Author's response to reviews

Title: Improving the outcomes of primary care attenders with common mental disorders in developing countries: a cluster randomized controlled trial of a collaborative stepped care intervention in Goa, India

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Author's response to reviews: see over
Reviewer’s report:
This is a nicely done trial and I would like to see the protocol be published. I have two comments.

1) It would be nice to see further details of randomization. In particular, I was looking for details of procedures that would ensure that randomization could not be interfered with. It seems possible, for example, that the statistician could misallocate a practice or a researcher change allocation later. To prevent this, you need some procedures. For example, what about something like:

The researchers randomly assign code numbers to each GP practice.
The list of the codes numbers is sent to the statistician, who assigns each code number to the intervention or control group.
The statistician sends the list of code numbers and allocations back to the researchers.
At the end of the trial the statistician’s list and researcher’s list can be reconciled to check that all practices were allocated as they should have been.

Response: We used a specific seed number for the randomization so the allocation be replicated. This guards against misallocation or changes in allocation by researchers. We intend to use the same process for allocating GP practices, which has not yet been carried out. We have amended the paragraph on randomization as follows:

**Selection of Facilities/Randomisation:** The sampling frame for phase 1 consisted of PHCs with minimum space available for the intervention team and which were not involved in preliminary phases related to the intervention development, and which have at least 350 attenders per month. Facilities were stratified into three strata; urban with a visiting psychiatrist (VP), rural with a VP, rural without a VP. Two intervention and two control PHCs were selected at random from each stratum, using the www.randomization.com software by the MANAS trial statistician (HW). A given seed number was used to enable the randomization procedure to be reproduced. This guards against misallocation or changes in allocation at a later stage. The sampling frame for phase 2 will consist of all GPs with adequate clinic space and who consent to participate, and will be similarly stratified.

2) In the statistical analysis, I disagree with: "Any of the a-priori defined confounding factors for which randomization did not achieve balance between the two arms at baseline will be adjusted for". Such an approach is data dependent, and is not 100% reproducible (e.g. different statisticians might disagree as to what counts as an acceptable level of "balance"). Moreover, a variable that is predictive will improve statistical precision even if there is no imbalance. I therefore suggest that the authors write down a list of variables that they believe are likely predictive of outcome and then include those as covariates in the final analysis, irrespective of differences between groups or lack thereof. Incidentally, baseline mental health scores must go in the model, as doing so dramatically improves power (see Frison and Pocock, Stat Med 1992).
Response: We agree with the reviewer that variables to be adjusted for should be defined a-priori. As the reviewer suggests, the most important variable is baseline mental health score and we will adjust for this. However, as this is a cluster-randomised trial with relatively few clusters, there is likely to be some degree of imbalance between arms with respect to other confounding factors. We plan to carry out secondary analyses adjusting for these other factors which have been listed in the paper.

The paragraph on analysis has been amended as follows:

The primary analyses will be intention-to-treat, regardless of adherence to the intervention, and will be based on outcomes 6 months after diagnosis. Logistic regression generalized estimating equations with robust standard errors will be used to compare case prevalence in the two arms, allowing for any within-facility clustering resulting from the cluster randomized design, and adjusting for baseline mental health score. Further analyses will adjust for any other of the a-priori defined confounding factors list above for which randomization did not achieve balance between the two arms at baseline. These analyses will be carried out for the different patient groups defined in Table 3, with their respective outcomes as described above. For each of these primary outcome analyses, we will present an estimate of the effect size as an odds ratio and 95% confidence intervals, and a coefficient of intracluster correlation. A number of secondary analyses are proposed, which are listed in the Trial Registration protocol.