen-2021-055521 on 18 April 2022. Do	
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	(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)	Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by	10 studies with moderate concerns about adequacy. Minor or very minor concerns about methodological limitations, coherence and relevance.
mention of providing smoking cessation information and advice from the Patient information leaflets" to avoid smoking stigma.				9, 2024 by guest. Protected by copyright	

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Changes planned before the full trial to address barriers related to Integration of the trial into	(7-9,18)	No or very concerns about adequacy	Minor concerns about coherence (3 studies with well-grounded	-20	4 studies with no or minor concerns about methodological limitations,
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.		00, 10	changes and one study with unclearly linked changes)	High confidence-055521 on 18 April 2022. Downloaded from http://bmjopen.bmj.com/	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	(8,22)	No or very concerns about adequacy	No or very concerns about coherence	High confidence Fril 19, 2024 by guest. Protected by	2 studies with no or very minor concerns about methodological limitations, coherence, adequacy and relevance.

Page 10	9 of 111		BMJ Op	en		.1136/bm	
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3 4 5 6 7 8 9	both within and outside the parameters of research.					136/bmjopen-2021-055521 on 18 Ap	
10 11 12 13 14 15 16 17 18 19 20 21	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	April 2022. Downloaded from http://bmjo	2 studies with moderate concerns about adequacy and coherence. No or very minor concerns about methodological limitations and relevance.
22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40	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	pen.bmj.com/ on April 19, 2024 by guest. Protected by	2 studies with moderate concerns about coherence. No or very minor concerns about methodological limitations, adequacy, and relevance.
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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
<ol> <li>Aim</li> <li>Synthesis methodology</li> </ol>	State the research question the synthesis addresses 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)	Introduction 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 o synthesis
17. Coding	Describe the process for coding of data (e.g. line by line coding to search for concepts)	Methodology o 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 <i>Theme Matrix</i> 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 - <i>Theme Matrix</i> 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 fullscale 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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BMJ Open 2022;12:e055521corr1. doi:10.1136/bmjopen-2021-055521corr1

Check for updates

**Correction:** Using qualitative methods in pilot and feasibility trials to inform recruitment and retention processes in fullscale 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

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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BMJ Open 2023;13:e055521corr2. doi:10.1136/bmjopen-2021-055521corr2

