Reviewer's report

Title: Effects on mortality of a nutritional intervention for malnourished HIV-infected adults referred for antiretroviral therapy: a randomised controlled trial

Version: 1 Date: 27 November 2014

Reviewer: Wafaie Fawzi

Reviewer's report:

The paper reports the findings of a randomized controlled trial to examine the effect of nutritional interventions among undernourished individuals who were ART-naïve and beginning to be initiated on ART. The trial addresses an important research question given the high mortality among patients with low BMI.

- The Introduction focuses primarily on the role of macronutrients in the context of ART and HIV/AIDS management. But the trial is in essence examining the additional effect of micronutrients vs not on top of a base that includes varying quantities of macronutrients. The rationale for examining the efficacy of micronutrients is not clearly stated.

- It would be good to report that duration that each of the two nutritional regimen/phases of the trial (mean, Median, standard deviation).

- It would be important to present the results of the two phases of the trial, recognizing there may limited statistical power to examine them separately. Thus, the results could be presented comparing mortality and outcomes in the two treatment arms from recruitment until 2 weeks post-ART; and separately from 2 weeks of ART when the second nutrition regimen was introduced until the end of follow up.

- Magnesium levels were reported to have been examined in a subset of specimens but the results were not of clinical interest with the other data. The reason for exclusion of the results is not clear, and the results may be of interest to some readers.

- The findings from secondary analyses related to phosphate levels are not clearly presented. It is not clear what the significance of the findings in Figure 3 is.

- Low adherence is a concern as the authors have noted. Could there have been similarly low adherence to ART? It would be good to report that as it may also explain the high mortality noted in the study population. It is also important to discuss the generalizability of the findings – in essence the trial did not test the effect of the interventions in a large part given the low adherence.
Mortality was substantially higher than expected as compared to other populations initiating ART in developing settings. The team had assumed mortality rates to be 25 per 100 person-years but they found it to be more than 80 per 100 py. It would be helpful to discuss this level in absolute terms regardless of the intervention arms, and how it compares with other populations. Presenting mortality pre-ART and after ART initiation would be helpful.

The discussion related to potassium could be clearer. It appears the authors are saying the dose they used is established to be safe, and actually lower than what they may have considered but the dose used was the maximum the manufacturer could include in a tablet. Bu then the authors speculate that the amount given ‘appeared to be more than their metabolism could handle”. How was that determined? It would be helpful to present results on potassium levels at baseline; levels as an outcome, and levels as a modifier.

The discussion (page 14, para 1) states that the ‘control group received LNS which contained innate vitamins and minerals …”. This point could be made clearer in the Methods section as well. Could the authors clarify what these innate nutrients are and in what quantities.

The Discussion section overall could be better organized. Findings of other trials of vitamins and minerals are worth noting – what they found, how their findings differed or were in agreement with this new trial, and why. There is very little discussion of other trials in the context of HIV/AIDS(pre- and during ART) and their findings.

The authors refer to ‘fairly high dose of vitamins and minerals’ (Page 12, para 1): please quantify how high.

Figure 1 – it appears that 36 patients in one arm and 25 in another were excluded because of BMI>18.5 after randomization but were still followed up. Is that the case? If so, it seems reasonable to include the data in the analyses and report the findings per intent-to-treat principle. It is also fine to present additional results with these data excluded.

Quality of written English: Acceptable

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

Declaration of competing interests:

I have no conflicts of interest