Reviewer's report

**Title:** cART prescription trends in a prospective HIV cohort in rural Tanzania from 2007 to 2011

**Version:** 2  
**Date:** 19 December 2013

**Reviewer:** Kerry Uebel

Reviewer's report:

RE REVIEW COMMENTS DATED 19 DECEMBER 2013
I HAVE INCLUDED MY RE-REVIEW COMMENTS IN CAPITAL LETTERS UNDER MY ORIGINAL COMMENTS BELOW.
ON THE WHOLE THE MANUSCRIPT IS MUCH IMPROVED AND THE AUTHORS HAVE RESPONDED TO MOST OF MY COMMENTS. HOWEVER THE MANUSCRIPT IS STILL NOT SUITABLE FOR PUBLICATION AS THERE ARE STILL MAJOR CHANGES NEEDED.

**MAJOR COMPULSORY CHANGES**

1. THERE ARE MANY SECTIONS WHERE THE LANGUAGE IS POOR AND THE WHOLE MANUSCRIPT NEEDS A LANGUAGE EDIT. I HAVE MADE SOME SUGGESTED CHANGES TO ILLUSTRATE THIS, BUT I CAN NOT DO A MAJOR LANGUAGE EDIT FOR THE AUTHORS. PLEASE SEE ALL MY COMMENTS DIRECTLY IN THE MANUSCRIPT

2. SOME OF THE AUTHORS DESCRIPTION OF RESULTS SEEM TO BE INCORRECT. SEE MY COMMENT ON LINE 99 OF THE MANUSCRIPT. THE AUTHORS STATE THAT PRESCRIPTION OF AZT 3TC EFV HAS INCREASED WHEREAS IT HAS DECREASED FROM 42% TO 33% FROM 2009-2011

3. THE MANUSCRIPT DOES NOT INCLUDE ANY COMMENT ON SOME IMPORTANT FIGURES IN THE TABLES: THE 40% DECREASE IN NUMBER OF NEW INITIATIONS IN 2009-2011 (WHY THE DECREASE?) THE LOW NUMBER OF PATIENTS ON REGIMEN 2. THEY NEED TO COMMENT ON THESE FIGURES

4. IT IS NOT AT ALL CLEAR WHAT IS THE DENOMINATOR FOR THE 16.4% OF PATIENTS THEY SAY HAVE BEEN CHANGED FROM STAVUDINE CONTAINING REGIMENS IN LINE 130.

5. IN LINE 196 IT IS NOT AT ALL CLEAR WHAT HAPPENED IN TANZANIA WITH SUPPLIES OF STAVUDINE. HAVE THEY STOPPED ALTOGETHER? ARE ORDERS BEING SCALED DOWN? HAVE PROTOCOLS CHANGED? IF IT IS TRUE THAT THE GOVT HAS CEASED SUPPLYING STAVUDINE THAT WILL CERTAINLY HAVE A PROFOUND EFFECT ON THIS COHORT AS THE MAJORITY OF PATIENTS ARE STILL ON STAVUDINE. THE AUTHORS NEED TO EXPLAIN THIS BETTER

I HAVE INCLUDED HERE MY PREVIOUS REVIEW COMMENTS WITH MY
PRESENT RESPONSE IN CAPITALS

Abstract

Minor changes

In the Background section the second sentence should be changed: “Country based information on the uptake of these recommendations is needed to monitor their implementation.” I do not agree that the information is scarce There is good data in the WHO Global report of 2011.

In the Methods describe was this pharmacy data? Clinical data?

In the Conclusion section “switch patients off “is slag usage Please reword

ALL THESE CHANGES HAVE BEEN ATTENDED TO

Background

Minor changes

Please include a reference for WHO guidelines in Intro

ATTENDED TO

Reword first 2 sentences of paragraph 2. They are awkward and do not read well.

THERE ARE STILL SOME LANGUAGE PROBLEMS. I HAVE MADE SOME SUGGESTED CHANGES

Consider replacing cART with the phrase HAART a more widely understood acronym

I ACCEPT THE AUTHORS COMMENTS THAT THEY WOULD LIKE TO RETAIN THE TERM cART

Major changes

In the third paragraph the authors comment that the HIV guidelines of the NACP of Tanzania changed the preferred first line regimen in Feb 2009 from d4T/3TC/NVP to AZT/3TC/EFV with TDF/3TC/EFV as an option. It would be helpful here to state what these guidelines said about patients already on a d4T containing regimen. Was there any advice that all these patients should be changed to the new regimens? Or that patients on d4T should stay on it and only be swapped if they experienced side effects? When they comment that d4T/3TC/NVP was still a valid first line combination what do they mean? Do they mean it was a valid regimen for initiation OR for patients already on this regimen? Which regimen was recommended as the first line regimen? Under what circumstances was d4T/3TC/NVP considered a valid first line regimen? This would help to interpret their findings.

ATTENDED TO

There is no discussion of the evidence on usage of d4T AZT and TDF based regimens in different countries. The authors have stated that information on usage of different regimens is scarce. This is not so. The authors refer to the WHO report on the Global HIV epidemic of 2011 but do not discuss any of the finding in this report. There is a lot of data from many different countries in this
report on usage of the different regimens. They should summarise and discuss the findings of this report to put their findings in perspective.

THIS HAS BEEN ADDRESSED IN THE DISCUSSION

Methods

Major changes

What was the data base used? Pharmacy database, clinical records? A research data base or a programmatic database? Was it an electronic data base? It appears the researchers conducted a retrospective review they did not do prospective data collection for the purposes of the research?

ATTENDED TO

How did they get all subjects to sign consent if this was a retrospective review of data in the database?

ATTENDED TO

Results

Minor changes

The word enrolment is spelt wrongly throughout the text. Please do a spell check

I HAVE DONE A SPELL CHECK FOR ENGLISH UK. I AM NOT SURE IF THE JOURNAL IS USING AMERICAN OR ENGLISH SPELLING. MY APOLOGIES IF THE JOURNAL IS USING AMERICAN SPELLING.

Major changes

It would be useful if the authors could give more description of the 3008 patient cohort. In Table 3 it is stated that 1846 patients were assessed for 2011. What happened to the other 1162 patients (how many deaths, how many LTFU, how many transferred?) Also could they give details of how many new patients were initiated each year? It also seems strange that the number of prescriptions assessed for 2009 2010 and 2011 have not increased that much 1758,1787 and 1846. What happened to the rest of the cohort. It wold be useful to know how many new initiations how many were lost to the cohort through deaths and transfers and LTFU. It looks as if the number of people lost to the cohort was almost the same as the number initiated each year.

THIS HAS BEEN ATTENDED TO. HOWEVER IT IS CLEAR THAT THE NUMBER OF NEW PATIENTS INITIATED ON ART DECREASED BY ABOUT 40% IN THE LAST 3 YEARS. THERE IS NO COMMENT ON THE POSSIBLE REASONS FOR THIS DECREASE

The figures on changes in regimen 1 are confusing and there is no table of this data. Could the authors not put in a table for these 242 changes with figures for how many patients were changed to which regimens for each year?

ATTENDED TO. HOWEVER IN THE RESULTS THE AUTHORS COMMENT THAT 242 PATIENTS IS 16.4% OF THE TOTAL PATIENTS ON STAVUDINE. BUT THEY DO NOT GIVE THE TOTAL NUMBER OF PATIENTS ON STAVUDINE AND WHERE THEY GOT THIS DENOMINATOR FROM SO IT IS
DIFFICULT TO SEE WHERE THEY GOT THE FIGURE OF 16%
The results presented would be much stronger if there was data on any evidence of side effects in patients remaining on d4T regimens and those who changed away from d4T regimens. 
THE AUTHOR HAS ATTENDED TO THIS BY EXPLAINING THAT THIS DATA IS NOT AVAILABLE

It would also be helpful if there was any data on the number of patients who were assessed as having good treatment response. The authors report on the number of patients on Regimen 2 but give no indication of how many patients still on regimen 1 have evidence of treatment failure. In the discussion they comment that treatment is monitored clinically and immunologically. Do they have access to such clinical data in their database? If so they should present it as it would make the point more strongly that there seem to be a low percentage of people on regimen 2.

THE AUTHORS SEEM TO HAVE TAKEN OUT OF THE TEXT THE COMMENTS ON THE LOW PERCENTAGE OF PATIENTS ON REGIMEN 2. I THINK THESE COMMENTS SHOULD BE INCLUDED AND THEY SHOULD COMMENT ON THE LACK OF VIRAL LOAD RESULTS AND THE IMPACT THIS MAY HAVE ON LOW RATES OF SWITCHING TO REGIMEN 2

Discussion
Minor changes
The word counterindicated has been used in the first paragraph. I think they mean contraindicated.
ATTENDED TO

Major changes
The authors have commented on the changes in NACP guidelines but it is not clear what the 2009 guidelines recommended for patients already on d4T and under what conditions they should be changed to another regimen. The 2009 guideline is the one most relevant for this data.
ATTENDED TO

The third paragraph is poorly written and needs rewriting as the meaning of some sentences is not clear (first and last sentence particularly are not clear).

THE LANGUAGE REMAINS POOR IN A NUMBER OF PLACES AND I HAVE COMMENTED ON THIS EXTENSIVELY IN THE MANUSCRIPT. THIS MANUSCRIPT NEEDS A FULL LANGUAGE EDIT

I think this is the main point of the article and it is not coming through clearly ie despite good uptake of WHO and national recommendations to initiate new patients on regimens other than d4T regimens, a large number of patients remain on d4T containing regimens and these patients are likely to develop side effects. Efforts should be made to implement new WHO recommendations to phase out Stavudine. The authors also need to discuss the WHO recommendations on phasing out Stavudine in the 2011 Global HIV report which they have referenced.
(Ref 10) but they have not discussed in the Background or here in the discussion. The last paragraph of the discussion is not well written. It should be stated that there were limitations to their report and what these limitations are.

THE LANGUAGE IS STILL POOR

References

Major changes

References are incomplete. No URLs for Ref 10 and 15. Are references 8,9,11 and 12 available on the internet? If so please include URLs. In all of these references 8,9,10,11,12 and 15 the reference includes the abbreviation In. but there is no indication of in what? These references need to be redone.

ATTENDED TO
1. Is the question posed by the author well defined?
No. I cannot see any clear research question in the Background

THIS IS NOW CLEARER
2. Are the methods appropriate and well described?
Methods need some Major changes see above

THESE ARE NOW WELL DESCRIBED
3. Are the data sound?
The data appear to be sound but could be improved see above for Major changes

IMPROVED BUT ONE PROBLEM REMAINS. SEE MAJOR CHANGE NUMBER 2. LISTED AT THE TOP OF THIS DOCUMENT
4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
Yes
5. Are the discussion and conclusions well balanced and supported by the data?
Their conclusions would be stronger if they reported on more clinical data as outlined above

THIS HAS IMPROVED
The writing in the discussion and conclusion is poor and not always clear. Some sections need rewriting see Major changes above.

THE LANGUAGE IS STILL POOR IN MANY SECTIONS
6. Are limitations of the work clearly stated?
This section is there but needs to be more clearly stated that these are the limitations

THIS PARAGRAPH IS STILL POORLY WRITTEN
7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
Not necessary
8. Do the title and abstract accurately convey what has been found?
Yes
9. Is the writing acceptable?
There are a number of sections that are poorly written and some spelling mistakes wrong words and use of slang terms See above comments
THE LANGUAGE IS STILL POOR IN MANY SECTIONS

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited

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