Reviewer's report

Title: Safety, immunogenicity and effectiveness of licensed vaccines in HIV-infected persons: a systematic review protocol

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Reviewer: Regina El Dib

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Major Compulsory Revisions

1. When I first read the title "Safety, immunogenicity and effectiveness of licensed vaccines in HIV infected persons: a systematic review protocol" I thought the authors was planning to perform a systematic review in order to verify the effectiveness and safe of vaccines versus no intervention in the quality of life, adverse events, etc on HIV-infected patients. Besides that, in the abstract the authors mentioned "We are therefore conducting a systematic review to assess the vaccine safety, effectiveness and durability of protection in HIV-infected persons."...the authors never mentioned about non infected HIV person. However, throughout the background section I noticed that the authors will evaluate infected- and non infected- HIV persons. So, I am not sure whether the study design adequately test the authors's hypothesis because their objective is "Our aim is to compare the immune responses induced by vaccination between HIV-infected and uninfected persons." So, I wonder whether a systematic review of prognosis will be more adequate here taking into account that they have a case group (infected-HIV people) and a control group (non infected-HIV people) and the authors wish to verify the immune responses (outcome) from vaccination (an exposure factor). If this is the case, RCT is not the study design authors wish to identify and the authors should plan to do a prognosis SR.

2. At the last paragraph authors said "To understand the impact of HIV infection on the immunogenicity, persistence of vaccine-induced immunity as well as safety and effectiveness of vaccines, we will conduct a comprehensive systematic review focusing on children and older individuals." Here is the place where authors should make more explicit the aim of their study. Why don't say something like: we will conduct a prognosis systematic review to verify the patterns and safety profile of immune responses to the WHO recommended vaccines in HIV-infected persons and compared them in a non-infected population?

3. Also, the authors proposed as a secondary objective to assess "the impact of ART, repeated vaccinations, nutritional supplementation and immunomodulatory agents on the vaccine-induced immunity in HIV infected persons" which now this is an interventional systematic review. I particularly disapprove the conduction of two different clinical questions (prognosis versus intervention) in one systematic review as for each clinical question we have different plans of actions in the study
design, population criteria, statistical analysis and so on.

4. The authors mentioned "Additionally, there is insufficient evidence as to whether immunogenicity/effectiveness of vaccines specifically targeted at HIV infected adolescents/adults are immunogenic and efficacious in this group (compared to HIV uninfected)." How do authors know there is insufficient evidence on it if they haven't done a systematic review to scrutinize the literature yet and drawn a conclusion?

5. In the item "Assessment of risk of bias in included studies", the authors said "The quality of studies will be assessed using the Cochrane Collaboration’s tool for assessing risk of bias for experimental studies and the Scottish Intercollegiate Guidelines Network (SIGN) checklist for other study designs." Although they are corrected in the use of the Cochrane tool (Higgins 2011) to assess the risk of bias in RCTs included, why did they mention the SIGN checklist here? First, the SIGN has implemented the GRADE process, please see it: "As part of the changes related to GRADE, SIGN decided as of 2013 not to continue with the ABCD grading of recommendations that had been in use since 2001. Reasons for this decision are set out in a separate policy document." Second, one thing is to assess the risk of bias and, other is to rate the strength of evidence and drawn a conclusion based on some variables such as indirectness, heterogeneity, applicability and risk of bias which GRADE system provides it. So, accordingly to those variables (which include the risk of bias) one can drawn a conclusion and recommend the use of such an intervention from a very low evidence to a very high evidence. Furthermore, accordingly to GRADE system, authors will then downgrading the evidence based also in the design of the study (i.e., observational studies will not start from the very high evidence). So, authors have mixed between to grade evidence using a grading system and to assess the risk of bias using Cochrane tool.

6. Under "Sensitivity analysis" item, the authors also mixed the planned analysis between sensitivity (the effect of study designs) with a subgroup (immunological assays used and the geographical settings) analysis. I would suggest the authors to separate by clinical and methodological diversities.

7. Why authors did not consider run the search on both EMBASE and LILACS?

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:

I declare that I have no competing interests.