

PCI Infections Article #90 Decision Round 3

Title: HIV self-testing positivity rate and linkage to confirmatory testing and care: a telephone survey in Côte d'Ivoire, Mali and Senegal

Arsène Kouassi Kra et al. doi: <https://doi.org/10.1101/2023.06.10.23291206>

Dear Authors,

Thank you for the work you have done to improve this manuscript, and explanations where clarity was needed.

There are just a few things that remain to be addressed before I can provide my recommendation. Truly sorry for the fine-toothed comb, but I think it is prudent that the important results and methods here are not overshadowed by the questions these additional details raise. All line numbers are from the tracked changes PDF. I've been as detailed as possible so that the authors can respond quickly.

1. The line corrected in the abstract with "consistent response" remains slightly awkward, should be corrected for singular/plural and uses "negative" instead of "non-reactive". If not changing to the original suggestion ("X% responded with an interpretation (i.e., reactive or non-reactive) consistent with the reported results of the test (i.e., 'non-reactive' for 1 line reported, 'reactive' for 2 lines reported)'), maybe reverse the order to: "X% reported (a) consistent response(s) between the number of lines on the HIVST and their interpretation of the result (i.e., 'non-reactive' for 1 line, 'reactive' for 2 lines). See below.
2. In several other places, "(in)consistent response" needs to be consistently plural or singular. It should say either "(in)consistent responses" or "a(n) (in)consistent response". Please check lines 246, 304.
3. Line 54: remove period.
4. Line 78 - missing the word "project" outside of the parentheses: "The HIV Self-testing in Africa (STAR) project... "
5. Line 38-40: This still needs work. The suggested revision does not explain what central hypothesis, low and high are inside of the abstract, which should stand alone. The sentence prior explains that there was a proportion of the responses that were not consistent. So, it is more logical if that is referenced, such as: "Overall positivity rate based on self-interpreted HIVST results was 2.5% considering complete responses, and could have ranged from 2.X% to 10.X% depending on the interpretation of incomplete responses." The second sentence needs to have some basis in the results. In the results, the authors found that only Education levels differed significantly, but NOT

sex or age or anything else. So the sentence should read something like "Positivity rates were significantly lower among respondents with higher education." The authors could also add that no evidence for differences in positivity rates between other socio-demographic categories was found.

6. Several references are incomplete. Please double-check all references for the following issues. E.G. Ref #45 is not complete. A brief internet search for "La notice d'utilisation du fabricant suffit-elle dans un contexte multilingue et de faible alphabétisation ? L'exemple de l'autodépistage du VIH en Afrique de l'Ouest." Results only in a poster at an event but which is inaccessible. Authors need to either provide the correct reference or change the wording e.g., is likely needed, no ref; or has been shown to be useful in other ATLAS project studies (pers comm, unpublished data). E.G. Ref #50 does not give the DOI or the preprint server. Please provide all DOIs where they exist. This is a requirement of PCI. E.G. R citation needs to include publishers and URL : R Core Team (2021). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. <https://www.R-project.org/>. E.G. Ref # 32 gives a WHO document but no link. A link is very helpful for these types of documents.
7. Line 259: typo (positity → positivity) , but also probably should say "lowest possible positivity" and "highest possible positivity" - because neither are likely to be true, but instead represent the range of potential truths.
8. Lines 262-263: First, the authors did not stratify sex and distribution channel separately - either remove the comma and say 'sex and distribution channel' or say 'key population profile (based on sex and distribution channel)' (see comment below). In either case, would be good to make a more logical and direct liaison with the following paragraph explaining why these were combined (i.e., not as a separate paragraph, saying "We combined sex and distribution channel into a single variable for stratification because the key population profile should differ..."). So just turning the phrase around.
9. Lines 262-263: Second, the authors still have not explained what statistical tests were conducted. Did they use one large multiple logistic regression testing all factors together (I would have done this)? It says two analyses, so I'm guessing this is the case rather than testing each factor separately. Clearly, a likelihood ratio test was done to get significance of each factor (either together or separately), but how were the factor levels then tested (Table S1 shows both results)? Was a Tukey or Bonferoni correction for multiple comparisons conducted? How were the factors 'deemed' necessary for stratification? Why not marital status or prior history of testing? Might be better to say simply "We stratified positivity by x,y, w and v, and z."

Or better yet, something like "We tested for differences in HIVST result positivity between age groups, key population profiles, ... using a multiple logistic regression analysis with likelihood ratio tests and compared factor levels for each variable using Tukey tests to correct for false discovery bias."

10. Line 268: the authors, should they choose, could go one step further and call this variable "key population profile" for more direct clarity. Not a requirement, I know the authors will be anxious to complete their revisions. Just a suggestion.
11. Lines 320-322: Again, here, this needs to be changed to match the rest of the manuscript revisions to report the central hypothesis with low and high possibilities parenthetically. For instance, the reporting of these results is done best in the discussion's second paragraph (lines 400-406). Why not move this to the results section and remind the readers only of the central hypothesis results in the discussion? The authors need to remove the focus from the larger positivity levels based on an extreme assumption about missing data that is unlikely to be true. While the range is fine to present, the only valid testable result is the central hypothesis (unless imputation methods had been used, which they were not).
12. Lines 323-326: The explanation now given by the authors is very clear about why they combined sex and channel. It seems like there might have been a difference between channels, but that breaking up the categories removed power from being able to detect it. While the authors can say how the numbers differed, they cannot conclude that this difference was statistically significant (i.e., unable to reject the null hypothesis of being due entirely to chance). That is what the overall likelihood ratio test gives. There is no evidence that the pairwise comparisons were performed with the appropriate correction (e.g., Tukey test) for multiple comparisons. Had this been done, the only key population profile that might have remained significantly lower would have been for male partners of FSWs. Furthermore, it was only evident for self-reported HIVST results. However, I do find it highly interesting that this is a general trend - that there are significantly lower self-reported positivity rates among male+FSW, female+FSW, and highest education level participants, while there are no significant differences when considering the number of lines on the tests. Seems there could be social/economic reasons for this - a bias towards not wanting to see a positive test. Do the authors have any discussion points to add for this?
13. Lines 327-333: Same as with sex and channel. The authors should immediately report on the multivariable model showing that none of the socio-demographic factors tested had a significant effect on positivity (except for self-interpretations among participants with higher-education). A discussion point about this is that with very low

positivity numbers, there is very little statistical power to detect differences.

14. Line 333: Why aren't the results of education level or marital status reported here?
15. Line 328: it should be either "aged between 15 and 24 years old" or "aged 15 to 24 years old".
16. Line 409-410: This seems irrelevant, because that reference (42) also found that positivity was highest among 35-50 yo men. I could not find, and would not expect to find, that the age structure of participants differed greatly between this study and that of Ref 42. I would remove this sentence. Unless the authors can provide the missing information.
17. Line 411-412: I would move to the end of the whole argument (line 447). Lines 400-439 should all be one paragraph, then 440-447+411:412 would be a separate paragraph.
18. Lines 302, 432, 335: Number needs a comma (but no space!) to separate thousands. Please check throughout the manuscript.
19. Table S1 no longer gives positivity rates. It gives the effect of each variable on the positivity rate (results of logistic regression and multiple comparisons/whatever was done).
20. Table S4: In the description/title, I thought MSM and FSW channels both included facility and outreach?
21. Table S4 and Lines 269-275: I believe the authors followed my previous suggestion, but have mis-stated their methods. Binomial regression = Y variable has two levels (e.g., Yes or No). Multinomial regression = Y variable has more than two levels. Multivariate regression = multiple Y variables. Multiple or Multivariable regression = multiple X variables. Multiple multivariate = multiple X and multiple Y variables tested all together. Bivariate = 2 variables: one X and one Y. Multinomial bivariate = X and Y where the Y variable has more than two levels.
Thus, it is not a "multivariate" model at all, but a "multinomial multiple regression" model, with the Y as group = the three groups of respondents and the X as a list of all of the socio-demographic factors. Bivariate is technically correct, but it is a "bivariate multiple regression" model. So the headings of the columns listing the p-values should say "simple regression model" and "multiple regression model". The test statistic for a likelihood ratio test approximates Chisq for large sample sizes. That's why you get roughly the same response with a chisq test and a likelihood ratio test on a bivariate multinomial regression model.
22. A final possibly informative thing is that I do wish the authors had looked at positivity rates among only complete AND consistent responses - those where the number of lines and the interpretation matched. I am NOT suggesting that they spend the effort to add it at

this stage, but if they did I would be really interested to see how that compared to prior estimates. I do understand that it could mean reduced power, which was in short supply already here.

23. Not a big deal, but conventionally, Appendices should be added after the References, acknowledgements, tables and figures, etc. of the main text.

PS - I can't believe medRxiv rejected a figure with French written in it. Seems quite counter-productive in a manuscript such as this where the precise wording matters. I think I will write a letter to them to raise the issue. You should too!