Reviewer's report

Title: Immune correlates to CD4 decline in HIV-infected patients experiencing virologic failure before undergoing treatment interruption

Version: 1 Date: 5 September 2007

Reviewer: Adriana Perez

Reviewer's report:

General
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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

This manuscript presents the results of a observational, longitudinal secondary analysis of data from the Asset and health Dynamics Among the Oldest Old Survey (AHEAD). The authors were interested in comparing the risk of falling for people reporting a lot of difficulty in an activity of daily living. Results of their findings are reported for two sub-populations: those who needed assistance most of the time and those who needed some occasional or no assistance. Data was measured between 1993 and 1995.

General:
The authors are assuming that the readers are very well familiar with their terminology and notation when reporting the results of their study as well as familiar with the methods implemented by the authors and the population of study.

Abstract:
-What is PBMCs in the abstract, it is not previously referenced.
-what is pre-T1 definition by the authors in this abstract?
-What is IQR and r in this abstract?
-What is the author’s definition of “drug holiday”? 

Background:
Please provide the reference for the SMART trial

Methods:
 Authors used statistical methods for the description and interpretation of their findings. Authors used statistical inference techniques to report their findings. The use of statistical methods in inferential process is based on the assumption that there is a sample selected from a population of interest. Statistical methods are also known for samples that were randomly selected from the population of
interest with some known probability to proceed with the inferential process.

The authors lacked to describe the population of interest and how those 13 patients were selected for their analysis. From which country are these patients? Why these patients represent a particular population? Among how many these patients are only available? What was the inclusion and exclusion criteria for these individuals? Why was a retrospective study chosen and from where was that retrospective information collected? Which format, form, or questionnaire was used to collect systematical information on these patients? Why there is not description of the precious drugs used by these patients and why was not important for the authors? It is unclear how other readers will be able to compare their patients with the description of the patients provided here, i.e. other countries? Other hospitals?

-What was the purpose of dichotomizes the count of CD4+T cell decline?
-Which subpopulations were studies? It is unclear in this current version of the manuscript.

-What are the responses evaluated in the figures presented in this paper? They are described differently than in the text or they are different variables presented?
-What are the values reported in each contour plot for figures 1, A?
-What was the purpose of the individual contour plots? Why was not described in the methods of this manuscript?

-Why only 13 patients?
-What was the timeframe for collecting these patients? What are the biases associated with this?
-Statistical significance is not established by p-values, 0.05 but due to sample size selection from the population of interest using a type I error level of 0.05. Authors should correct their statement in the methods section.
-How many observations per patient were used for the analyses presented?
-How authors handled missing data, specially because this is a retrospective information collected?

- Which statistical method was used for testing trends as described in the results section?
-How was the sample size calculated and power used for selecting the patients for this analysis?

Results:

-Unclear what is IQR for these authors. If IQR represents interquartile range, it is just a number and not two numbers as the authors reported. Are they presenting minimum or maximum, quartiles? This raised major concerns in the statistical aspects of this paper.

-Authors should report gender in percentages instead of absolute values
- Unclear why, how, and where the Mann-whitney test is reported in figure 1.
- Unclear paragraph on page 8, what are the comparison groups and the test presented for comparing what with what?
- What is the definition of the authors for immune predictors?

Discussion:

- Authors should minimize their discussion substantially for example authors claimed that their results presented “SHOWED” clear evidence for their findings, however there is not a clear population study or description that they have enough sample size for their conclusions or hypothesis of interest.
- Author lack to motivate readers to compare their findings with other because it is impossible to know from where these patients come from to use their results, especially because authors indicate that this is key for those using “drug holidays”. Implications and links to real clinic is lacking in this version of the manuscript.
- Authors lack to evaluate all the potential biases found in their sample in terms of the epidemiological components.
- What are the limitations of this research and your findings?

Figure 1
- Please review titles.
- Are the correlations across multiple measures in time for these patients?
- What does the rectangle measures in figure 1 section A?
- Why are graphs presented for selected patients instead of all patients? What is the message they want to communicate to readers? Why are these contour graphs important in measuring the correlation?
- Why there is a different notation in this graphs and the text? What is CD4 count change??? In time???
- It seems authors think that a not statistical significant p-value for a spearman correlation coefficient indicates lack of correlation. However, their graphs indicated that they are measuring is linearity of their correlation which is usually the case with Pearson correlation. Authors need to review what are their testing when reporting each p-value in their manuscript and figure.
- Graphs in section B do not include 13 patients, why? What the line represents in these graphs? How the assumptions for the line provided here were evaluated?
- Why the correlation coefficients are different between text and figure?
- When were these variables measured?
- What are the socio-demographic characteristics of these patients?

What next?: Reject because scientifically unsound
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

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

Declaration of competing interests:

I declare that I have no competing interests