Reviewer’s report

Title: Developing Substance Use Programming for Person-Oriented Recovery and Treatment (SUPPORT): Protocol for a pilot randomized controlled trial

Version: 0 Date: 19 Oct 2017

Reviewer: Susanna Dodd

Reviewer’s report:

Thank you for submitting this well-written, interesting study protocol. I have a few comments relating to the structure of the paper and statistical issues:

1) Please add "Protocol for" before "a pilot randomized controlled trial" in the title of the manuscript.

2) It would be helpful to add two sections to the end of the "Background": firstly relating to the study "Hypothesis" and secondly the "Aims and Objectives" of the study. There may be primary and secondary objectives, which would link to the primary and secondary outcomes of the study (see next point). The primary objectives of a pilot study should relate to the demonstration of feasibility/acceptability/deliverability/safety etc of the interventions/outcome assessments/recruitment/randomisation, etc or to provide reliable estimates for sample size calculation for a future definitive trial.

3) Please clarify the primary and secondary outcomes. The primary outcomes of a pilot study should link directly to the pilot/feasibility objectives; therefore, there should be primary "feasibility" outcomes as well as primary (and/or secondary) "patient-centred" (or "efficacy") outcomes of interest. Please label your primary and secondary outcomes accordingly (eg as primary feasibility outcomes, primary efficacy outcomes, secondary efficacy outcomes, etc).

4) The description of the randomisation process (using a pre-established list) suggests that there is no allocation concealment. Allocations must be concealed in order to prevent selection bias; can you provide information on how this will be achieved (e.g. through the use of sealed opaque envelopes or telephone randomisation)?

5) Analysis of a pilot study should focus on confidence interval estimation, rather than hypothesis testing or statistical modelling, as the limited sample sizes used in pilot studies mean that they are typically underpowered for statistical testing. Although it is interesting to explore possible outcomes, inferential statistics should be used with great caution. As such, please could you rephrase the statistical analysis section, clarifying that the analysis will focus on confidence interval estimation, and that any hypothesis testing will be considered entirely exploratory in nature. The authors may be interested in the following useful references with regards to this issue:


Eldridge et al (2016) CONSORT extension to pilot trials is also a useful reference and contains examples. Pilot and Feasibility Studies, 2:64

6) Please could you clarify the sample size statement? Pilot studies are not usually powered to detect significant differences between randomised groups, as the purpose of pilot studies is not to provide definitive results in terms of powered statistical comparisons. Instead, sample sizes are usually justified in terms of providing sufficient precision for estimation of parameters to inform sample size estimation for future definitive clinical trials. The authors may be interested in the following additional references in relation to this issue:


You have quoted a minimum clinically important difference (MCID) of 10 days between groups (after 1 year of treatment) in your sample size calculation - and the justification for this is an average of 7 days observed after 6 months of IN-ATR treatment. This would suggest that you expect the treatment effect to increase from (at least) 7 days after 6m to (at least) 10 days after a year's treatment - is this realistic? Also, the power calculation suggests in excess of 99% power, using the parameters provided in the sample size section - please could you clarify the MCID on which the power calculation has been based?

7) Pilot studies should be assessed in terms of progression criteria related to the feasibility objectives of the study. Please could you describe the feasibility criteria on which the pilot study will be assessed (eg recruitment/consent rate > 50%, acceptability or retention > 70%) with threshold values for each criterion, which would inform the readers if a future study is indeed feasible.

8) I understand that the CAPI interviews at 15m are carried out in the SUPPORT group only, "to understand retention of treatment effects three months post discharge". Is it not equally important to assess treatment effect retention in the TAU group, to allow comparison with the SUPPORT group?
9) When follow up data are missing due to incarceration, would it be possible to use this information ("negative" reason for missingness) to inform meaningful interpretation of the missing results (eg imputing a poor outcome for these patients in a sensitivity analysis)?

10) The data monitoring section refers to "preliminary analyses of the data (at 6, 12 and 15 months)”: please can you specify what these analyses will involve, to ensure transparency relating to multiple testing of outcome data? For example, will these analyses relate only to safety outcomes, or will there be between-group interim analyses conducted prior to the end of the study? If the latter, do you have stopping rules on which to base any decisions in relation to stopping the trial early, which will account for the impact of multiple testing on subsequent interpretation of the final analyses?

I have a few minor comments (note that page numbers relate to those in the pdf, rather than the number at the bottom of each page of the manuscript, which is one less than the pdf page numbering):

p8 line 12: add a full stop after coach

p8 line 31: put a semi-colon (rather than comma) between "vouchers" and "rather"

p8 line 41: replace "few" with "fewer"

p11 line 12/14: please check this sentence for meaning ("attendance at self-report attendance...")

p12 line 41: add a comma after "eligibility"

p12 line 53: add closed bracket ")" after "technology"

p17 line 17: add "and" between "organizations" and "a more diverse group..."

p30 line 39: add apostrophe after "subjects" (ie subjects') and comma after "date of birth"

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An article of importance in its field

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Please indicate the quality of language in the manuscript:

Acceptable

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