Author's response to reviews

Title: Which adults in the Paris metropolitan area have never been tested for HIV? A 2010 multilevel, cross-sectional, population-based study

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Author's response to reviews: see over
Dear Editor,

Thank you for considering the attached, the second, completely overhauled version of our article entitled “Which adults in the Paris metropolitan area have never been tested for HIV? A 2010 multilevel, cross-sectional, population-based study”.

A title page with names, institutions, and emails addresses and an abstract were included.

At the end of the method section we added "The participants provide their verbal informed consent. Written consent was not necessary because this survey did not fall into the category of biomedical research (as defined by French law) and did not collect any personal identification data."

We have replied to and incorporated all of the reviewers’ suggestions, where warranted.

As you can see from our reply to the first reviewer, we have explained why the issue of people never having been tested for HIV is an important topic, namely, the hidden HIV/AIDS epidemic in France, which is largely described by other authors and which justifies the primary objective of our study. The ultimate goal of our study was not to increase the detection of acute and early-stage infections, given the seroprevalence in the general population.

Please note as well that this article is not a mere replication of an older analysis, but rather one involving original data collected 5 years later with the support of France’s two main HIV/AIDS research funding institutions, using a questionnaire developed, in the interval, specifically for studying HIV screening uptake.

Thank you again for your consideration.

Sincerely,

Veronique Massari

Responses to reviewers’ comments

Reviewer’s report: James McMahon

This study seeks to identify individual and neighborhood-level predictors of lifetime HIV testing in a sample of adults residing in the Paris metropolitan area in 2010. Data sampling methods are adequately described to allow evaluation and replication. The authors correctly apply multilevel modeling methods to accommodate the nested structure of the data. The manuscript adheres to the relevant standards on reporting of observational studies. The limitations of the work are clearly stated. The writing, organization and use of tables are satisfactory.

Weaknesses in the study and manuscript are as follows:

Major Compulsory Revisions:
The research question posed in the last sentence of the Introduction is clear, although terms such as “non-uptake of HIV testing” have not yet been defined. However, despite its clarity, one wonders if the researchers are truly asking the right question. If the ultimate goal is to develop effective interventions to increase the detection of acute and early stage HIV infections (as the background implies), is it informative to identify the determinants of “never having an HIV test” among a representative sample of the general population of Paris? If high-risk individuals have had a single HIV test a decade ago, should this be coded as a “success” in the prediction model?

The ultimate goal of our study was not to increase the detection of acute and early-stage infections,
given the seroprevalence in the general population, but rather to identify individuals who have never been tested and who are participating in the hidden epidemic at a time when France’s public health authorities are recommending proposing universal screening in the general population. This issue and this objective (different from that consisting in increasing test uptake by at-risk individuals) are now explained in the introduction.

It would seem to be more informative to identify barriers to repeated testing among those at highest risk of HIV infection.

Others, apart from us, are interested in this topic, especially among men who have sex with men. In the general population, the proportion of high-risk individuals is too low (even in Paris) for one to observe anything in sample surveys (at least those consisting of a few thousand individuals).

2. The data sampling methods appear to be sound. As previously mentioned, the primary outcome variable “no lifetime HIV testing” is not well matched with the ultimate goal of the study, which is to use the results of the analysis to inform the development of effective interventions to increase the frequency of early stage HIV diagnosis. As defined, the outcome would place individuals with a single HIV test twenty years ago in the same category as those who undergo repeated HIV testing every few months. This lack of discrimination renders any findings from the analysis uninformative in relation to the ultimate goal of the study.

We agree with this comment, but it is not exactly the subject of this article (see previous comment).

3. The first two paragraphs of the discussion simply list, again, the significant predictors of the HIV testing outcome. This is redundant from the Results section and unnecessary.

We have deleted these two paragraphs from the discussion

Throughout the discussion the authors related their study findings to an interpretation of “risk for late detection” of HIV (e.g., lines 369-371).

However, as mentioned, the outcome variable of “ever tested for HIV” versus “never tested for HIV” lacks validity to differentiate early versus late diagnosis of HIV.

We have deleted this argument from the discussion.

In another example, the authors compare their observation of an association between history of STIs and increased “ever testing” for HIV to a U.S. study that found a prior history of STIs was lined to decrease likelihood of a recent HIV test. The authors seem to think they can directly compare findings using the two different outcomes: ever tested and recently tested (U.S. study), but these outcome measure very different testing behaviors. Thus, such interpretations and comparisons are not valid.

We agree with this comment. This reference has been deleted.

4. The author’s conclusions are unsatisfactory because they do not offer any firm recommendations for policy changes based on their findings. Indeed, my contention is that they cannot provide any such recommendations because their outcome does not allow them to make any conclusions about predictors of early versus late HIV diagnosis.

The conclusion has been changed.

Minor Essential Revisions

5. Gender is listed as a demographic independent variable, but separate analyses were performed by sex, so technically, gender was not included in any of the models as an IV.

We agree with this comment. Gender has been deleted from the list of independent variables.

6. The authors use an automated backward stepwise selection method for model building, but this method has be empirically discredited in the statistical and methodological literature, as it has been
shown to require arbitrary thresholds, and can lead to model misspecification, bias, overfitting, and inflated Type I error (e.g., Mundry & Nunn, 2009, The American Naturalist, 173:119). Superior approaches are available, such as Least Absolute Shrinkage and Selection Operator (LASSO) or the Allen-Cady modified (non-automated) backward selection procedure (see Vittinghoff et al, 2012, Chpt 10, Predictor Selection, in Regression Methods in Biostatistics). Alternatively, the authors should simply present the full models (after checking for multicollinearity), adding each block of independent variables in sequence so the reader can see how the coefficients change with each added block. 

Contrary to what the reviewer thought he understood, we did not use automatic selection but rather manual selection for each block of variables, using the usual method recommended by Lemeshow and checking for multicollinearity. This point has been added. 

Tables 2 and 3 are constructed exactly as the reviewer recommends: "the authors should simply present the full models (after checking for multicollinearity), adding each block of independent variables in sequence so the reader can see how the coefficients change with each added block."

7. The authors provide OR and 95% CIs for all significant predictors in the abstract accept one: >44 years in females. It is not clear why the parameter estimates for this one predictor were omitted in the abstract. Alternatively, it is not clear that these parameter estimates are needed in the abstract and are more appropriately given in the results section of the manuscript. This omission was a mistake and has been rectified. We have deleted the ORs and 95% CIs to shorten the abstract.

8. The meaning of last two sentences of the Results subsection of the abstract (lines 57-59) and unclear. Use proper terminology. Do the authors mean: “In women, demographic and socioeconomic variables moderated the relationship between HIV testing history and neighborhood of residence.”

Yes, this is what we call (as other authors do) the “composition effect” in the discussion (line 415): the observed differences in prevalence can be explained by differences in neighborhood composition (the residents’ individual characteristics) rather than by the level 2 characteristics of the neighborhoods.

9. The conclusions in the abstract do not relate to the results. Specifically, the conclusion drawn is that the results can help “target people furthest from the offer of screening”, but there is no mention of distance to HIV testing sites as a determinant in their models. Was the sentence simply miss-worded?

We agree with this comment. We were referring to psychological distance as opposed to geographical distance.

Discretionary Revisions
10. The writing and organization are satisfactory, as are the tables. The differences between the Model 1, Model 2 and Model 3 results in Tables 2 and 3 are sufficiently minor that perhaps presentation of only Model 3 is preferable.

We preferred to follow the advice given in comment 6.

Reviewer: Karen Champenois
Reviewer's report:
The manuscript reports a multilevel analysis of factors associated with no lifetime HIV testing in a representative sample of the Paris inhabitants in 2010 (cross-sectional study).
The paper is well writing, the Methods part is very clear; Results are well discussed. A lot of variables were took into account in the analyses, and a lot of results are presented leading to difficulties to distinguish the main messages of the manuscript. Authors might highlight two or
three key messages. In the discussion, a paragraph where results would be compared to the literature on this issue might be added. Some studies about HIV testing barriers in high-income countries are cited in the manuscript (references 1 to 7 of the manuscript). For example, Deblonde et al., in a systematic review in Europe, found that the main barriers to get HIV testing are low risk perception (one of the paper results), and fear of HIV disease and of HIV diagnosis disclosure (not assessed here), and health services accessibility (assessed in another paper on the cohort). De Wit et al. found a better access to HIV testing when people perceive the benefits from HIV testing. These points might be discussed.

Thanks for these suggestions. We have incorporated them into the discussion.

This paper is an update of a study published in AIDS Care 2011 on the second wave of data collection in the SIRS cohort in 2005 (reference 11). The main results are the same. The authors might discuss deeper the similarities, the differences and the evolution in the 5 years between the two studies.

In reality, the two analyses are different, since in 2010, we took a larger number of variables into account (intentionally included in the 2010 survey), such as those concerning sexual behaviors, attitudes toward people living with HIV, and HIV prevention behaviors (variables that we did not have in 2005). As a result, the models cannot be compared on a one-to-one basis. The changes observed between 2005 and 2010 by the KABP surveys are mentioned in context.

No major revisions

Minor revisions

1. Title: Some factors associated with no lifetime HIV testing are characteristics of individuals like age, or STIs history for example. The word 'barrier' is not the best word in all the situations.
   
   We agree with this comment. The title has been changed accordingly.

2. Abstract: > 350 words. The authors should reduce
   
   The summary has been revised (350 mots).

Results part.
3. Methods, line 154: The authors might explain how they assess the participants' self-perception of HIV risk. What were the question(s) asked to participants?

   The question asked was “Have you ever been afraid of having been infected with the AIDS virus?” (yes, very much; yes, a little; no, not really; not at all)

4. Methods, line 154: The authors might state how the stigma score has been validated

   This score has not been validated, strictly speaking.

5. Methods, line 164: The authors collected the number of sexual partners of each sex, but no results are presented in the Results part or in the Tables.

   We used this variable to create the one/multiple partner variable.

   It did not seem useful to us to provide more details because this variable was not associated with our outcome in univariate analysis.

   We have added a sentence explaining that we are only presenting in our tables the variables that were, in the end, significantly associated with our outcome.

6. Methods, line 167: The authors might specify which STIs were taken into account.

   The interviewees were asked about their STI history by means of a single question: “Have you ever had an STI?” (with no further details). This has been added in the Methods section.

7. Results, lines 220-2: The authors might give details about the area with the smallest and the
highest HIV testing prevalence.

For your information: In men, the neighborhood with the lowest prevalence was the Cité 4000 in La Courneuve (classified as a ZUS, or sensitive urban area), and that with the highest prevalence was the Centre Nord neighborhood in Ormesson-sur-Marne (a middle-class neighborhood). In women, they were, respectively, a working-class neighborhood in Bondy and a working-class neighborhood in Montfermeil. There is, therefore, no apparent correlation between the type of neighborhood and the observed prevalence (this is, moreover, what multilevel analyses are all about!).

8. Results, Table 2: Sexual partnerships during the previous 5 years is not significant in Models 2 and 3. There is probably a link between sexual partnerships during the previous 5 years and lifetime number of couple relationships. The authors might explain why they kept this not significant variable into the models.

We decided to show all the variables introduced into the model, even if they no longer proved significant in the final model. We now present only the variables that were significantly associated at the 5% cutoff.

9. Results, line 259: In factors associated with no lifetime HIV testing in women, being self-reported as heterosexual but also not answered OK. This has been added on line 244.

10. Results, Table 3: Stigma score, feeling of being supported and living alone are not significantly associated with lifetime HIV testing in women, but these variables are still in the models. The authors might explain why they kept these variables in the model (for example, low income with p<0.05 in the univariate analysis was removed from the model). In the text line 274, authors stated that stigma score is significantly associated with the outcome.

This was a mistake. We now explain and present only the variables that were significantly associated at the 5% cutoff.

11. Discussion, lines 334-44: Young people have more sexual partners and use less likely condoms than others. But specific-population HIV prevalence is also an important indicator of potential HIV exposure. I think that the HIV prevalence in young heterosexual people is quite low.

We have reworked this point in the discussion, taking your comment into account.

12. Discussion, line 383-9: In the example (line 386), the factors associated with HIV testing in the past year were assessed but the time period of the history of STI was not specified. The recommendation to test for HIV is not applied only if the history of STI considered was in the past year.

In France, in a study in newly-diagnosed HIV-infected people performed in 2010, only half of people with STIs during the 3 years prior to HIV diagnosis (period when they were probably HIV-infected and unaware of their infection) received an HIV testing proposal by healthcare providers (Champenois et al; BMC infectious diseases 2013) suggesting the recommendation is not always followed.

We agree with this comment and have included these results and this reference in the discussion.

Discretionary revisions

13. Introduction : The authors might further clarify the issue or the work hypotheses of the study.

The introduction has been revised.

14. Methods, lines 119-120: People lost to follow-up were younger and wealthier than others at the time of the second wave of data collection?

This is true: Those lost to follow-up were younger and better off (it was they who moved the most
between the two dates), but our final sample was not so select that we had reason to fear this. On the one hand, since those whom we were unable to reach were less well off, slightly older (active but during irregular hours, for example)... and, on the other, since half of the sample was ultimately renewed in 2010 (by the same random procedure).

15. Results, line 218: The authors might explain what is the difference between the HIV test during a systematic or routine examination and at physician's request. For prenatal HIV testing, the test is at the initiative of the physician.
We agree with this comment. We had indicated in the questionnaire that a systematic examination included pregnancy, marriage, blood donations and preop exams. “On a physician’s advice” included because of clinical signs or risk-taking.
Also, the reason for the last test was an open-ended question, and we systematically classified prenuptial tests with routine tests. This point has been added in the Methods section.

16. Table 1: Authors might recall in the title or in the first line of the Table the total number of men and women
Done.

17. Discussion: The authors might highlight the strengths of the sampling et statistical methods, in particular the relevance to use the median OR.

18. Discussion, line 288: and no history of STIs
Corrected.

19. Discussion, line 331: KABP
Corrected.

20. Discussion line 346, ANRS-VESPA2 studied social determinants of HIV-infected people in France. It found that at the time of HIV diagnosis, older people were also at higher risk for late diagnosis and late presentation to care.
Results of Vespa2 in people born in Africa should be more interesting in the context of the present study than in MSM
Corrected.

21. Discussion, line 411-412: high stigma score
Corrected.