Reviewer's report

Title: Depression symptoms and cognitive function among HIV-positive individuals in Uganda

Version: 1 Date: 5 November 2009

Reviewer: Anne Mijch

Reviewer's report:

1. Is the question posed by the authors well defined?
   Yes this aimed to measure prevalence of depressive symptoms in a population of HIV infected Ugandans compared to a HIV uninfected control group

   Then the authors aim to examine association of depressive symptoms with cognitive function at baseline and follow-up on 3 and 6 months of HAART

2. Are the methods appropriate and well described?
   Yes this is a component of an ongoing cohort study in Uganda.(ref 18)

   Further clarification in this report of the cohort inclusion criteria is needed. The study selects attendees at substantial risk for dementia; (International HIV Dementia Scale [IHDS]) with a score #10 which has shown a sensitivity and specificity for HIV dementia of 80% and 55% respectively in a prior Ugandan cross sectional study) together with substantial immune dysfunction, a CD4 <200/uL.

   Succinct description of the population from which the 102 individuals were recruited would assist the reader, enabling more generalisability of findings (e.g. is this an inpatient or outpatient, specialized referral service or general HIV treatment service and what proportion of all patients does this cohort would represent)?

3. Are the data sound?
   Yes. The tool used to measure depressive symptoms is Center for Epidemiologic Studies Depression Scale CES-D, essentially a well validated screening tool which requires followed up with a clinical interview to establish the diagnosis of depression (DSM-IV). The authors should include any confirmatory data. Otherwise “depressive symptoms” would be better terminology than depression throughout the report.

   Similarly the cognitive impairment is measured using a screening tool International HIV Dementia Scale (IHDS) defining abnormal as < 10. Reference to a lack of association with the clinically validated MSK score should be clarified both in terms of explanation of the “MSK” (i.e. Memorial Sloan-Kettering score) and consideration of inclusion of summary results as in reference 18 to the full neurocognitive assessment used to allocate a dementia categorization according
4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
   Yes in general

   The results of the longitudinal analysis (table 1) should identify denominators from which the prevalence is calculated so as to clarify the loss to follow-up of 9 individuals (8.8%) by month 6.

   The method of dealing with those individuals lost to follow-up in analysis of associations should be stated.

   Do the authors have any data on risk factors for depressive symptoms (eg FH, alcohol use, baseline immune function or plasma HIV RNA). Is there any confirmatory data on those screened with depressive symptoms in this group?

   Would a time to event analysis (time to recovery of depression, time to normalization of cognitive screen) clarify the outcome of those treated with HAART with and without depressive symptoms at baseline.

   The meaning of the statement “There were 81 HIV-positive individuals with CD4 cell count <=200 at baseline. Among these, there was no association between increasing CD4 cell count and decreasing CES-D score over the study period (p=.168)” is not clear. How this fits with published inclusion criteria and whether this is a valid examination in the absence of data about HIV RNA suppression or CD4 changes in the entire cohort population (Is there any correlation between markers of treatment response and depression symptoms?) Are the numbers large enough to have the power to exclude a type 11 error?

   Could the authors distinguish between the somatic and affective symptoms in the CESD and did both correlate with HIV+ status and did both improve to the same extent with HAART?

   Were any patients treated with anti-depressants or other treatments?

   There are minor discrepancies between reports of this cohort with reference 18 which should be clarified (e.g. Karnofsky Score 98 v 91 in controls, and dementia case in controls).

   One decimal point in age, other demographics is sufficient.

5. Are the discussion and conclusions well balanced and adequately supported by the data?
   Yes excepting in relation to the lack of association between treatment outcome and improved depression symptom scores. This could be clarified by including HIV RNA data or further clarification of actual clinical and immune measures.

6. Are limitations of the work clearly stated?
Yes

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
Yes

8. Do the title and abstract accurately convey what has been found?
Perhaps consider changing
Depression symptoms and cognitive function among HIV-positive individuals in Uganda
to
Depression symptoms and cognitive function amongst high risk HIV-positive individuals treated with HAART in Uganda

9. Is the writing acceptable?
Yes

A few typographical errors page 4 HIV dementia.

1 Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

1.1 Further clarification in this report of the cohort inclusion criteria is needed to identify the fact that those selected are HIV infected attendees at substantial risk for dementia.

1.2 Succinct description of the population from which the 102 individuals were recruited would assist the reader.

1.3 “Depressive symptoms” would be better terminology than depression throughout the report

1.4 Consideration of inclusion of summary results of dementia categorization according to MSK (based on full neurocognitive battery used as in reference 18) to the IHDS screening tool results in order to further strengthen analysis of association with depressive symptoms

1.5 Further interesting information included if available. Do the authors have any data on risk factors for depressive symptoms (eg FH, alcohol use, prior AIDS opportunistic infections (esp CNS), baseline immune function or plasma HIV RNA). Is there any confirmatory clinical data on those screened with depressive symptoms in this group (DSM IV defined depression)? Were any individual treated for depression?

1.6 Could the authors distinguish between the somatic and affective symptoms in the CES-D and did both correlate with HIV+ status and did both improve to the same extent with HAART?

1.7 The method of dealing with those individuals lost to follow-up in analysis of associations should be stated.
1.8 The meaning of the statement “There were 81 HIV-positive individuals with CD4 cell count <=200 at baseline. Among these, there was no association between increasing CD4 cell count and decreasing CES-D score over the study period (p=.168)” is not clear. How does this fit with published inclusion criteria and is this a supportable statement in the absence of data about HIV RNA suppression or CD4 changes in the entire cohort population (Is there any correlation between markers of treatment response and depression symptoms?) Are the numbers large enough to have the power to exclude a type 11 error?

2 Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

2.1 explanation of the “MSK” (i.e. Memorial Sloan-Kettering)

2.2 The results of the longitudinal analysis (table 1) should identify denominators from which the prevalence is calculated so as to clarify the loss to follow-up of 9 individuals (8.8%) by month 6.

3. Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

Nil