Reviewer's report

Title: Psychological distress and its relationship with non-adherence to TB treatment: findings from a multicentre clinical trial

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Reviewer: John Metcalfe

Reviewer's report:

The study by Theron and colleagues is of great interest and clearly warrants publication. The topic is timely and the parent study impressive.

Major

My single major inquiry has to do with the definition of non-adherence. Granted that no single accepted definition exists, use of one missed DOTS visit seems to lack clinical significance. The fact that some allowance for intermittent dosing has been acceptable in WHO guidelines suggests a certain degree of flexibility in dosing schedules. Most desirable would be to look at treatment default, or adherence as a continuous measure (proportion of doses taken). If these options are not feasible, sensitivity analyses using greater cut points could be an alternative.

Minor

Non-specific psychological distress is less compelling than well-validated psychiatric diagnoses. I believe the authors should do a better job in the Introduction of making the link between the K-10 and actual DSM diagnoses (as in the Myer Soc Science and Med 2008 citation).

It would be great if the study hypothesis could be clearly stated in the Introduction. Was the primary aim to examine covariates associated with K-10, or predictors of non-adherence, or correlates of improvements in morbidity?

Should multivariate analyses account for clustering in the data? There is evidence that the sites are quite different (in particular with respect to psych distress), and therefore I might be cautious about interpreting the observations as independent. On the other hand, there are few clusters and adjustment for site may do nearly as well. Do the authors have thoughts on why reported distress is much higher in Harare and Mbeya, even after adjustment for other pertinent covariates?

Line 228 on page 12: although the difference is statistically significant, some indication of the minimally important clinical difference in K-10 should be noted.

I may have missed it, but do the authors define delay in seeking care? This is mentioned in the Discussion.

With these data, could the authors posit that mental health treatment could potentially improve patient outcomes, as has been shown for HIV? Or not? Should advocating for mental health treatment be imperative in its own right
given the authors’ findings of a high prevalence of psychological distress?

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**
I declare that I have no competing interests