Applying person-centred care to support trial recruitment and retention in a randomised trial for patients with refractory breathlessness and advanced disease: a qualitative study.

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Abstract

Background Recruitment and retention in clinical trials remains an important challenge, particularly in the context of advanced illness. It is important to understand what affects retention to improve trial quality, minimise attrition and reduce missing data. Person centred care (PCC) has been shown to improve patient outcomes in advanced disease or complex needs. Therefore, we considered whether the same principles could be applied to clinical trials. This study aimed to explore what influenced participants to take part and remain in a feasibility trial of mirtazapine for chronic breathlessness. Methods Qualitative study embedded within a double blind randomised trial. Participants with cancer, Chronic Obstructive Pulmonary Disease (COPD), Interstitial Lung Disease (ILD), or Chronic Heart Failure (CHF), with a Modified Medical Research Council Dyspnoea Scale grade 3/4 were recruited from three UK sites. A purposive subsample completed qualitative interviews after the trial. Interviews were analysed using thematic analysis. Results were interpreted in relation to the core elements of PCC. Results 22 participants were interviewed. 11 had a diagnosis of COPD, 8 ILD, 2 CHF, and 1 lung cancer. Median age was 71 years (56-84). 16 were male. 20 had completed the trial, 2 withdrew due to adverse effects. Three main themes were identified as important for recruitment and retention; the relationship between patient and professional, the context, and potential benefit to self and others. Within ‘relationships’ the personal attributes of the researcher, and continuity of research team were identified as particularly important when considering why people remained in the trial. We interpreted results in relation to PCC and developed a model of the person centred trial. Conclusions We propose that a PCC approach can improve recruitment and retention in clinical trials. The importance of the relationship between the patient and professional, and continuity within the research team has implications for future funding of clinical trials, the focus of which is often based on monthly recruitment targets and not on retention. Future work should aim to evaluate this model across other settings and in countries outside of the United Kingdom. Trial registration Registry name: ISRCTN Registration number: ISRCTN32236160 Date of registration: 13/06/2016

Background

Recruitment and retention in clinical trials remains an important challenge which can impact on the validity of results by introducing bias and reducing power. Of 151 randomised control trials funded and published by the UK's National Institute for Health Research (NIHR), the target sample size was only achieved in 56% (1). Recruiting to palliative care trials can be particular challenging, with eligibility and access important considerations (2-6). However, despite overcoming these barriers, a high proportion of approached eligible patients often decline to participate in research, 57% in a recent large multicentre observational palliative care study (7).

What influences potential participants to take part in a clinical trial (or not) is recognised to be a complex multifactorial process. The research decision making model identified nine factors which predicted cancer clinical trial participation; disease context, socio-demographics, hope, quality of life, trust in healthcare system, trust in health professionals, preference for research decision control, understanding

of risk, and information (8). Many of these concepts are supported by research conducted in advanced cancer and palliative care. Results from a survey identified that financial cost, invasiveness of trial interventions, potential for side effects, and the concept of randomisation were all deterrents to taking part in a clinical trial, and that length of trial, and understanding of complex trial related information were important considerations (9). Qualitative interviews have further explored patients' and carers' preferences and expectations regarding research in the palliative care setting, and identified four motivations to take part in research: 1) altruism, 2) to have someone to talk to, 3) to provide feedback on services, and 4) to seek information (10). Awareness of what motivates participants can help to guide recruitment strategies in a clinical trial.

Retention in clinical trials is equally important, and attrition remains a well-recognised problem. A review of clinical trials in advanced cancer identified a median attrition of 26% at the primary end point, increasing to 44% at the end of the study (11). Reasons for attrition included a high symptom burden (21%), patient preference (15%), hospitalisation (10%), and death (6%)(11). Attrition can lead to high levels of missing data, the level of which, in a recent systematic review of palliative care trials, was associated with study duration and an increasing number of study questionnaires and/ or tests (12). A review of 108 randomised controlled trials of palliative care interventions found that the reason for missing data was unclassified in 53%, recorded as loss to follow up or withdrawal with no further details of the underlying reason (13). It is therefore important to understand what affects retention so that we can minimise attrition and ensure high quality clinical trials of palliative care interventions in the future.

Research within clinical trials units (CTUs) has considered methods that may improve recruitment and retention, and a survey of staff identified areas that may be important, focusing on CTUs, and how education is provided to staff (14). However, strategies to improve recruitment into trials have had variable success (15). A delphi survey of 48 CTUs identified that; methods to boost recruitment, methods to minimise attrition, and choice of appropriate outcomes need to be prioritised (16). In addition, a qualitative study of staff working in CTUs recommended that; additional support and training should be provided for researchers and clinicians, focus needs to be placed on studies which consider the effectiveness of retention strategies, and that the balance of organisational and funding body emphasis on recruitment and retention needs to be addressed (17).

It is increasingly recognised that healthcare should be centred on the needs of an individual, a concept referred to as person centred care (PCC). This approach has been shown to improve patient outcomes in advanced disease (18-20). While there is no globally accepted definition of PCC, core elements have been identified and include; patient participation and involvement, the relationship between the patient and the healthcare professional, and the context in which care is delivered (21). If we recognise the importance of PCC in delivering healthcare, then the same principles may apply to clinical trials. A person centred approach may improve patient experience and impact on recruitment and retention rates.

Improving retention in clinical trials has recently been identified as a top priority (16, 22). However, to our knowledge no studies seeking to understand recruitment and retention in palliative care trials, have

focused on participants' trial experience, and why they chose to take part in and remain within a clinical trial. This study aimed to explore patient experience in a randomised controlled trial of mirtazapine for refractory breathlessness, and what influenced participants to take part and remain in the trial.

Methods

Design

Qualitative study using in-depth interviews embedded within a randomised trial, reported in accordance with the consolidated criteria for reporting qualitative research (COREQ) (23). Interviews were conducted with patients who had taken part in a double blind randomised feasibility trial of mirtazapine for refractory breathlessness. Ethical approval was received from the UK Health Research Authority (16/LO/0091) and the trial was prospectively registered (ISRCTN 32236160).

Setting

Participants were recruited from three UK sites; King's College Hospital, Nottingham City Hospital NHS Trust, and Castle Hill Hospital. Potential participants were identified through inpatient clinical teams, multi-disciplinary team meetings, hospital clinic lists, and hospital databases. At each site there was a small dedicated research team who were involved in both the recruitment and follow up data collection across all time points of the trial.

Study participants and sampling

Those eligible for the feasibility trial were adults with cancer, Chronic Obstructive Pulmonary Disease (COPD), Interstitial Lung Disease (ILD), or Chronic Heart Failure (CHF), with a Modified Medical Research Council (mMRC) Dyspnoea Scale grade 3 ("I stop for breath after walking about 100 yards or after a few minutes on the level") or 4 ("I am too breathless to leave the house" or "I am breathless when dressing"), with no current diagnosis of severe depression, not currently prescribed an antidepressant medication. For full eligibility criteria see appendix 1. A purposive subsample completed qualitative interviews. Purposive sampling was used to achieve maximum variation within the trial population and enable exploration across a diverse group of people. Sampling was based on primary diagnosis, trial completion / non-completion, and age (<65 years / >65 years). Participants were approached by telephone or in-person to arrange an interview. All participants provided written informed consent prior to their interview.

Data collection

Qualitative interviews were conducted at the end of the trial, during which participants had received mirtazapine or placebo for 28 days. Interviews were conducted in a place of the participants choosing. This was usually their own home, but some interviews were conducted in hospital. The topic guide was developed using existing literature and refined following feedback from patient representatives and the Trial Management Group (1-6). The interview schedule included questions about experience of recruitment to the trial, why they had decided to take part, what their expectations were, and their

experience of being in the trial (taking the trial medication, experience of trial visits, and experience of completing the trial questionnaires).

Open questions were used to ensure that participants were not restricted in their answers. Interviews were digitally audio recorded and transcribed verbatim. A distress protocol was used to minimise the risk of potential harm. All interviews were conducted by one researcher (NL) who has a medical background, and had completed training in in-depth interviewing. Interviews took place between January 2017 and December 2017.

Analysis

The qualitative interviews were analysed through Braun and Clarke's framework for thematic analysis [29] using NVIVO version 10 (QSR International (UK) Ltd.). Transcripts were read and re-read and then coded inductively for themes relating to; reasons to participate in the trial, reasons not to participate in the trial, reasons to remain in the trial and reasons to discontinue the trial. Following coding the results were considered and interpreted in relation to the core elements of PCC (21). Three transcripts were double-coded by another researcher (SE) who produced their own coding frame. Areas of agreement and disagreement were then discussed until consensus was achieved.

Results

22 participants were interviewed. 11 had a diagnosis of COPD, 8 ILD, 2 CHF, and 1 lung cancer. Median age was 71 years (range 56-84). 16 were male. 20 had completed the trial, whilst 2 withdrew due to reported adverse effects of the trial medication. The mean interview duration was 33 minutes (range 15-104). See table 1 for participant characteristics based on the sampling frame.

Table 1: Characteristics of participants based on sampling frame

We identified three overarching themes which were important for both recruitment and retention; the relationship between the patient and professional, the context, and potential benefit to self and others (see table 2 for coding frame).

Table 2: Coding frame

Recruitment

Relationship between the patient and professional

Relationships were identified as an important influence when considering whether to participate in the trial. Many chose to participate because of their relationship with their usual clinician. Being approached by a familiar clinician appeared to validate the authenticity of the trial.

'It came through erm when I was at the erm, IPF meeting and my consultant was there actually that day giving a talk as well, so I figured that, you know, it was bona fide, cause you, lets face it, you don't know.'

1010, Female with ILD >65 years old

The ability of their usual clinician to listen and communicate effectively further instilled trust, and made patients more likely to participate.

'My doctor, yes, he said 'well try it, anything's worth a try'. Its our GP, yeah. Yeah, we've known him for a while, yeah. And he's a doctor that listens to you… he's very good like' 1022, Male with COPD >65 years old

The initial encounter and subsequent relationship with the research team was also important. Clear communication of trial related material established confidence in the research team.

'The interviewer, interviewers (research team) were very pleasant, very helpful, they explained everything to me and I agreed to it' 1001, Male with COPD >65 years old

One participant worried about the expectation that might be placed on them, and felt reassured when the initial assessment was tailored and focused to their individual needs.

'I thought well, you know, I hope they're not going to push me too much, you know, cause I'll just have to refuse to do it. But everything was fine, you know, spot on, you know. They understood my needs' 1014, Male with COPD <65 years old

The context

Context was important when deciding whether to participate and was considered in relation to both trial processes and the intervention. The opportunity to be visited at home instead of going into hospital was a positive influence and made people more likely to participate in the trial.

'I didn't have to go to the hospital… you do home visits, and that, that made my mind up even more to do it. Because of the struggling to walk and everything else, so I was more than happy' 1003, Male with COPD >65 years old

Although we only interviewed people who had participated in the trial, the interviews did provide some detail of influences relating to the intervention which would have made people less likely to participate. Concerns about potential adverse effects were a deterrent and one of the participants who withdrew during the trial period after experiencing adverse effects felt that more information could have been provided about the trial medication:

'It wasn't a great deal of information about the actual drug, to be honest' 1016, Male with heart failure >65 years old

Whilst some participants expressed concerns about taking an antidepressant medication, this was mostly offset by trust in the clinicians and researchers, and a belief that they wouldn't be given anything which could cause harm.

'That was my thought when they first said antidepressant 'oh, do I want to be taking something like that?' but at the end of the day, they're not going to do anything that's going to put you at any risk' 1020, Male with COPD <65 years old

Some participants explained that it was important that the trial design enabled them to continue to take disease specific medications.

'I'd contacted erm, I rang up the hospital and asked, and they said, 'yeah, you'll be ok, ones for your brain and ones for your lungs" 1010, Female with ILD >65 years old

Potential benefit to self and others

The possibility of potential benefit was a large contributing factor when deciding whether to participate in the trial. Most commonly participants described hoping for an improvement in symptoms, above all their breathing. One women living with COPD stated.

'I was prepared to try anything that would help with me breathing' 1015, Female with COPD >65 years old

Many viewed the trial as an opportunity to have extra input from clinical services. This included additional assessments prior to enrolment, as well as regular monitoring throughout the trial.

'I had a full, er, a medical before I started on the course, which was good, it eased my mind' 1015, Female with COPD >65 years old

'They just told us, as I say that we would be, regularly monitored', 1010, Female with ILD >65 years old

One participant felt that he had benefited from seeing a specialist as part of the trial.

'It opens doors at the hospitals for you, like I've got to see a specialist through it' 1022, Male with COPD >65 years old

For many, living with chronic breathlessness can be an isolating experience, and therefore the social aspect of participating in the trial was perceived as a potential benefit, with the trial providing an opportunity to meet other people who were in a similar position.

'I was gonna gain and that I would be meeting a few more people' 1009, Male with COPD >65 years old

Participants appeared to understand the concept of randomisation and were mostly accepting of the fact that they may not receive the active medication.

'Erm, well somebody's got to get it I think, you know, it, I, I don't really, I just sort of tried to take it in my stride, and whi- whichever I get, I get, cause there's not a lot you can do about it' 1001, Male with ILD >65 years old

Some participants did express concerns about receiving the placebo medication and therefore not experiencing a potential benefit.

'Only if it wasn't the drug… then it might not be a chance of it working… which you in my case seems it wasn't the drug or it wasn't working… I lost hope, lost hope in it' 1008, Male with ILD <65 years old

Altruism was also commonly described, individuals wanted to participate to help others, regardless of whether they would experience a direct benefit. One man with COPD explained that he did not expect the trial to help him, but hoped it might benefit others in the future.

'It won't do me any good but it might help other people in the future, you know. So, my expectations are in the ways that it'll help other people in the future, you know, by me taking a part in these trials' 1014, Male with COPD <65 years old

Participants also talked about their individual experience of receiving healthcare, often over a number of years, and many felt that the trial was an opportunity to be involved, and give something back to the health service.

'I have had some wonderful service from the NHS (National Health Service), and I thought well this is a chance to pay something back by taking part' 1004, Male with COPD >65 years old

Some people recognised the importance of clinical trials in the context of research, and wanted to participate to advance science, and help to develop new treatments.

'People need to know about these things… if it is going to help then I'll take part in these trials. To, you know, help, help science' 1005, Male with ILD >65 years old

Retention

Relationship between the patient and professional

The importance of the relationship between participants and the research team was identified across all interviews, and was substantial when considering the reasons why participants remained in the trial. Attempts by the research team to minimise burden and ensure a calm environment were recognised by participants.

'I found the people extremely helpful, nothing was too much trouble. Everything was explained in meticulous detail really, it was, it was so easy, everything was done for you, the drugs were all measured out you had the right number for the right days. All I had to do was wake up and pop the pill, you know. The people were lovely, it was a very very rewarding experience in a lot of ways' 1020, Male with COPD <65 years old

'Like Jen (research nurse) said, if there's any problems and you can't make it, just give us a ring or anything like that, there's no, you must arrive or that sort of thing. And it's a relaxing place, when you go

there, there's no hustle and bustle or owt.' 1013, Male with COPD >65 years old

The personal attributes of the researcher were also central to remaining in the trial. Participants described the importance of effective communication, and not feeling rushed during trial visits.

'When you came here people took the time and they listen to you. They actually ask you a question, but they listen to you, they didn't jump in and try to answer for you, you know, which I thought was good. As I say, everything was so relaxed, so calm and, you know, if I'd come here and I'd been under pressure I'd have says nah I'm not going there again' 1014, Male with COPD <65 years old

'You come to this clinical trials unit here and the girls (research nurses) are absolutely brilliant, and that does make a difference, you know that you're going to walk in there and come what may- You feel part of the family actually, now -you know, chatting, and they explain things so well don't they, and they're so patient and you know, they must get some cantankerous people in here and yet their attitude never changes in there does it?' 1012, Male with ILD >65 years old

Continuity was also important and enabled participants to build up a relationship with the research team. One participant explained that while they didn't always see the same member of the research team, someone that they had met before always made an effort to come and say hello when they first arrived at the trials unit.

'I'd go in and sit down, they'd maybe make me a cup of tea if I was waiting and whatever, then they'd come through. It wasn't always the same person, but Kim (research nurse) would pop in and say hello and she'd say so-and-so's seeing you today'. 1020, Male with COPD <65 years old

In contrast not being given clear trial related information and feeling rushed by members of the research team was reported by one participant who chose to withdraw from the trial. The participant stated that they had chosen to withdraw due to adverse effects of the trial medication, however it is possible that these two sub-themes which sit within the overarching theme of relationships may have contributed to, or influenced this decision.

'It wasn't a great deal of information… it was a bit rushed wasn't it, yeah' 1016, Male with HF >65 years old

The context

The context of trial processes and the intervention was important when considering the reasons why participants remained in the trial. The research team providing clear information appeared to ensure that the trial ran smoothly, and the offer of home visits made it easier to participate.

Being at home was perfect, you know, they were always on time, and prompt so yes, no problem whatsoever there. Oh the home visits are quite good you know. Saved me a lot of bother not going to the hospital' 1002, Male with COPD >65 years old

Participants found the questionnaires straight forward to complete and the research team were always there to provide help if required.

'If there were any problems then they would run me through the questions'. 1020, Male with COPD <65 years old

The intervention was simple and well tolerated and participants found the chart provided a useful reminder.

'It was tablets and I took them every day as I was asked to, um we made a note of them in a chart to make sure I had taken them, it was no problem at all' 1001, Male with ILD >65 years old

Trial duration was also important with a shorter duration felt to be more manageable.

'I thought that as it was also only over a 28-day period I thought yeah, I'd, I'd be quite happy to try.' 1010, Female with ILD >65 years old

Adverse effects of the intervention were an important influence for participants discontinuing the trial and were reported by both participants who were interviewed after withdrawing from the trial.

I just sat up in bed looking at the tablets and thinking, should I chance it tonight or not, because I knew how I might feel a bit groggy the next day, so it put you off taking the tablet' 1019, Female with ILD >65 years old

Potential benefit to self and others

Perceived benefits motivated participants to remain in the trial. An improvement in symptoms was described by a number of individuals.

'Everything was so much better. I would sleep better, so if I sleep better that means by breathing is better when I wake up in the morning, which it never was before… they have definitely really helped. Everything has just changed for the better, you know, you know I am so glad that I have done it.' 1003, Male with COPD >65 years old

Participants also perceived the regular monitoring they received during the trial to be beneficial. They felt taken care of and were therefore more likely to remain in the trial.

'I think the way you've conducted the trail has been very very good, the follow up has been very good. I was seen at weekly intervals to see how things were progressing, and if there were any problems, so I felt I was being taken care of in terms of the trial' 1017, Male with ILD >65 years old

The social aspect was an additional benefit for many participants and provided an interruption to an otherwise sometimes isolating existence. This was described by participants visited at home but also those who were reviewed in the trials unit.

'I quite enjoyed the experience of having somebody to come in and talk to me' 1001, Male with ILD >65 years old, visited at home

'They could've come to my home, but I prefer to come here cause it gets me out the house for an hour or two… its nice just to come somewhere and as I say, meet different people, see different people, which is half the battle when you, you know' 1014, Male with COPD <65 years old, attended the trials unit

It was important that participants felt actively involved and as though they were contributing to the trial. Knowing that the trial may benefit patients in the future, as well as providing an opportunity for individuals to give back were motivating factors for completing the trial. Several participants described how they found the trial process rewarding on an individual level.

'I just felt as though I was doing some good. It was personally rewarding for me, because I felt as though I was contributing, you know' 1020, Male with COPD <65 years old

The three important considerations which appear to improve recruitment and retention in clinical trials closely relate to the core elements of PCC identified by Kitson (21). We therefore propose a model of PCC in clinical trials which incorporates three components: prioritisation of the relationship between the patient and the professional; ensuring a person centred context; and enabling the patient to participate and be involved (Figure 1). We believe that this approach may improve recruitment and retention by ensuring that clinical trials are person centred and focused around the needs of the individual.

Figure 1: Person centred care in clinical trials

Discussion

This study identifies three important considerations closely related to PCC which may influence the decision to both participate and remain in a clinical trial; the relationship between the patient and professional, the context, and potential benefit to self and others. In this trial recruitment targets were met and attrition levels were low, suggesting that a person centred approach can improve recruitment and retention rates. We therefore propose a model of PCC in clinical trials (figure 1).

In this study the relationship between the patient and professional was crucial, and particularly important when considering what influenced people to remain in the trial. Feeling listened to, being treated with respect, and having their needs understood were important influences supporting retention. The continuity of the research team was also important, and enabled participants to build up a trusting relationship over the trial duration; one participant referred to this as 'feeling like part of the family'. In addition participants praised the research team for the extra time taken during trial visits, to ensure that individuals did not feel rushed, and that paperwork and assessments could be completed in the participant's own time. These finding have implications for the set-up of research teams across trials, to

achieve both continuity and also ensure that researchers have enough allocated time to spend with participants.

The context was another consideration for recruitment and retention. Provision of clear trial related information, the opportunity for home visits, and assistance with trial related questionnaires are all examples of how a trial can be adapted to be person centred. This approach minimises the burden placed on patients and can have a positive influence on recruitment and retention by ensuring that the trial works around the patient, and not the other way around.

The results of this study have important implications for policy and funding. Of particular interest are our findings relating to the care relationship within trials, supporting continuity of the research team. This contrasts with current funding models in the UK where the funding allocated for recruitment is often separate to the funding allocated for the rest of the trial duration. This means that the members of the research team who are funded to recruit to a trial may be different to those funded to complete trial visits after enrolment. Our results suggest a distinct benefit to having the same team working across all stages of a trial. Our results also suggest a benefit to ensuring that the research team has enough time allocated to spend with participants whilst completing trial related assessments and paperwork, so that participants do not feel under pressure or rushed. The James Lind Alliance has recently conducted a priority setting exercise involving researchers, patients, and the public, and aiming to agree priority research questions to improve retention in randomised trials. Priority question number one (from a total of 10) has been identified as: 'What motivates a participant's decision to complete a clinical trial?" (Personal Communication with The PRioRiTy II (Prioritising Retention in Randomised Trials) Study Team). We believe that this study provides initial ideas about what motivates people to remain in a trial, and we hope these results can spark the debate for future work.

Strengths and limitations

To our knowledge this is the first study to consider what influences people to take part and more importantly remain in a clinical trial in the context of advanced illness. The study used in depth interviews and purposive sampling to achieve maximum variation. While a single researcher conducted all of the interviews, interpretation bias was minimised by use of a reflexive diary, double coding of a random subset of transcripts, and discussion of findings within the research team.

The study was limited by one researcher (NL) with a medical background conducting all of the interviews. In addition some of the interviewees had met this researcher during the feasibility trial, therefore increasing the risk of social desirability bias, with participants reluctant to offer criticisms about the trial intervention and/ or processes. Some interviews were conducted with a carer present which may have impacted on the answers given. Although we achieved a balanced sample of trial participants, we only interviewed two participants who did not complete the trial, and were not able to interview anyone who declined to participate in the trial. Finally our findings are not necessarily transferable to other populations and/ or settings, and future work should aim to explore this further.

Conclusions

This study identifies importance considerations which influenced the decision to participate and remain in a feasibility trial of mirtazapine for chronic breathlessness. We propose that prioritisation of the relationship between the patient and the professional, ensuring that the context is as person centred as possible, and enabling the patient to participate and be involved can improve recruitment and retention by ensuring that a trial is person centred. Our model of PCC in trials should be considering when designing or developing a clinical trial, ideally at the pre funding stage. The results of this study have implications for the future funding of trials, and highlight the importance of a dedicated research team who have the opportunity to build up a relationship with participants across the duration of a trial. Future work should aim to evaluate this model in other settings including different populations and countries.

Abbreviations

Clinical trials unit CTU

Criteria for reporting qualitative research COREQ

Chronic Heart Failure CHF

Chronic Obstructive Pulmonary Disease COPD

Interstitial Lung Disease ILD

Modified Medical Research Council Dyspnoea Scale mMRC

National Institute for Health Research NIHR

Person centred care PCC

Declarations

Ethics approval and consent to participate

Ethical approval was received from the UK Health Research Authority (16/LO/0091). All participants provided written informed consent.

Consent for publication

Not Applicable.

Availability of data and material

Requests for data should be made to the corresponding author.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

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References

1. Walters SJ, Bonacho Dos Anjos Henriques-Cadby I, Bortolami O, Flight L, Hind D, Jacques RM, et al. Recruitment and retention of participants in randomised controlled trials: a review of trials funded and published by the United Kingdom Health Technology Assessment Programme. BMJ open. 2017;7(3):e015276.

2. Rinck GC, van den Bos GA, Kleijnen J, de Haes HJ, Schade E, Veenhof CH. Methodologic issues in effectiveness research on palliative cancer care: a systematic review. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 1997;15(4):1697-707.

3. Hanson LC, Bull J, Wessell K, Massie L, Bennett RE, Kutner JS, et al. Strategies to support recruitment of patients with life-limiting illness for research: the Palliative Care Research Cooperative Group. Journal of pain and symptom management. 2014;48(6):1021-30.

4. Ewing G, Rogers M, Barclay S, McCabe J, Martin A, Todd C. Recruiting patients into a primary care based study of palliative care: why is it so difficult? Palliative medicine. 2004;18(5):452-9.

5. McWhinney IR, Bass MJ, Donner A. Evaluation of a palliative care service: problems and pitfalls. BMJ (Clinical research ed). 1994;309(6965):1340-2.

6. Jordhoy MS, Kaasa S, Fayers P, Ovreness T, Underland G, Ahlner-Elmqvist M. Challenges in palliative care research; recruitment, attrition and compliance: experience from a randomized controlled trial. Palliative medicine. 1999;13(4):299-310.

7. Stone PC, Gwilliam B, Keeley V, Todd C, Kelly LC, Barclay S. Factors affecting recruitment to an observational multicentre palliative care study. BMJ supportive & palliative care. 2013;3(3):318-23.

8. Biedrzycki BA. Factors and outcomes of decision making for cancer clinical trial participation. Oncology nursing forum. 2011;38(5):542-52.

9. White CD, Hardy JR, Gilshenan KS, Charles MA, Pinkerton CR. Randomised controlled trials of palliative care - a survey of the views of advanced cancer patients and their relatives. European journal of cancer (Oxford, England : 1990). 2008;44(13):1820-8.

10. Gysels M, Shipman C, Higginson IJ. "I will do it if it will help others:" motivations among patients taking part in qualitative studies in palliative care. Journal of pain and symptom management. 2008;35(4):347-55.

11. Hui D, Glitza I, Chisholm G, Yennu S, Bruera E. Attrition rates, reasons, and predictive factors in supportive care and palliative oncology clinical trials. Cancer. 2013;119(5):1098-105.

12. Hussain JA, White IR, Langan D, Johnson MJ, Currow DC, Torgerson DJ, et al. Missing data in randomized controlled trials testing palliative interventions pose a significant risk of bias and loss of power: a systematic review and meta-analyses. Journal of clinical epidemiology. 2016;74:57-65.

13. Hussain JA, Bland M, Langan D, Johnson MJ, Currow DC, White IR. Quality of missing data reporting and handling in palliative care trials demonstrates that further development of the CONSORT statement is required: a systematic review. Journal of clinical epidemiology. 2017;88:81-91.

14. Bower P, Brueton V, Gamble C, Treweek S, Smith CT, Young B, et al. Interventions to improve recruitment and retention in clinical trials: a survey and workshop to assess current practice and future priorities. Trials. 2014;15:399.

15. Boland J, Currow DC, Wilcock A, Tieman J, Hussain JA, Pitsillides C, et al. A systematic review of strategies used to increase recruitment of people with cancer or organ failure into clinical trials: implications for palliative care research. Journal of pain and symptom management. 2015;49(4):762-72.e5.

16. Tudur Smith C, Hickey H, Clarke M, Blazeby J, Williamson P. The trials methodological research agenda: results from a priority setting exercise. Trials. 2014;15:32.

17. Daykin A, Clement C, Gamble C, Kearney A, Blazeby J, Clarke M, et al. 'Recruitment, recruitment, recruitment' - the need for more focus on retention: a qualitative study of five trials. Trials. 2018;19(1):76.

18. Kane PM, Murtagh FE, Ryan K, Mahon NG, McAdam B, McQuillan R, et al. The gap between policy and practice: a systematic review of patient-centred care interventions in chronic heart failure. Heart failure reviews. 2015;20(6):673-87.

19. Burton CD, Entwistle VA, Elliott AM, Krucien N, Porteous T, Ryan M. The value of different aspects of person-centred care: a series of discrete choice experiments in people with long-term conditions. BMJ open. 2017;7(4):e015689.

20. Chenoweth L, Forbes I, Fleming R, King MT, Stein-Parbury J, Luscombe G, et al. PerCEN: a cluster randomized controlled trial of person-centered residential care and environment for people with dementia. International psychogeriatrics. 2014;26(7):1147-60.

21. Kitson A, Marshall A, Bassett K, Zeitz K. What are the core elements of patient-centred care? A narrative review and synthesis of the literature from health policy, medicine and nursing. Journal of advanced nursing. 2013;69(1):4-15.

22. Kearney A, Daykin A, Shaw ARG, Lane AJ, Blazeby JM, Clarke M, et al. Identifying research priorities for effective retention strategies in clinical trials. Trials. 2017;18(1):406.

23. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. International journal for quality in health care : journal of the International Society for Quality in Health Care. 2007;19(6):349-57.

Tables

Table 1: Characteristics of participants based on sampling frame

	Male	Female
ILD		
<65 years old	1	
>65 years old	5	3*
COPD		
<65 years old	2	1
>65 years old	5	1
CHF		
<65 years old		
>65 years old	2*	
Cancer		
<65 years old		
>65 years old	1	1

*1 did not complete trial

Table 2: Coding frame

Overarching theme	Theme	Subtheme
Relationship between the patient and professional	Relationship with usual clinician	Established relationship
		Trust in clinician
		Reassurance provided by clinician
		Clinician suggested to take part
	Relationship with research team	Trial explained clearly
		No pressure to participate
		Researcher provided reassurance
		Visits not rushed
		Therapeutic environment
		Attributes of professional including communication skills
		Continuity of team
		Flexibility of team
The context	Trial processes	Home visits
		Help provided with completing questionnaires
		Easy to contact team if concerns or questions
		Diary (as a reminder for participants)
	Intervention	Simple intervention
		Low risk intervention
		Able to take other medications at same time as trial medication
		Short duration of trial
		Risk of adverse effects
Potential benefit to self and others	Altruism	To help others
		To give back to the healthcare system
		To advance science
		The feeling of doing a good thing
	Benefit	Assessed before trial
		Monitored during trial
		Improvement of symptoms
		Social interaction
		Access to specialist
		Randomisation

Each of these themes is discussed below in relation to recruitment and retention.

Figures

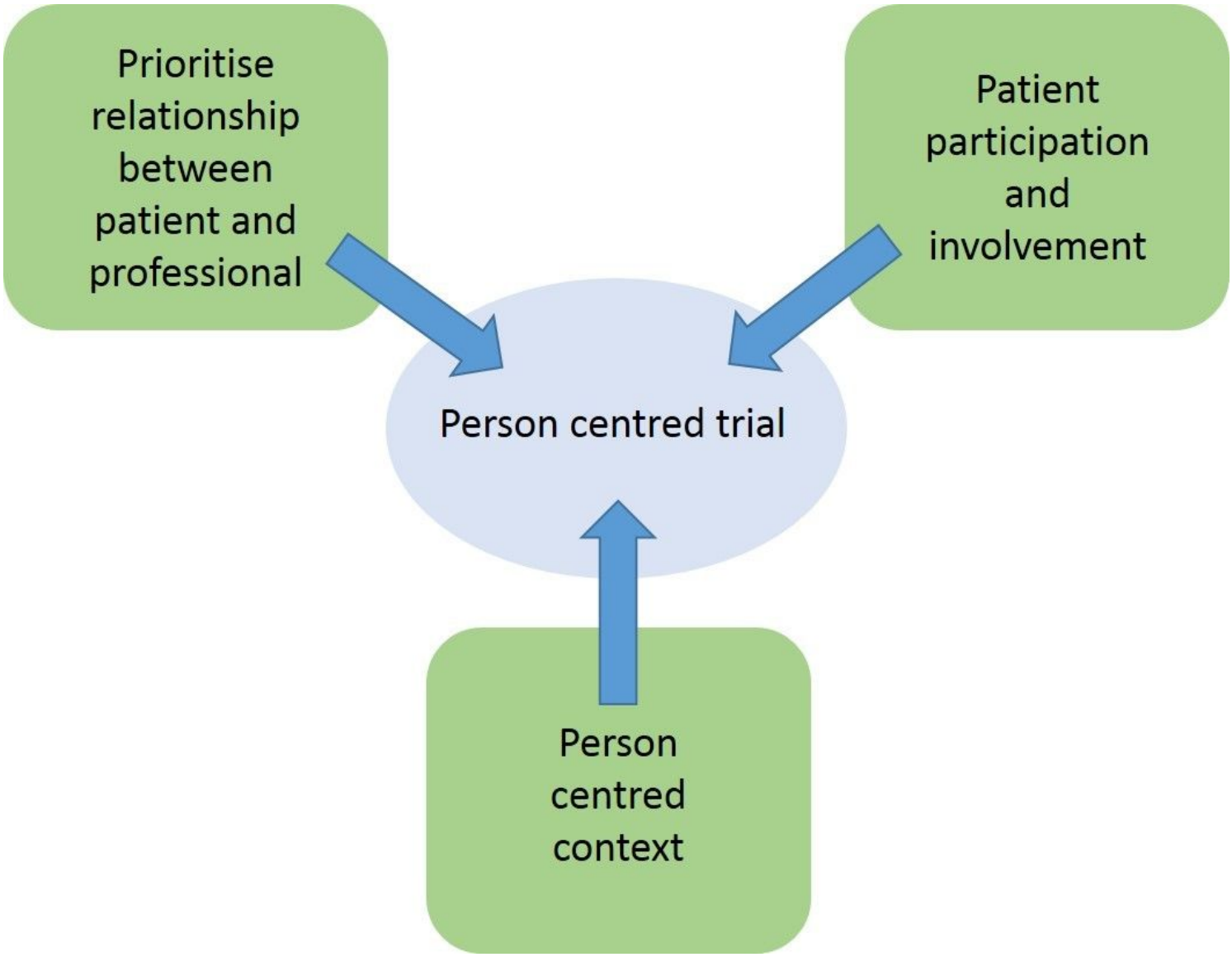

Figure 1

Person centred care in clinical trials

Supplementary Files

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