Author’s response to reviews

Title: A feasibility study of the Mini-AFTER telephone intervention for the management of fear of recurrence in breast cancer survivors: a mixed-methods study protocol

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Version: 1 Date: 31 Mar 2017

Author’s response to reviews:

Editor comments:

In addition to the reviewer comments below:

- Please include more information on how exactly the objectives will be assessed and the methods used to address each objective

Thank you to the reviewers for their comprehensive and helpful comments. This has given us the opportunity to bring out more clearly some of the real strengths of this study and its development. We hope we have addressed their concerns in full and have made significant changes to the manuscript. These include: a number of changes to the methods section, included a diagram outlining our use of the sequential explanatory mixed method design, restructured certain sections and added more detail as requested. As a result, our tables appear in a different order than previously submitted and have been labelled accordingly. We have addressed all the comments made by each reviewer to strengthen each area.

- Please would you include the ethics approval number
Number included
Reviewer 1

If this is a feasibility study with intention to undertake a full trial, it would be strengthened by including study objectives related to assessing feasibility and progressing the findings. Perhaps authors could consider objectives about identifying what data can be collected, what outcomes measured and what criteria should be met in order to assess whether a full trial can be undertaken. This would then require the addition of prospectively agreed progression criteria. Without predefined boundaries, it will be difficult to interpret feasibility ie how to decide if a trial is worth doing - and know what steps are needed to build on this study. The authors could consider whether a pilot would be required before moving to full trial since this study is only investigating theoretical acceptability by nurses, not actual adoption and implementation nor patient perspectives.

Response

This study is designed to address a specific and important element of the feasibility of delivery of a specific intervention – i.e. whether breast care nurses would be prepared to deliver an intervention to address fear of cancer recurrence. Current evidence would suggest that they are reluctant to do this. Without establishing what the barriers are to delivery and developing training to overcome this a full trial is likely to fail. As such this study is not designed to test trial feasibility objectives and further piloting would be required. We have rewritten the paper to make this clearer.

The study does not appear to have any public and patient involvement (PPI) which is a concerning omission. PPI is a requirement of much UK funding and is recommended as best practice in undertaking research. There is a strong tradition of involvement by cancer patients, including breast cancer, in relevant research. The authors should review this omission as a matter of urgency. Advice is available from INVOLVE http://www.invo.org.uk/ and other sources which are listed on that website.

Response - The study meets all the requirements for PPI. One of the co-authors (EB) is a patient representative and has been involved since the beginning and is a co-applicant. Another co-author (KS) represents the charity Breast Cancer Care and has also been involved since the beginning as a named collaborator.

Background

P3 para 1 line 7,9 - could authors clarify what they mean by patients' fears not being addressed - is it that clinicians don't recognise or treat FoR or that the fears are unfounded?
Response - This sentence has been changed to offer better clarity

P3 para 1 line 10-20 - The background would be easier to follow if the sentence 'this protocol....' were moved to the end of the introduction before the Aims of the Study paragraph.

Response - This has been moved

P3 para 3 line 58 - Also, what do the authors mean by 'manualised'?

Para 3 pp3 and 4 Please clarify whether AFTER was developed for breast cancer or any cancer.

Response - The term “manualised” has been slightly changed. However the term is widely used in psychology to indicate an evidence-based therapy that has been committed to paper in a detailed format to contain the elements and techniques for use, and hence adding to its credence when used clinically.

P4 line 12-17 - 'More generally...follow up services': please provide a bit more information here to evidence potential of the intervention.

Response - This has been changed to provide more detail.

P4 para 2 - The authors state that the mini-AFTER intervention is suitable for breast cancer nurses to deliver. If the intervention was developed for that patient group, what was the anticipated route for delivery? Was any work done to establish that nurses are suitable? If so, what and why is this additional study required. If not, why not and why are nurses now being identified.

Response - The original AFTER intervention was developed, and is now delivered by trained psychologists and specialist cancer nurses. Knowing that nurses could deliver psychological interventions, the Mini-AFTER was developed for people with breast cancer and therefore the breast cancer nurse specialists was the ideal healthcare professional due to their current role providing psychological support (ref21). Preliminary work on this development has included detailed discussions with a local group of BCN’s, assessment of fears of recurrence system, and the creation of a supervision fidelity check model. It has been tested primarily in a small controlled environment and it now ready to be tested more widely. However, we are unclear whether BCN will widely embed and integrate this intervention into their everyday clinical practice and therefore this study is a necessary step towards a trial.
I am unclear what the process has been to develop and implement the mini-AFTER intervention.

Response - The Mini-AFTER is referenced (21) and we have provided the detailed rationale for its development (page 5). Its development has been documented more clearly in the introduction. It is now ready to be tested in clinical practice.

Methods

The methods section would benefit from restructuring and better explanation of how the two study phases are planned and build on each other.

Response - We have restructured the methods to reflect various comments made by all the reviewers. In addition, we have added a diagram to illustrate the design more clearly for the reader and how the two study phases are planned. In addition, we have included a further explanation about the normalisation process theory and provided an example of how the analysis of the survey data will inform the direction of interviewing in the methods section.

I found the layout of the methods confusing. It would be easier to follow if the detailed methods were described when each phase is introduced, rather than have these reported afterwards.

Response - See comment above – we have considered all the sections of the methods and laid it out more clearly to reduce confusion.

Phase 1 domains: could the authors explain how these link to the NPT categories? The survey is said to investigate barriers but these are not mentioned in the domains.

Response - Firstly, table 1 has made it more explicit how the phase 1 feasibility domains align with the NPT framework. Questions about barriers are included in the survey and we have added in two examples into the table of questions to illustrate this. Feasibility domains align well within the NPT framework - Acceptability – coherence; demand and practicality - cognitive participation; adaptation – collective action; integration – reflexive monitoring.

Table 1: section 4, q2: how can this be measured by a scale when there does not appear to be any numerical element to the question 'how is the issue of FoR generally raised?' How do respondents report barriers and challenges to implementation without the opportunity to fill in a
free text box. Please explain how this survey was compiled and what knowledge was it based on?

Response - The table numbers have changed this is now table 2. The survey has been developed by the research team with full and frank consultation by all the team members, then reviewed by BCN’s, Breast Cancer Care nurses before it was circulated. It needed to balance the requirement to illicit the right information for the study while also being practical (not too long) to be completed by clinically based nurses.

We have amended our table to make it clearer how a scale is used – the question how is the issue of FoR generally raised is a general statement and there are sub questions such as – what proportion of your patients mention FoR in their clinic.

Phase 2: issues covered in the domains underpinning the interview schedule don't appear to match the study objectives. Could the authors look at this again? Could the authors explain how these link to NPT?

Response - Table 1 is the topic guide for the survey/interviews that was written to address overall study objectives based on the NPT framework. It provided a structure that ensured data about all the component parts that fit with barriers, challenges, successful delivery from an individual and organisational perspective, are included appropriately. In phase 1 we have asked about barriers in direct questioning (added to table 2). However in the interviews we will explore barriers (objective 3) through NPT coherence (questions about the goals and activities of the organisation), cognitive participation (the point of the intervention, skills required and investment of time, energy to deliver), collective action (exploring what promotes or impedes their work, and therefore the embedding of this intervention). The flexibility comes with the design of the study that allows analysis of phase 1 to inform phase 2.

Table 2: some of the example question topics are not questions and some are leading. It would be helpful if the authors could include something more closely matching the interview schedule showing how it links to stud objectives. At present, it does not appear to address barriers and facilitators.

Response - Please see above. Table 2 has now become table 1 with the re-ordering of the manuscript. It has been changed to reflect some of ways the topic guide translates into survey/interview questions although this will be further informed following analysis of phase 1 data.
Interview analysis p9: Normal practice is for several study team members to collaborate on developing analysis themes. More detail would be helpful here with clearer referencing to support how the process will happen.

Response - More clarification is provided

The authors do not mention how the data from phase 1 will inform phase 2. There is a strong argument in favour of using the interviews to explore in detail issues which arise in phase 1, particularly as there doesn't appear to be any existing evidence about this population using this intervention. Yet they term it a 'sequential' method. Could the authors look again at this.

Response - More detail is included

Reviewer 2

Abstract: I am a little unclear as to how the aim of Phase 2 will be achieved if the nurses are not actually delivering the intervention; could this be rephrased in terms of perceived/anticipated feasibility issues with delivery/implementation of intervention?

Response - Some changes have been made to the abstract to rephrase the aims of phase 2.

Abstract: I think that the section under discussion could be revised and expanded on slightly. I am not clear what a "neglected area of implementation" is. It would also be good to highlight what are the key feasibility issues that this study will address and how the study will be further expanded on in future research (e.g by future pilot evaluation).

Response - We have made several changes which we believe addresses this area.

Introduction

There seems to be some overlap and repetition between the first and second paragraph; I would suggest merging/condensing into one paragraph. It might also be better to move sentence regarding the protocol towards the end of the introduction, after clinical context/importance has been described.

Response - The first two paragraphs have been shortened, due mainly to the removal of the sentence regarding the protocol to the end of the introduction.
Do you have any data regarding the % of patients who actually seek help from HCPs regards FoR? Also, what type of HCPs do they typically engage with?

Response - In a study by Kanatas (2014) which we referenced, 62% of breast cancer patients wanted to discuss FoR with a health care professional. In breast cancer services it is typically a doctor (surgeon, oncologist or radiologist) and a Breast Care Nurse who engage with these patients regularly, the Breast Care Nurse providing most of the psycho-social support.

For references 7 and 8, respectively, I don't think it's necessary to quote page number or p-value.

Response - P value removed. Page number retained as this is a requirement of the Journal.

A reference should be included for Mini-AFTER at the end of third paragraph (page 4) and also when referred to in the fifth paragraph.

Response - added (21)

Reference to secondary outcomes in sentence one line 49 seems strange - would it be better just to state that "the intervention has also been shown to reduce XYZ...."?

Response - changes made

Reference 24-28 refer to other nurse led interventions; it would be good to know how these are different to the current intervention and why the proposed research is needed.

Response - We have clarified why the interventions differ. FoR is a major concern for patients. FoR has a quality of being stable once it has developed, hence forward-looking approach by introducing Min-AFTER is to attempt to reduce the likelihood of FoR increasing to a high level. The BCN is the key health professional providing emotional and psychological support and follow-up services for people with breast cancer. If no follow-up services are provided NIICE recommends all patients have access to a BCN for on-going support (viewed to encompass psychological, physical, social). Hence, they are best placed to assess fears of cancer recurrence and intervene early.
When referring to "individuals", do the authors mean breast cancer patients?
Response - Changed to patient for consistency throughout the paper.

Aims
I can't see an explanation in introduction as to FoR is classified; how are "moderate levels" differentiated from other levels of severity? Would the intervention be suitable for patients with severe FoR?
Response - We have clarified this within the introduction and referenced.

I would suggest rephrasing aims to start each bullet point with an action verb, e.g. to identify, to determine etc.
Response - this has been changed

I don't think separate headings of Design and Methods are needed - suggest using one or the other after the aims
Response - Agree. Used the heading methods only

Suggest including a reference for NPT
Response - an additional reference has been included

In describing the four main components of NPT it would be useful to cross-reference to the table which provides examples It would be useful to expand briefly on the specific data that will be gathered and inform a future RCT.
Response - All tables are cross referenced. They have been ordered differently and an additional diagram added

Is it necessary to refer to "quantitative responses"? Could you not just say that a web based survey will be administered?
Response - changed

I think it would be useful to specify that you are referring to breast cancer patients.
Response - Agree. We have changed and are consistently using the term patient throughout.

Based on some of the descriptions of issues investigated under various domains, I am not clear if they clearly align with feasibility issues? How does engagement with a training programme assessed integration?
Response - More clarification is provided

As per previous comment regarding "quantitative responses", I think you could just say that qualitative telephone interviews will be conducted.
Response - Agree and changes made

The flow/information presented between sections "study population" and "data collection" is not quite right. Recruitment/sampling of interview participants is discussed before sampling of questionnaire recipients. It might be useful to include the heading "sampling and recruitment" after study population;
Response - We have made some changes to this to improve the way we have presented the information.

It would also be helpful to highlight how questionnaire respondents will be sampled/recruited before discussing recruitment of interview participants.
Response - This is changed

How was 20 decided as the number of interview participants? Have the authors considered data saturation with the qualitative interview data?
Response - This point has been addressed more fully in the text
Data analysis

I am not clear what the "same centre" is? Or how the authors would be able to determine this

Response - Some centres have more than one BCN working there, some up to 15. We will control for this through the analysis. We specifically ask them to give us their place of work on the survey. Hence we will be able ascertain whether there is multiple membership of responders from the same ‘unit’ or ‘hospital’

I am not clear as to what the "xtmixed" and "xtmelogit" procedures are - are there more commonly used terms that can be used?

I am not clear how you will be able to "predict effective delivery" if the intervention isn't actually being delivered in the study or assessed under RCT conditions.

Response - We have clarified this and changed the section. Xtmixed and xtmelogit are well recognised statistical routines in STATA for analysing multi-level models or data that is effectively clustered. Without taking account of the clustering of the data there is a real risk of biased estimates and interpreting a statistically significant result – when in effect there was not one after all. We are aware that there may be some unfamiliarity of these multi-level methods however we are sure that the journal will support the use of techniques that will prevent biased reporting. We have supplied a reference source for interested readers to follow up our methodology. The reference we have supplied is written by the acknowledged experts in this field.

It would be useful to include a brief overview of how framework analysis will be employed in the analysis.

The study is described as "sequential explanatory" - so it would be useful to be more explicit as to if/how survey responses will be built into phase 2

Response - We have included more detail about framework analysis. The sequential explanatory process has been illustrated more clearly within diagram 1 and more detail provided within the text.

Discussion

I am unclear as to what "exacerbated FoR" is and if this is distinct from the "moderate" levels that the authors have previously referred to.
Response - We have clarified the use of terms throughout and referred to high or moderate FoR for ease of understanding.

Is this intention to go straight to an RCT after this study?

In the final sentence the authors state that they aim to develop and deliver the intervention - has the intervention not already been developed? Is development part of this study? Were the authors involved in the development process?

It would also be good to highlight what are the key feasibility issues that this study will address and how the study will be further expanded on in future research (i.e. in any future evaluation).

Response - You are right, the intervention is already developed and we have included more details about this to strengthen our manuscript. We will probably have to do a further pilot to test manual adherence, ICC estimation etc which we have clarified in the text but this work will enable us to know whether the conditions to delivering the intervention in practice can be achieved and therefore the likelihood of a future trial being successful.

Hopefully the restructuring of the methods and increased detail has addressed some of this. Although we don’t want to assume what happens next before data are gathered, we have indicated the importance of understanding all the difference component parts to understand if we should proceed to another pilot.

Reviewer 3

"a sequential explanatory mixed-methods study" - this study design is mentioned several times, but never defined for the non-specialist (this journal must have a wide readership!). It becomes clearer over the course of the article what is meant, but a clear explanation and references at its first mention will help.

Response - We have included a diagram adapted from Ivankova (ref 30) to explain the design more fully to a non-specialist.

Similar issue with "eight point adaptive quadrature procedure" (p.9 line1): explain and/or give references.

Response - We have continued to include this term as it a statistical method that will be used but have given more information in the analysis section on both the xtmixed and xmetogit procedures. A reference is also added (42).
Say more in the design section (Phase 1) about other variables being collected: age, gender, seniority(?), as I assume these will be adjusted for or stratified by in the analysis of the survey responses?

Response - Demographic variables are now described in the sampling and recruitment section plus examples of how this translates into the survey is included in table 2. Yes ,we will stratify/adjust for age, location, yrs qualified, yrs in BCN position etc.

More should be said in the limitations section e.g. about the potential biases that might impact the findings from the possible low response rate, and by only recruiting from the Breast Cancer Care Nursing Network

It would be beneficial to the study if other sources of nurses could be found to take part in the study. Have the authors considered emailing other nursing organisations, websites/newsletters that target nurses, all hospitals that have a breast cancer MDT? If they have and decided not to, this should be detailed in the paper

Response - We have re-written the limitations section. There are many nurses who care for people affected by breast cancer but we are only targeting Breast Cancer Nurses (BCN) as the intervention was developed specifically for this group to use. It is possible to access these nurses through other networks and we have used these networks to raise awareness of the study and share the link. However, based on data reported by Macmillan (reference 36-39) and Breast Cancer Care, the Breast Cancer Care network is pretty comprehensive and the only known database. We acknowledge this may have limitations accessing BCNs through a single point and have therefore taken measures (described in recruitment and limitations) to raise awareness of the study through national and regional means.

Background

I would move the end of the first paragraph, to the end of the Background: from "This…” (p. 3 line 10) up to "…intervention." (p.3 line 20)

Response - This has been done

Reference the Delphi Study (p.3 line 29)
Response - We had already referenced the paper but made it clearer that the FoR definition was derived through a Delphi technique.

The acronym AFTER needs to be explained where it first appears; suggest moving the two sentences from "The acronym…” (p.4 line 3) to "…symptoms [16,17]" (p.4 line 10) to p.3 line 59 after "…levels of FoR."

Response - Good idea. We have moved it.

Design

*Say more about the RCT planned

Response - we have included more information

How was the sample size of 20 nurses to interview determined?

Response - We have included more detail about this as we will be using a purposive sampling matrix.

p.8 line 17: give details here of the eligibility criteria. These should also be included in the online survey in case ineligible nurses try mistakenly to fill in the survey

Response - A more detailed explanation of this is provided

The purposive sampling is described, but it would be useful to know more about how the criteria listed will be allocated among the 20 participants. What groups will there be e.g. number of years qualified: over 5 vs less than 5 years etc? Is there an aim of 4 nurses with each of the 5 criteria?

Response - This is provided in more detail as described above

I assume the nurses who test the survey will not be eligible for the main study. How many will test it?
Response - The BCN population is static. Full exposure to the intervention has been limited to enable this population to be used in a future cluster randomised trial.