Reviewer's report

Title: Diagnostic utility of zinc protoporphyrin to detect iron deficiency in Kenyan preschool children: a community-based survey

Version: 0 **Date:** 10 Mar 2017

Reviewer: Madeleine Verhovsek

Reviewer's report:

This study presents analysis of clinical and laboratory data collected as part of an RCT. The authors are trying to determine the diagnostic utiligy of ZPP alone or in combination with other laboratory values (e.g. hemoglobin concentration) in identifying cases of iron deficiency. The manuscript is generally well written, however there is a focus on long descriptions of statistical analyses and presentation of results without sufficient placement in the clinical context.

Major comments:

- Overall the authors have not made it clear why this is an important clinical question, and how they feel ZPP could add to the currently available tests. In particular, the authors note that both ZPP and ferritin are elevated in inflammatory states. Therefore ZPP seems to have the same test limitations as ferritin, which is a widely used and available test.

- The definition of iron deficiency was based on ferritin <12 ug/L, which is a very strict definition. This cut-off is likely quite specific but not sensitive, therefore missing out on cases of iron deficiency with higher ferritin levels. This is most clear in the results section where it appears that very few of the children with inflammation or Plasmodium infection were classified as having iron deficiency (32.1% in the no inflammation/infection group vs. 17.1% in the group as a whole). This is not clinically plausible and suggests that very many cases were missed by using exclusively the strict ferritin cut-off for case identification.

- A major study limitation is the lack of ability to definitively identify and confirm all cases of iron deficiency. Understandibly, the gold standard of hemosiderin stain on bone marrow sample would not be practical in this study setting.

Abstract

- No context or background is provided as to why this is an important study question.

- It is likely unnecessary to include all inclusion and exclusion criteria in the abstract - this listing takes up a large portion of the word allowance.

Background

- Page 4, last paragraph - The authors indicate taht ZPP has "little diagnostic utility as a screening marker to manage iron deficiency in pregnant women". Please explain why you would then decide to study this test again in the current population

Methods

- Exclusion criteria - why were children with twin siblings and those with Hb <70g/L excluded?

- Earlier in the manuscript it is noted that this was an analysis of data collected in an RCT. It would be helpful to the reader if you briefly describe the nature and purpose of the RCT

- Were the children tested for thalassemia?

Results

- As noted above, the lower rates of iron deficiency identified in children with inflammation/infection vs. children who were well make it clear that ferritin alone was not an appropriate test in this population for case identification

- The authors have not explained the reasons for testing both whole blood ZPP and erythrocyte ZPP. Please explain the differences between these tests, and what the anticipated differences would be in test results.

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 recommend additional statistical review

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

Acceptable

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

I agree to the open peer review policy of the journal