Author's response to reviews

**Title:** Derivation and Validation of an Accurate Estimation of CD4 counts from the Absolute Lymphocyte Count in Virologically Suppressed and Immunologically Reconstituted HIV Infected Adults

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**Author's response to reviews:** see over
Dear Dr Logan,

Re:

MS: 1658368154172199
Derivation and Validation of an Accurate Estimation of CD4 counts from the Absolute Lymphocyte Count in Virologically Suppressed and Immunologically Reconstituted HIV Infected Adults
Barnaby E Young, David C Lye, Oon Tek Ng and Yee Sin Leo

Many thanks for your assessment of this manuscript and to the reviewers for their comments. Please find below a point-by-point response. We have amended the manuscript in light of these comments and the additional editorial requests.

We look forward to your reply,

Yours sincerely

Dr Barnaby Young

Reviewer number 1

Reviewer's report: This is a well thought-through study assessing the validity of ALCS in predicting CD4 counts in virologically suppressed patients. The use of case-control design to examine factors associated with a variability >25% and then using these in a validation cohort is an excellent concept.

There is only one minor comment that the authors may want to address in the discussion. How would they envisage that this would be used in clinical practice? Clearly, the cases in which one would want to estimate CD4 counts in post-cART immune reconstituted patients; virological failure, immune suppression for other reasons (immune suppressive therapy for example) would be the cases where ALCS would not work. Bringing this up in the discussion would be useful for readers.

- Thank you for your review. The limitations of ALC values to predict CD4 thresholds and virologic failure have been well documented – and perhaps at the cost of appreciating that their inaccuracy is largely due to variation in the CD4 percent. We agree that CD4 estimates are most accurate in the population where knowledge of the value has least clinical utility. The wording of the discussion has been amended to clarify that we anticipate the utility of CD4 estimates is primarily to help support reduced CD4 testing.

Reviewer number 2

Reviewer's report: Thank you for asking me to review this paper As the authors state cd4 count are no longer routinely monitored in most centers and not advocated in most guidelines once the viral load is suppressed and immune reconstitution has taken place. Although I agree that this causes some anxiety this is a question of education not of alternative tests This paper would be far better targeted in the use of this strategy in patients with a detectable viral load, not on therapy, and whether it could reduce cd4 monitoring or in identifying individuals previously suppressed who had new virological failure I disagree that full blood count is a routine part of care in such patients Was
there any clinical utility in knowing the cd4 count in these patients Were patients matched for art especially efavirenz which may be associated with lower cd4 counts as would hepatitis c?

- Thank you for your review. We agree that reducing CD4 monitoring can cause anxiety amongst health care providers and patients, and this provided the impetus behind the study. CD4 estimates from the ALC could be a practical solution to help bridge this anxiety. 3-12 monthly FBCs are recommended as part of routine care by the EACS and DHHS guidelines. Patients were not matched for ART. We note in the discussion that frequent use of zidovudine and stavudine in the cohort may have reduced the accuracy of CD4 estimates. HCV infection is uncommon locally, and have updated the discussion to clarify this.