Author's response to reviews

Title: Using mobile technology to deliver a cognitive behaviour therapy-informed intervention in early psychosis (Actissist): study protocol for a randomized controlled trial.

Authors:

Sandra Bucci (sandra.bucci@manchester.ac.uk)
Christine Barrowclough (christine.barrowclough@manchester.ac.uk)
John Ainsworth (john.ainsworth@manchester.ac.uk)
Rohan Morris (rohan.morris@manchester.ac.uk)
Katherine Berry (Katherine.berry@manchester.ac.uk)
Matthew Machin (matthew.machin@manchester.ac.uk)
Richard Emsley (richard.emsley@manchester.ac.uk)
Shon Lewis (shon.lewis@manchester.ac.uk)
Dawn Edge (dawn.edge@manchester.ac.uk)
Iain Buchan (buchan@manchester.ac.uk)
Gillian Haddock (gillian.haddock@manchester.ac.uk)

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Author's response to reviews: see over
Dear Editor

Thank you for the suggestions made by the reviewer and the editorial comments regarding our manuscript re-titled: “Using mobile technology to deliver a cognitive behaviour therapy-informed intervention in early psychosis (Actissist): study protocol for a randomized controlled trial”. Each of the points made by the reviewer has been considered and addressed, and the amendments are outlined below. Please find the reviewer’s comments below (in bold), followed by information on how we have addressed each of the points raised and text we have inserted in the manuscript (in italics).

Reviewer’s report


Thank you for highlighting this point. We have added the following information in the background of the manuscript:

Cognitive behavioural interventions have been the most robustly evaluated psychological approach for psychosis. Wykes and colleagues [6] carried out a meta-analytic review of 34 CBT trials targeting people with a schizophrenia-related diagnosis across various countries. There were overall beneficial effects for the target symptom in 33 studies (effect size = 0.400; 95% CI = 0.25, 0.55) as well as significant effects for positive symptoms (32 studies), negative symptoms (23 studies), functioning (15 studies) and social anxiety (two studies) with effects ranging from 0.35 to 0.44. Overall, results from this meta-analysis indicated a ‘modest’ effect size in improving positive symptoms compared to standard psychiatric care (TAU). Jauhar and colleagues [7] recently updated the Wykes et al. [6] systematic review and meta-analysis of Cognitive Behaviour Therapy (CBT) for core schizophrenia symptoms and found results from randomised controlled trials were broadly consistent with previous results. Fifty-two studies from various countries were included in the meta-analysis. There was an overall significant but modest impact of CBT on psychotic symptoms, with blinded studies showing lower effect sizes on overall symptoms and positive symptoms, but not for negative symptoms. However, this latter meta analysis has been criticised for its over-simplification of the complexities of psychosis presentations and psychological interventions.
Given the available evidence, CBT is recommended as a first-line intervention by NICE [3].

2. Similarly, a balance view of strengths and limitations of the use of mobile phone device or information technology for behavioral interventions should be explained and how (some of) these weaknesses will be addressed in your proposed study.

We have added a section in the Discussion section of the manuscript highlighting the strengths and weaknesses of mHealth research, and in particular how we attempt to overcome some of the weaknesses. Three weaknesses we have identified include using appropriate trial methodology so that trials can match the pace of software development, affordability of smartphones for low income individuals, and developing ways to measure therapeutic alliance with mobile devices. These points are addressed in the Discussion as follows:

Mobile, wearable and ubiquitous technologies are advancing at an unprecedented rate. Therefore, a major research challenge is being able to rigorously evaluate mobile health (m-health) interventions using robust scientific methods, such as RCTs, appropriately. One possible way to evaluate mHealth interventions is to adopt more sophisticated trial methodology. In standard RCTs, the intervention is fixed at the onset of the trial and is not permitted to evolve during the trial duration. Indeed, for many drugs under investigation or complex interventions, this is reasonable. However, for digital interventions, this is problematic due to the pace of change in such interventions; fixing the intervention at trial onset can render it obsolete by the time the trial results are available. Apps can also costly and can be time consuming to develop, such that the app might be out-dated by the time it is completed. Therefore, ideally, trials of digital interventions need to be adapted to allow the intervention, and potentially the control arm, to evolve as the trial progresses. Another anticipated challenge in the mHealth field is that low income individuals may not be able to afford smartphones or indeed the sufficient levels of data necessary to run apps and other smartphone functions. To overcome this potential problem, we provide participants with mobile phone handsets and cover data network charges. However, factors such as these could be a practical barrier to continuous mHealth services. From a psychological perspective, therapeutic alliance is a key predictor of outcomes in psychological therapy [53]. Mobile technology has been criticised for lacking this essential therapeutic ingredient. Nonetheless, there is an emerging literature regarding the concept of therapeutic alliance in the context of electronic health (eHealth) and mHealth ranging from alliance service users may form with any therapist supporting the technology to ‘relationships’ that service users may form with mobile devices or apps themselves [54]. We propose to contribute to this emerging literature by developing a measure of alliance to the Actissist app and determining the feasibility of administering the new measure. Furthermore, if trials such as Actissist are effective, a major challenge is for mental health services to recognise and incorporate digital interventions into mainstream health service delivery. Indeed, compatibility issues could pose significant barriers to real-world implementation due to the fast paced development in mobile
technology and platforms. One possibility for future research following this trial would be to run a pragmatic trial of the Actissist intervention in routine mental health services.

3. Please also explain why the service users are randomly allocated at a ratio of 2:1 into the study groups.

Since this is a feasibility study, we aim to find out as much information as possible from service users who are allocated to and use the Actissist intervention. Therefore, we ensure that most of our service users in the study are allocated to Actissist. As hypothesis testing is not the aim of this study, we are not concerned by the (slight) loss of power arising from an unequal allocation ratio. We have added a line on page 8 to highlight why we are using 2:1 allocation as follows:

Since this is a feasibility study, we aim to find out as much information as possible from service users who are allocated to and use the Actissist intervention. Therefore, we ensure that most of our service users in the study are allocated to Actissist by using a 2:1 allocation ratio.

4. Please describe any criteria or clinical assessment to confirm the service users are early psychosis or any co-morbidity allowed in your study.

Our inclusion criteria is such that participants are required to be registered with, and receiving treatment from, early intervention for psychosis teams in the North West of the UK. As such, all participants will have completed a rigorous assessment procedure including PANSS administration, clinical assessments and regular reviews with the team’s consulting psychiatrist, psychologist and care co-ordinator input. We have deliberately kept our inclusion criteria as broad as possible as the primary driver of our study is to increase access to psychological interventions for psychosis and related problems. This is reflected in the statement we included in the ‘Inclusion and exclusion criteria’ section of the manuscript. We also believe this approach improves the external validity of the trial.

5. Sample size estimation or not done should be described and explained. It is also important to explain how the sentences under Statistical Analyses section: ‘The proposed sample size is sufficient size for establishing feasibility and obtaining parameters to inform a robust power calculation for such a later trial’ be proved or supported by relevant literature on sample size or power calculation, statistics or any related research.

In order to estimate the standard deviation of our outcome variables to inform a future sample size calculation, sample sizes between 24 and 50 have been recommended. Julious (2005) recommends 24 participants, Lancaster, Dodd & Williamson (2004) recommend an overall
sample size of 30 and Sim & Lewis (2012) recommend at least 50 participants. Hence our proposed sample size of 36 is within the range recommended in the literature. We have added a section on sample size on page 15 of the manuscript and include the following references:

*Since hypothesis testing is not the objective of this study, formal power calculations are not appropriate. In order to estimate the standard deviation of our outcome variables to inform a future sample size calculation, sample sizes between 24 and 50 have been recommended [44-46]. Our proposed sample size of 36 is within the range recommended in the literature and is sufficient for establishing feasibility and obtaining parameters to inform a robust power calculation for such a later trial.*

Additional references include:


6. **There is not a clear plan for testing or comparing the outcome data at the post-tests between groups, using inferential statistics. Please further elaborate.**

We disagree with this comment. In the statistical analysis section on page 14, we state that: “To inform potential effect sizes for a future definitive trial we will use linear regression to examine the effect of random allocation on the secondary outcomes at post-treatment, adjusting for outcome measures at baseline. Presentation of the analysis will focus on point estimates and associated 95% confidence-intervals rather than statistical significance (P-values).”

We are planning to conduct a linear regression, with the post-treatment secondary outcome measure as the dependent variable and random allocation and baseline secondary outcome measure as independent variables. This is equivalent to an ANCOVA approach. In this study, we are not concerned with inferential statistics (p-values), but will present point estimates and 95% confidence intervals (which we expect to be large, due to the small sample size).

Thank you for the opportunity to respond to the reviewer’s comments. We look forward to your response.