Reviewer’s report

Title: Anaemia and blood transfusion in African children presenting to hospital with severe febrile illness

Version: 1
Date: 23 September 2014

Reviewer: John Myburgh

Reviewer’s report:

This is another high quality analysis from the landmark FEAST trial.
This paper follows the previous publication of transfusion volumes in Ugandan children and is a comprehensive and detailed analysis of transfusion practice, thresholds and outcome in patients who were transfused in FEAST.

The most important aspect of this trial is an assessment of compliance with WHO transfusion guidelines from a specific geographical (low-income) region that will draw substantial commentary questioning the external validity of the results.

The hypothesis and objectives are clear and explicit. It is not stated whether this post hoc analysis was pre-specified before or during FEAST.

Overall, the methods are sound, well described and accurately presented, although there is extensive space and words given to describe the methods used in FEAST. As an understanding of FEAST is essential in interpreting this post hoc study, this section should be substantially shortened with a reference to the New England Journal of Medicine publication.

The methods used to define and analyse variables defined in this paper should only be presented in this paper.

Specifically, a number of methods or definitions are presented in the results section, e.g. nutritional status and quantification of parasitaemia. These should be clearly defined in the methods section (that can be substantially shortened) and this will make the results section easier to read.

A key objective of this analysis is to determine compliance with WHO guidelines – while these and other jurisdictional guidelines are summarised in Table 1, an assessment of compliance with these should be presented in the methods section and included in the results.

The Forest plot definitions outlined in the methods are not the same as presented in the results – these need to be consistent – either define these according to haemoglobin cut off level (as presented) or by severity of anaemia (as is presented throughout the paper). My recommendation is the latter.

The results are very long and there is an extraordinary large amount of data presented. As indicated above, this section can be substantially shortened by removing methodological definitions and details description of data that are
clearly presented in the tables, particularly clinical characteristics (table 2) and site data (table 3).

Similarly, the data presented in table 4 is clear and the information presented in the results section can be substantially shortened to focus on the clear positives and negatives.

The KM graphs should be redone and simplified to show the probability of starting a transfusion for the 3 groups of patients according to Hb - this is a key outcome of this analysis. The site data for each group can be presented in tabular form or as supplemental material.

It is not clear why only two groups are presented in the KM graphs.

Similarly, the discussion needs to be extensively revised and substantially shortened to focus on the objective and aim of this important analysis.

There is substantive repetition of the results and the inclusion of new results within the discussion section.

This section needs to solely focus on a statement of principal findings written factually without editorial commentary, a summary of these findings to high-quality published literature, a summary of weaknesses and strengths, that should include a statement about generalisability and applicability of these results, implications for clinicians and policy makers, specifically a comment about the lack of compliance to WHO guidelines and potentials for this and a stronger statement about potential future research that includes the investigators phase III trial.

Major compulsory revisions:

1. Substantially shorten the description of the FEAST methods and specifically define methods applicable to this analysis in the methods section.
2. Include an analysis of determination of compliance to the WHO Guidelines
3. Revise the KM graphs to present only the groups per Hb level
4. Standardise the Forest plot to the same as the FP data
5. Substantially shorten and revise the discussion and outlined and remove redundant and editorial commentary.

Minor essential revisions:

1. State whether this analysis was pre-specified before or during FEAST

Discretionary revisions:

1. Nil

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I have no competing interests in relation to this paper.