**Reviewer’s report**

**Title:** The performance of rapid plasma reagin (RPR) titer in HIV-negative general paresis after neurosyphilis therapy

**Version:** 0  **Date:** 28 Aug 2017

**Reviewer:** Tim Read

**Reviewer's report:**

Thanks for asking me to review "The performance of serum rapid plasma reagin (RPR) titer in HIV-negative general paresis after neurosyphilis therapy" which examines RPR titres in patients with general paresis before therapy and in a small subgroup, after therapy. Patients with RPR+ CSF are compared with those who are RPR negative. General paresis is currently rare in high-income countries but may become more common in one or two decades as a result of the current resurgence in syphilis in MSM. This study provides useful information on whether changes in the serum RPR after treatment can be used to monitor response to treatment, or whether the CSF RPR is a better measure. Opportunities to study general paresis are rare because it is not often seen in settings with good resources for research, so this paper is potentially valuable.

I have three major concerns which I believe should be addressed before the paper is published:

1. From the information presented I have some doubt that all patients had general paresis. Could some have had alcoholic dementia, or some other form of dementia, affecting their MMSE, combined with reactive syphilis serology? This is especially relevant to those with normal CSF or non-specific changes in their CSF. It would be helpful to readers, and strengthen your case, to know more about the clinical features of the cases: eg proportions with neurologic signs (eg pupillary changes, hyperreflexia, speech changes) and proportions with personality or affective changes or delusions/hallucinations. It is inevitable that there may be some uncertainty, as it is a diagnosis of exclusion, but this shouldn't deter you from providing more clinical information.

2. This study has several significant limitations, but these are not listed in the discussion. Please provide a limitations paragraph which mentions: a) any diagnostic uncertainty (I find it hard to accept that you can be certain of diagnoses of neurosyphilis when the CSF RPR is negative particularly when the serum RPR is also negative), b) the very large losses to follow-up and c) any other caveats readers should consider alongside your data.

3. There are frequent errors in English grammar and word-usage throughout the manuscript that are potentially confusing. It would be worth enlisting the help of someone fluent in English. Lines 11 and 12 in the Results are just one example. Another is the use of declined (suggesting refused), instead of "decline in" (meaning a reduction) in the results. See also lines 7-9 in Methods.

Other comments:

- Was there any correlation between serological and clinical improvement? Was the MMSE more likely to improve in patients with a decline in CSF RPR?
- You need a more understandable running title. Include the words general paresis in full. Also in the text, the acronym GP is confusing as this frequently refers to general practitioners. Consider writing general paresis a little more often.
- Say in the abstract and in the text of the results, how many patients are in each of the two groups (CSF RPR+ and RPR-).
- Table 1: suggest delete the row: Reactive CSF RPR and replace the NA with dashes for the CSF RPR- group.
- Table 2. Remove MMSE from footnotes and superscript a from P values, as these seem unnecessary. I wonder whether you should drop the P values from this table; your definitions of the two groups...
are different and so different rates of non-RPR abnormalities are almost guaranteed. The most interesting finding is that there is no difference between groups in the third row. Table 3 - replace "declined" with "decline in" or similar. State that this is the median MMSE value. NA should be replaced with a dash, as this is simply not applicable. Table 4 gives little additional information to the text and can be deleted. A comment can be added to the text explaining that this is an odds ratio.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

**Declaration of competing interests**
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?
4. Have you received reimbursements, fees, funding, or salary from an organization that holds
or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below.
If your reply is yes to any, please give details below.

I declare that I have no competing interests.

I agree to the open peer review policy of the journal. I understand that my name will be included
on my report to the authors and, if the manuscript is accepted for publication, my named report
including any attachments I upload will be posted on the website along with the authors'
responses. I agree for my report to be made available under an Open Access Creative Commons
CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments
which I do not wish to be included in my named report can be included as confidential comments
to the editors, which will not be published.

I agree to the open peer review policy of the journal