Author's response to reviews

Title: Relating Therapy for voices (the R2V study): study protocol for an external pilot randomized controlled trial

Authors:

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Author's response to reviews:

Thank you for the helpful comments from reviewers. Below we have outlined how we have responded to reviewer comments.

Reviewer 1

Major Compulsory Revisions:

1. Research Objectives: The objectives are clear and appropriate for a feasibility study. Could the authors clarify what they mean by ‘disturbance’ associated with distressing voices and how disturbance differs from distress?

Response - Thank you for this comment. Following the recent publication of an analysis of PSYRATS-AH data (N=711) using structural equation modelling (Woodward et al, 2014), we have revised our hypotheses. The Woodward study identified 4 subscales – Distress (negative content, distress, and control), Frequency (frequency, duration, and disruption), Attribution (location and origin of voices), and Loudness (loudness item only). We hypothesise that Relating Therapy will impact primarily upon the Distress subscale. The manuscript has been revised to reflect these changes to the hypotheses.

2. Hypotheses:

• Hypothesis 1 – is the focus on general distress or voice-related distress? Please clarify.

Response – this hypothesis concerns voice-related distress as measured by the Distress subscale of PSYRATS (as identified by Woodward et al, 2014). The manuscript has been revised to reflect this.

• One of the aims of Relating Therapy is to re-balance the hearer-voice relationship with regard to both power and proximity, yet there does not appear to be a hypothesis about power/proximity. Unless hypothesis 2 measures these
dimensions, an additional hypothesis regarding power/proximity is required. If this is implied in hypothesis 2, then the terms power/proximity should be explicit in the hypothesis.

Response – the influence of power and proximity is captured by the second of the secondary hypotheses. Specifically, reductions in Distress will be mediated by a reduction in VAY Voice Dominance (power) and reductions in Voice Intrusiveness and Hearer Distance (proximity). The manuscript has been revised to reflect these more precise definitions.

3. Methods/Design: Is the Cognitive Therapy Checklist really an appropriate measure of adherence? Would the authors consider developing a specific Relating Therapy adherence measure of the purpose of this trial?

Response – We will use the general therapy items from the CTS-Psy (feedback, understanding, collaboration, etc.) to assess therapist adherence to general therapeutic principles, in combination with dedicated therapy specific items which have been written, using the CTS-Psy format, to assess adherence to relating therapy. We have piloted this approach on a selection of recordings and it appears a viable means of verifying quality control, appropriate to this stage of trialing the intervention.

4. Participants: It is not clear to me why a primary diagnosis of substance misuse is an exclusion criterion?

Response – this is a standard exclusion criterion that my colleagues and I have adopted in trials of psychological therapy for voices (e.g. Dannahy et al., 2011). This criterion is adopted to reduce the likelihood of participant engagement in therapy being disrupted by the altered state of consciousness that can be associated with significant use of illicit substances. The focus upon a ‘primary’ diagnosis of substance misuse attempts to restrict exclusion to people who have significant problems with substance misuse.

Minor Essential Revisions:

1. Introduction: The Introduction is well-written. However, I think the Introduction would benefit with mention of the fact that more recent CBT for psychosis trials, and CBT trials for distressing voices, no longer focus on voice reduction as their primary outcome (i.e. the aim of these trials is not to eradicate voices).

Response – a sentence has been added to the introduction stating that: A factor that may have limited the effect of CBTp upon voices concerns outcome measurement – as early trials used measures of voice frequency and severity, despite CBTp not focusing upon the eradication of voices

2. Spelling: Separate out feasibility/pilot as these are two different things (rather
than or, as the ‘/’ symbol implies). Also, p. 6 – ratter should read ‘rater’.
Response – the study is an external pilot – and has been labelled as such. The
_typographical error has been addressed.
Reviewer 2
Minor essential revisions:
1. The authors describe their study variously as a ‘feasibility/pilot’ study and as
‘feasibility RCT’. It would be good practice to consider whether this is a true
feasibility study or a pilot study. The study appears to be a small scale
implementation of the full protocol and I would suggest the authors use a
consistent language to describe the study, possibly based on a referenced
previous discussion of these distinctions. I find the NIHR distinction of internal
and external pilot also a useful structure to consider.
Response – This was helpful advice and the design has been called an external
_pilot throughout. NIHR define an external pilot as a study which is a small scale
version of the full study to test if the elements of the full study function as
expected, such as recruitment, retention and completion of assessments. This
study is an external pilot because we do not intend for the data to contribute to
the definitive trial. The manuscript has been revised to reflect this description.
2. The authors should identify how many therapists they will be training to offer
the treatment
Response – five experienced clinical psychologists/nurse consultants will be
delivering the therapy. Two of the therapists (including the CI) are familiar with
the therapy having previously delivered it within the case series (Hayward et al,
2009). The three remaining therapists are experienced in the delivery of
psychological therapy for psychotic experiences within trials, and have been
trained by the CI on the delivery of Relating Therapy. The manuscript has been
amended to reflect these details.
3. The authors should state a little more about the pathway stage from which
participants will be recruited, in particular will the TAU arm systematically include
CBT for psychosis, or will participants have already been offered CBT?
Response – All participants will be receiving treatment as usual from an NHS
mental health service. This will include anti-psychotic medication and regular
contact with a member of their clinical team. Participants will be required to have
no definite plan to receive psychological therapy for voices at the time of
consenting to the study. There are no other requirements exist for previous or
future therapy. The manuscript has been revised to include this description of
TAU.
Discretionary revisions
1. The authors refer to a previous ‘feasibility’ study that established the acceptability of the intervention; it is not clear whether this study also reported core feasibility parameters such as described in the NIHR feasibility/pilot discussion paper (www.ccf.nihr.ac.uk/.../Feasibility%20and%20pilot%20studies.docx). It would be useful to clarify this.

Response – the previous study was a case series and has been accurately labelled as such.

2. In the participants section the authors assume a 20% attrition rate; they may wish to delete this assumption? Is this assumption taken from the earlier feasibility study and if not does this not pre-suppose one of the core outcomes of the study? In the analysis section the authors identify that the purpose of the feasibility study or external pilot is to establish the actual conversion from first approach to consenting and the actual attrition within treatment and to follow-up. For both true pilot and true feasibility it can be helpful to consider (and state) the levels of conversion and attrition that will suggest that the study is feasible and what levels would suggest it is not, if this is the case is the 20% attrition described a minimum level above which the study will not be considered as feasible for Phase III trial?.

Response – this is a helpful comment. The wording of the manuscript has been adjusted to reflect the expectation that there is likely to be attrition (and hence the need to over-recruit), but does not specify the likely attrition as this information will be offered by the proposed study.

3. The use of pilot studies to establish a simple effect size is open to significant discussion (e.g. Leon et al, J Psychiatr Res. May 2011; 45: 626–629) as the sample effect size may not be a good estimate of the population effect size. Other important parameters to determine the suitable sample size for the Phase III trial might include clinically significant change. The authors may wish to consider this issue in the analysis section.

Response – The suggestion to focus upon clinically significant change is welcomed. Taking a reduction of 1 point on a PSYRATS-AH item as having clinical meaning (i.e. representing a move from a higher response category to a lower response category), we propose that a difference in change scores (T0-T1 and T0-T2) between intervention and control groups of 5 points for the 5-item Distress subscale will represent a Minimally Clinically Important Difference. We expect the 95% confidence interval for the effect size to contain this. The
manuscript has been revised to include this additional aspect of the analysis.

4. Fidelity is covered relatively briefly, how significant will the adaptation of the CTC need to be to be able to identify the key differences in the relationally based therapy compared to other forms of CBT and are the authors confident this will not need significant work to establish the reliability of such ratings.

Response – see response to reviewer 1

Editorial requests:

1. Please ensure the title conforms to journal style for study protocol articles. The title should follow the format ?_________: study protocol for a randomized controlled trial.? 

Response – the title has been amended as requested

2. Please include the date of registration with your trial registration number at the end of your manuscript.

Response – the ISRCTN number and registration date have been inserted at the end of the manuscript

3. Please include a statement in your Methods section explaining that you obtained informed consent from each participant.

Response – a statement has been added to the Methods section.

4. Please include a figure title and legend section after the reference list.

Response – the figure title has been inserted at the end of the manuscript