

Rebuttal Letter

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

Summary

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.

We sincerely thank you for your constructive and detailed comments on our manuscript. We greatly appreciate your time and effort in examining our work with such precision. Your meticulous approach is understood and appreciated as it aims to enhance the quality and clarity of our research.

We have carefully considered all the points raised and made revisions accordingly. Please find below the point-by-point responses to your comments.

Comments

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.

L35-38: *We have corrected the error, and the sentence is now as follows:*

“Of the 2,615 initial participants, 89.7% reported a consistent response 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).”

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.

Throughout the text, we have consistently used the term ‘(in)consistent response’ in the singular form. These modifications are illustrated as follows:

Line 226-231: *“Based on phase 1 participants’ self-reports, we distinguished between those who provided a consistent response, i.e. the reported number of visible lines was consistent with the reported self-interpretation (2 visible lines reported as reactive, one line reported as non-reactive, or no/one line and interpreted as invalid), those who provided an inconsistent response, i.e. the number of visible lines was inconsistent with the self-interpretation of the result, or those who returned only a partial response (refusal to answer or answered “I don’t know” to one or both questions).”*

Line 276-284: *“Of the 2,615 participants recruited in phase 1, 2,346 (89.7%) reported a self-interpreted HIVST result consistent with their reported number of visible lines on the HIVST: 2,292 (88.0%) reported one line self-interpreted as non-reactive, 50 (1.9%) two lines self-interpreted as reactive, and 4 (0.2%) no/one line self-interpreted as invalid (table 1). In contrast, 48 (1.8%) reported an inconsistent response: 10 (0.4%) one line self-interpreted as reactive, 35 (1.3%) two lines self-interpreted as non-reactive/ and 3 (0.1%) no line self-interpreted as non-reactive. Finally, 221 (8.5%) reported a partial result: 147 (5.6%) reported 0, 1 or 2 lines but did not know how to interpret the result or refused to answer, 46 (1.7%) self-interpreted their result but did not know or refused to report the number of lines, and 28 (1.1%) did not know or refused to answer to both questions.”*

Line 54: remove period.

Thank you for pointing that out; the period has been removed.

Line 78: missing the word “project” outside of the parentheses: “The HIV Self-testing in Africa (STAR) project... “.

The word “project” was added to the sentence as follows:

Line 79-80: “The HIV Self-Testing in Africa (STAR) project carried in Eastern and Southern Africa and funded by Unitaid aimed to boost the global market for HIVST (<https://www.psi.org/fr/project/star/>).”

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.

It has been rephrased in the manuscript, indicating as the main result the estimates using complete responses and indicating a range based on the way to include or not incomplete responses.

In the abstract: L39-44: “Overall positivity rate based on self-interpreted HIVST results was 2.5% considering complete responses, and could have ranged from 2.4% to 9.1% depending on the interpretation of incomplete responses. Using the reported number of lines, this rate was estimated at 4.5% (ranging from 4.4% to 7.2%). Positivity rates were significantly lower only among respondents with higher education. No significant difference was observed by age, key population profile, country or history of HIV testing.”

Similar changes have been made in the methods and the results section.

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 .

Thank you for the remark. We have corrected it.

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).

Thank you for the identification of the typo. Following previous comment, we have reworded this paragraph.

Line 232-236: *“Due to the inconsistency of responses, we considered self-reported results and reported number of HIVST lines separately to estimate HIVST positivity rates. For each source, we calculated positivity rates for complete responses (excluding ‘don’t know’ and refusals (DK-R) from the numerator and denominator). We also calculated the potential range of positivity rates by including incomplete responses (highest possible rate, DK-R responses are considered reactive, and lowest possible rate, DK-R responses are considered non-reactive).”*

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.

Following another comment, we renamed this variable 'key population profile' throughout the text.

Line 220-225: *"As the profile of participants should differ substantially by sex and distribution channel (women from the FSW-based channel are more likely FSW while those from the MSM-based channel are more likely female partners of MSM; men from the MSM-based channel are more likely MSM while those from the FSW-based channel are more likely partners or clients of FSW, see Figure 1), we decided to combine distribution channel and sex into a single combined variable named key population profile."*

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 Bonferroni 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."

We have developed two distinct models of multiple (multivariable) regressions. The first model was based on positivity rates calculated from the reported number lines, while the second used interpreted results. To compare the level of each factor and reduce the risk of false discoveries, we applied the Bonferroni test. To simplify the interpretation of the results, we divided Table S1 into two distinct sub-tables, S1a and S1b. We have made the following modification in the body of the text:

L237-242: *"We conducted two separate multivariable logistic regressions, based respectively on self-interpreted results and on the reported number of lines, to analyse differences in positivity rates according of key population profile, country, age group, marital status, educational level, and first-time tester. Global p-values for each variable were computed using likelihood-ratio tests (using Anova() function from 'car' R package). To account for multiple*

comparisons, q-values were computed with the Bonferroni correction (using the R p.adjust() function)."

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.

As already mentioned, we now follow this proposal, and this variable is now called "key population profile" through the manuscript.

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? They 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).

This section has been rephrased in the results.

L291-309: *"Based on the self-interpreted HIVST results, the overall positivity rate was 2.5% when only complete responses were considered (Table 1). It would have been similar (2.4%) if DK-R responses were considered non-reactive (lowest possible rate). Considering DK-Rs as reactive would have increased the positivity rate to 9.1% (highest possible rate). Based on the estimated number of visible lines, the overall positivity rate was 4.5% (complete responses, lowest possible rate: 4.4%, highest possible rate: 7.2%)."*

Multivariable models did not show any significant effect of key population profile, country, age group, marital status, or being a first-time tester on positivity rates (Tables S1a and S1b). No effect of educational level was observed on positivity rates based on the reported number of visible lines. However, a significant effect of the educational level was observed on positivity rates based on self-reported HIVST results ($p=0.002$, $q=0.014$): individuals with a secondary or a higher level of education have a higher probability of reporting a reactive test (adjusted OR equal to 4.00 [95% confidence interval: 1.44 to 12.9] and 4.12 [1.76 to 12.1] respectively).

Although not statistically significant, we observed variations between key population profiles (Figure 3, Table S2). Based on self-reported results, positivity rates were 3.4% for men [possible range from 3.2 to 9.8%] and 1.0% for women [1.0 to 2.9%] in MSM-based channels, 1.7% for men [1.6 to 8.2%] and 2.7% [2.5 to 10.0%] for women in FSW-based channels, vs 0.8% for men [0.7 to 5.8%] and 1.5% for women [1.4 to 8.2%] in the other distribution channels (PWUD-based channels, index testing and STI consultations). Observed positivity rates varied by age group (Table S3): 2.4% for 15-24 years old [2.2 to 7.8%], compared to 2.9% for 25-34 years old [2.7 to 9.5%] and 2.0% for those aged 35 years or older [1.8 to 12.0%]."

We also updated the Discussion.

L373-379: *"According to our estimates, HIVST positivity rates in Côte d'Ivoire were 2.0% (complete responses, lowest possible: 1.8%, highest possible: 9.8%) based on self-interpreted results and 3.9% (3.8% to 5.4%) based on the number of lines reported. In Mali, these rates were respectively 3.6% (3.5 to 6.7%) and 5.0% (4.9% to 7.8%), while, in Senegal, they were 1.4% (1.2 to 15.0%) and 6.0% (5.4% to 14.9%)."*

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?

Please see previous points regarding the clarification of the methods.
Presentation of the results has also been rephrased.

We also added the following sentence to the discussion.

L415-418: *“It is also suggested by the fact that, in our multivariable logistic regression models, individuals with a low level of education were significantly less likely to report a reactive HIVST result, while no significant difference was observed regarding the reported number of visible lines.”*

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.

See previous answer, which shows how this section has been rephrased and how the results of the multivariable models are now being reported immediately.

We also added to the discussion a sentence about the limited statistical power of the study.

L451-452: *“In addition, due to the small number of observations, we had low statistical power regarding the estimates of positivity rates and linkage to confirmatory testing.”*

Line 333: Why aren't the results of education level or marital status reported here?.

They are now reported. Please see previous answers.

Line 328: it should be either “aged between 15 and 24 years old” or “aged 15 to 24 years old”.

That sentence has been rephrased. “Observed positivity rates varied by age group (Table S3): 2.4% for 15-24 years old [2.2 to 7.8%], compared to 2.9% for 25-34 years old [2.7 to 9.5%] and 2.0% for those aged 35 years or older [1.8 to 12.0%].”

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.

We have removed the sentence as suggested.

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.”

We have reorganised the text as required.

Lines 302, 432, 335: Number needs a comma (but no space!) to separate thousands. Please check throughout the manuscript.

The use of a thin space as thousands separators has been official policy of the International Bureau of Weights and Measures since 1948 (and reaffirmed in 2003) as well as of the International Union of Pure and Applied Chemistry (IUPAC), the American Medical Association's widely followed AMA Manual of Style, and the Metrication Board, among others. It is also the convention used by the Lancet journal.

The use of a comma for digits-grouping is common in English-speaking countries and widely used in US and UK, although not officially recommended for academic writing.

To please the reviewer, we adopted a comma as a thousand separator and updated the manuscript accordingly.

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).

Thank you for your comment. We have changed the title to read as follows:

“**Table S1a:** Factors associated (logistic regression) with positivity rate based on self-reported HIVST, among participants of the first survey phase in Côte d’Ivoire, Mali, and Senegal (2021).”

“Table S1b: Factors associated (logistic regression) with positivity rate based on self-reported HIVST, among participants of the first survey phase in Côte d’Ivoire, Mali, and Senegal (2021).”

Table S4: In the description/title, I thought MSM and FSW channels both included facility and outreach?

Indeed, the MSM and FSW channels both included facility and outreach. We have corrected this in the title.

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.

Thank you for the feedback. We have corrected this in the body of the text and changed the name of the columns in the S4 tables. In the body of the text, the modification made is as follows:

L248-250: *“Simple comparisons were conducted using chi-square tests, and multiple comparison was performed using a multivariable multinomial logistic regression model, followed by the calculation of likelihood ratio tests.”*

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 . 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.

Although not included in the text, we have produced a table showing the positivity rates for complete responses by country and by key population profile. These rates appear to be lower than previous rates.

country	MSM-based channels		FSW-based channels		Other delivery channels		Overall, N = 2 615
	man, n = 997	woman, n = 103	man, n = 620	woman, n = 685	man, n = 137	woman, n = 73	
Côte d'Ivoire	1.7% (11/650)	1.4% (1/73)	0.6% (2/339)	0.8% (2/245)	0% (0/60)	0% (0/23)	1.2% (16/1 390)
Mali	4.2% (13/306)	0% (0/29)	1.5% (4/269)	3.6% (13/360)	9.1% (1/11)	0% (0/9)	3.2% (31/984)
Senegal	4.9% (2/41)	0% (0/1)	0% (0/12)	0% (0/80)	0% (0/66)	2.4% (1/41)	1.2% (3/241)
Overall	2.6% (26/997)	1.0% (1/103)	1.0% (6/620)	2.2% (15/685)	0.7% (1/137)	1.4% (1/73)	1.9% (50/2 615)

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

Appendices have been moved after references.

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!

We have included a new version of this figure, which is an exact translation of the French brochure, the French version being available at <https://doi.org/10.5281/zenodo.11086135>.