Reviewer's report

Title: Predictors of mortality in HIV-infected patients starting antiretroviral therapy in a rural hospital in Tanzania

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Reviewer: Stephen Lawn

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This paper examines early mortality in a rural ART cohort in Tanzania. This is a well written paper, which I enjoyed reading. The fact that the data are from a rural cohort is very valuable as most other data are from urban settings where resources and infrastructure are likely to be much better. I am only aware of 2 other studies of rural cohorts ## both from Malawi (Zachariah et al. AIDS 2006;20:2355-60 and Ferradini et al. Lancet 2006;367:1335-42). The paper is well constructed and I have no major criticisms of the methods or results. A high given a number of suggestions / questions below that I think may help to strengthen the paper.

Major comments

Reported 1-year survival proportions from different programs in Africa are quite variable. The 1 year mortality estimate of 26% is high compared to many other programmes and may well reflect the fact that over half the patients presented with stage 4 disease (a proportion higher than in most other reports) as well as other differences in health care infrastructure. I think the authors might comment on the availability level of secondary health-care available at the adjacent hospital.

The lack of CD4 cell counts in this paper reflects the reality that most patients in Africa live in areas where CD4 counts are very limited or not available. In this regard, the lack of these data does not pose a problem. However, it makes comparison of the strengths of the associations with risk factors in the multivariate analyses for risk of death more difficult to compare with other studies.

Background, line 6. The authors have referred to the WHO 2002 ART guidelines. I think it would be worth pointing out that these have been updated on 2 occasions in 2003 and 2006, advocating earlier treatment each time. Earlier initiation of ART is probably the most important factor needed to reduce early mortality rates.

Out of 703 ART-naïve people assessed, only 366 had received ART at the time of data censoring. Why was that? I am interested to know if there is any indication whether (i) sicker patients tended to be treated preferentially as this might explain the high early mortality (ii) whether many patients died while waiting to start ART (we have reported from our cohort in Cape Town that many patients die waiting and that even short delays in treatment initiation may have a significant mortality cost AIDS 2005;19:2141-48). This has important implications for waiting lists / health systems delays.

If data were available on the breakdown of the Stage 3 and stage 4 defining illnesses, it might be informative. Natural history data from rural Uganda and our experience in ART programmes in South Africa shows that wasting syndrome (stage 4 illness), for example, has a particularly poor prognosis (this would fit in with the findings on BMI). If precise numbers were not known, a general statement in the results of what the commonest stage 3 and stage 4 defining illnesses were would help.

Discussion, paragraph 1. The authors speculate about causes of death and might refer to the relevant literature (the study by Zachariah cited [6] did not report causes of death and TB IRIS I am told is very infrequently seen in Malawi as ART isn’t commenced until the continuation phase of TB Rx).

Two studies from Africa have described causes of death (Etard et al. AIDS 2006;20:1181-89; Lawn et al AIDS 2005;19:2141-48). Drug toxicity was a very infrequent cause. Immune reconstitution disease is a more common cause of death, but cryptococcal more commonly than TB in South Africa (Lawn et al AIDS 2005;19:2141-48).

The authors might like to speculate on potential causes of anaemia eg. immune activation-associated haematopoietic suppression; disseminated TB involving the bone marrow; gastrointestinal blood loss from intestinal KS or TB; dietary etc. I agree that the finding of an association of thrombocytopenia and mortality has not previously been found in other reports from Africa.

The authors identify simple and strongly prognostic markers (BMI and anaemia). It begs the question as to whether there are measures that could be taken to address these risk factors to reduce mortality risk. I am not aware of evidence that nutritional support helps, for example. This should be discussed.

The over-riding issue appears to be that in this setting (as elsewhere in Africa), patients are accessing ART with disease that is too far advanced (58% stage 4, high proportion with anaemia and wasting). Perhaps the emphasis on identifying how patients can be diagnosed earlier and receive ART earlier might be increased.

Minor comments

Abstract, first line. Suggest changing this to Studies of antiretroviral treatment (ART) programs in Africa. 
Methods, page 6. It is probably unnecessary to state the HIV serology methods. Since CD4 cell count data are not presented, it is also probably not necessary to give the CD4 assay methods.

**What next?:** Accept after minor essential revisions

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

'I declare that I have no competing interests'