Author’s response to reviews

Title: Could caregiver reporting adherence help detect virological failure in early treated Human Immunodeficiency Virus-infected infants? Experience from the PEDIACAM study in Cameroon

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Version: 5
Date: 23 August 2015

Author’s response to reviews: see over
REVISIONS

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MS: 54 39 68 26 91 42 18 13

1) TITLE PAGE

The corresponding author has been stated. Furthermore, each co-author mailing address has been indicated.

2) ABSTRACT

- The abstract has been structured as background, Methods, Results and Conclusion

- The following statement «Unfortunately it is too expensive for resource-poor settings» was changed to “Unfortunately it is difficult to access in many resource-poor settings”.

- The following statement “We aimed to measure the diagnostic value of caregiver reporting adherence for detecting virological failure in routine practice during the first 2 years after cART initiation in infants.” was changed to “We aimed to measure the performance of caregiver reporting adherence for detecting virological failure in routine practice during the first 2 years after cART initiation in infants”.

- As suggested by a reviewer, we defined the virological failure in the abstract as following: “Virological failure was defined as having a viral load≥1000 cp/mL at 3 and 12 months after cART initiation or having a viral load≥400 cp/mL at 24 months after cART initiation.”
As suggested by a reviewer, we changed the following statement “However, cumulative missed dose may be useful for the detection of virological success, particularly after 12 months of cART, given its high negative predictive value” to:

“However, the cumulative missed dose measurement may be a reliable predictor of virological success, particularly after 12 months of cART, given its high negative predictive value”.

3) BACKGROUND

- “Introduction” has been renamed as “Background”

- The following sessions has been added below the discussion session: Competing interests, Authors Contributions and Acknowledgements

- References to additional files have been removed from the figure legends

- A reviewer commented that the assertion “viral load is the best marker of adherence to cART” is true when considering antiretroviral naive patients.

In page 3, lines 12-14: we have modified the phrase as following: “Viral load measurement is the best marker of response to cART which is strongly reflective of adherence to cART in patients whose strains are susceptible to antiretroviral treatment they are receiving.”

- In page 3 lines 14-15, we changed the following statement “...but is too expensive for routine use in resource-limited settings” to:

“But it is difficult to access for routine use in many resource-limited settings”

- In page 3 lines 22-24, we changed the following statement “...There is a corresponding need for reliable methods, cheaper than viral load determinations, for assessing infant adherence to cART in routine practice” to:

“...There is a corresponding need for reliable methods, easier to access than viral load determinations, for assessing infant adherence to cART in routine practice”
In page 4, lines 4-6, we changed the following statement “The main objective of this study was to assess the diagnostic values of caregiver adherence reporting questionnaires for detecting virological failure in routine practice during the first 2 years of cART in infants in Cameroon” to:

“The main objective of this study was to assess the performance of caregiver adherence reporting questionnaires for detecting virological failure in routine practice during the first 2 years of cART in infants in Cameroon”

4) METHODS

- In page 5, line 3, we replaced “M12” by “M24”

5) RESULTS

- In page 8, lines 17-18, we added the following phrase (written in italics):
  “Respectively 34% and 64% started cART with nevirapine-based and lopinavir-based regimens”.

- Importantly, most of the caregivers reported no difficulty in administering cART dose, that is 140/143, 119/122 and 76/79 respectively at M3, M12 and M24. Thus, in page 10, lines 20-21, we suppressed the assertion that emphasized the absence of association between reported difficulties and missed doses.

- A reviewer recommended that titles of the figures 1 & 2 should be under the figures instead of above. Revisions were made according to reviewer’s suggestions.

- In page 19, table 1 legend, we added a definition of CD4.

- The vertical segment of line in table 2, page 20, line 4, was removed.

- In page 20, table 2, “Accompanied by”: we made correction by changing “grandmother” to “grandmother”.

- In page 21, table 3, title, the table title was changed from: “value of reported adherence for detecting virological failure in HIV-infected infants treated early by
cART for at least 3 months” to “Performance of reported adherence for detecting virological failure in HIV-infected infants treated early by cART for at least 3 months”.

- In page 21, table3, line 12, a reviewer found errors when calculating the LR+ and the LR- of the “#2 cumulative missed (B)” at M12. We made revisions according to the reviewer’s suggestions.

6) DISCUSSION

- In page 11, lines 17-18, we suppressed “low” in the following statement “Here, prevalence of virological failure was low: 47.8% at M3, 23.8% at M12 and 27.9% at M24, which explains the high NPV. A cohort study in Uganda reported that 28.8% (17/59) of children had viral loads #1000 copies/mL at M12, and this is consistent with our findings (20).”

- In page 11, lines 4-6, we modified the following statement “Other children were classified as “adherent” although they showed virological failure at M12 or M24, leading to false negative cases and subsequently to decreased sensitivity, NPV and LR-” to “Other children were classified as “adherent” although they showed virological failure at M12 or M24, which would be considered false negatives, reducing the sensitivity, NPV and LR+ of caregiver adherence reporting as a test for virological failure”.

- In page 12, lines 13-15, we suppressed “resistance to ARV” in the following statement “Other factors which were not assessed by our study may be involved, such as resistance to ARV…”

- We also modified the comments in page 12, lines 8-11 and lines 18-22.