Reviewer's report

Title: Adherence with isoniazid for prevention of tuberculosis among HIV-infected adults in South Africa

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Reviewer: dick menzies

Reviewer's report:

General
1- Is the question posed by the authors new and well defined?
The literature on adherence with therapy is vast, and the literature on adherence with TB therapy particularly Isoniazid preventive therapy is quite extensive. Therefore the topic is not new. Use of INH urine test strips is also not novel although there are fewer papers on this. Use of in house test strips is even less reported. As such this is a relatively novel aspect to the paper and the procedure they follow to prepare the strips and use them is well described so that other readers could adopt this method in their own clinics. Given that it is inexpensive and not that time consuming to prepare it would seem appropriate for the type of setting in which it was tested – i.e., in low and middle income countries.

2- Are the methods appropriate and well described?
As noted above the methods for preparing the urine INH tests strips are well described and detailed enough that they could be reproduced elsewhere. However many other aspects of study methodology are not described in sufficient detail. In particular the selection of the study population is not well described. It appears that patients were taken at any time during therapy when they presented for their routine visits. Thus some may have been on therapy for years while others were on therapy only for a month or two. In addition the questionnaire is very poorly described. In fact one only gleams information about the questionnaire from looking at Table 1. It would be better for the questionnaire to be described in some detail in the methods section. Given that there are some questions regarding knowledge, attitudes and beliefs about TB it would be customary for the authors to describe where they got the questions from, whether these were validated particularly in this patient population before, if this questionnaire was pre-tested, and if so how?

3- It is a little unclear how they define adherence other than by using the INH test strips. For example I am not sure whether they mean that patients finally dropped out of therapy at a later date or whether this simply means that patients who are adherent on the time of the individual visit. In addition it is not clear whether patients were surveyed more than once. For example, if they came a month later were they included again?

4- Is the data sound and well controlled?
The authors suggest that they have validated the urine INH test strips clinically, but in fact they have compared urine INH test strip results with self reported compliance and reported a number of associations. However the vast literature on adherence is quite consistent that self-report is notoriously inaccurate when it comes to real treatment adherence. One can not validate measure such as urine INH test strips against self report. The authors should have validated this method in patients who are observed to take treatment and provide urine samples at varying intervals after ingestion of a dose.

5- Does the manuscript adhere to the relevant standards?
I have some comments regarding the Tables. Table 1 is too long and needs to be reduced (it would
have been helpful to have it included in the same file as well, but that is a much more trivial point). However the Table should be reduced substantially to the key variables.

In Table 2 the individuals who strongly agree that INH was bad for them were actually less likely to have negative tests than those who did not know i.e., there does not appear to be a “dose response relationship” between agreement or disagreement with the statement and having a negative test.

In Table 3, one question item is listed here but is not in Table 2, it is unclear why not. The parameter estimates can be dropped from this table and P Values similarly are not necessary when 95% confidence intervals are shown.

6- Are the discussion and conclusions well balanced and accurately supported?
Looking only at the conclusion – the authors focus on the INH test strips. It is true that they have shown that they are low cost and feasible in their setting. However they can not make any conclusion about accuracy of these test strips since they have provided no data regarding accuracy of the test strips in this paper.

7- Title and abstract
As noted above the title and abstract inaccurately suggest that the INH test strips have been validated. In fact they have not. This should have been the focus of this study. If they had validated the INH test strips properly then they could have gone on to a more interesting study about adherence. However the patient population selected i.e., those who had already been on therapy for a very long time, is a poor sample of patients to study for adherence and for side effects because this is clearly a select subgroup of all those who actually start therapy.

8- Is the writing acceptable?
The writing is clear throughout the text.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
1- As noted above the tables need some editorial work. For example Table 1 should be reduced somewhat to the key questions. Table 2 should include all the same factors as shown in Table 3. In table 3 the parameter estimates and P Values could be dropped.
2- In the description of the study population it would be important to specify how many were on HIV treatment. I note in Table 1 that very few were. This should be explained in the description of the study population (why in 2004 are relatively few being treated?).

3- Discretionary revision - Introduction paragraph 3 – non adherence with INH has not been shown, to my knowledge, to lead to drug resistance.

Discretionary Revisions (which the author can choose to ignore)

**What next?:** Reject because scientifically unsound

**Level of interest:** An article of insufficient interest to warrant publication in a scientific/medical journal

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

I declare that I have no competing interests.