

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Effect of comprehensive knowledge of HIV on risky sexual behaviors associated with HIV transmission among adult Ugandans: a propensity-score matched analysis
<b>AUTHORS</b>	Izudi, Jonathan; Kadengye, Damazo T.

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Maggie Zgambo Edith Cowan University
<b>REVIEW RETURNED</b>	08-Jun-2022

<b>GENERAL COMMENTS</b>	<p>I commend authors for conducting a study towards the fight against HIV and utilising a more reliable source of data for their analysis. There are, however, areas that need rectifying to enhance clarity and readability. The methods section needs extensive tweaking and the manuscript can benefit from extensive editing and proofing. Best wishes.</p> <p><b>Abstract</b></p> <ul style="list-style-type: none"><li>- Please follow the journal's guidelines.</li><li>- See applicable comments below</li></ul> <p><b>Background</b></p> <ul style="list-style-type: none"><li>- HIV should be written in full first . See also how UDHS, SSA, STI etc have been used throughtout the manuscript.</li><li>- Add a sentence of two about incidences of HIV infection in Uganda- between line 68 and 69</li><li>- Did you mean HIV uninfected partner?</li><li>- Reference are needed for lines 76 to 79. Which DHS data (year) is being referred to in this section?</li><li>- Reference needed for line 92</li><li>- Would the authors cite studies mentioned in line 94?</li><li>- A lot of information in this section needs references. Please revise accordingly</li><li>- There is a great deal of literature reporting correlations between HIV knowledge and sexual behaviours with results pointing to the direction of findings from this study. Some examples can be found in the links below. Would the authors justify the relevance of this study? Why this study after over 3 decades of HIV health educational campaigns in SSA? <a href="https://iussp2009.princeton.edu/papers/91553">https://iussp2009.princeton.edu/papers/91553</a> <a href="https://riviste.unimi.it/index.php/ebph/article/view/17457">https://riviste.unimi.it/index.php/ebph/article/view/17457</a> <a href="https://aphrc.org/wp-content/uploads/2019/07/Kadengye-DT-and-Shona-D-2018.-Social-intolerance-and-association-with-HIV-knowledge-among-Ugandan-adults.pdf">https://aphrc.org/wp-content/uploads/2019/07/Kadengye-DT-and-Shona-D-2018.-Social-intolerance-and-association-with-HIV-knowledge-among-Ugandan-adults.pdf</a></li><li>- It is good that knowledge of HIV and correlates have been discussed in this background, readers can also benefit from learning</li></ul>
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	<p>what is already known about the impact of knowledge on HIV risk behaviours</p> <ul style="list-style-type: none"> <li>- I would recommend streamlining the introduction to sexual risky behaviours in married couples to be more focused. What is known about married couples and HIV risk behaviours? This will be your problem statement which will justify why you are interested in married couples only.</li> <li>- I am not sure how the first and secondary objectives differ from each other considering that this study was conducted among men and women. Kindly review and provide more clear objectives</li> <li>- In general, HIV knowledge has been discussed at length in the introduction, but nothing is mentioned on condoms use.</li> <li>- Kindly review the introduction to highlight the magnitude on the problem</li> </ul> <p>Methods</p> <ul style="list-style-type: none"> <li>- The authors state that they used data from DHS database. This data is from surveys. Kindly confirm that this report is based on DHS data and not RCT?</li> <li>- Survey questionnaire should be explained in more detail</li> <li>- Who collected the data and how? How many people were interviewed per household?</li> <li>- If this is RCT, there is a lot of missing information including control group, duration of interventions, type of intervention etc</li> <li>- The variables are overlapping in this section. Kindly present them in a clearer pattern. What measurements were carried out to assess outcomes?</li> <li>- How were the interventions applied in this RCT .....and what are they?</li> <li>- How did the authors re-identify DHS survey participants and follow them up for 12 months?</li> <li>- line 186 How were the outcomes measured ?</li> <li>- Propensity score matching cannot be used where there is no control group. Please revise your data analysis methods to match you collected data</li> <li>- If it is an RCT ethical approval is a must</li> </ul> <p>Discussion</p> <ul style="list-style-type: none"> <li>- See my comments under the introduction section. What new conclusion are the authors making from this study? Health education has been there since the inception of HIV. What change or new approach can this study findings suggest to the society?</li> <li>- Line 395- clarify what other approached or environmental determinants mean in this context</li> <li>- The 'what next' is missing in this discussion. What do you recommend? Making sense out of your findings should be your main focus considering that there are other studies with similar findings. A conclusion should highlight the take-home message from the study and not just summaries of the narrations in the report.</li> </ul>
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<b>REVIEWER</b>	Shaonong Dang Xi'an Jiaotong University Health Science Center
<b>REVIEW RETURNED</b>	15-Sep-2022

<b>GENERAL COMMENTS</b>	<p>It is an interesting study where authors investigated association between comprehensive knowledge of HIV on risky sexual behaviors among Ugandans. Impact of knowledge on behavior could be limited but worthy of assessment. However, some technical issues could limit publication of this work as following:</p> <ol style="list-style-type: none"> <li>1. Although authors used PSM, the nature of study is still observational. So it is inappropriate to say that "Since no true randomization was employed, the study design is a non-randomized,</li> </ol>
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	<p>quasi-experimental study”. moreover, the title should be also changed because just association was investigated.</p> <p>2. It is unclear about exposure, what is group with comprehensive knowledge of HIV? Knowing any one knowledge among three or all of them?</p> <p>3. In PSM, it is little confusing about matching. What variables were used for matching? Generally, they are covariates but not outcome variables. Why did authors present table 2? It means that authors used outcome variables as matching variables? Or outcome variable are balanced between two groups with and without knowledge? Authors should check them carefully.</p> <p>4. For table 3, what covariates were adjusted in adjusted analysis?</p> <p>5. If authors conducted 1:1 PS matching, conditional Logistic regression should be used for PSM data.</p>
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### VERSION 1 – AUTHOR RESPONSE

#### Reviewer: 1

I commend authors for conducting a study towards the fight against HIV and utilising a more reliable source of data for their analysis. There are, however, areas that need rectifying to enhance clarity and readability. The methods section needs extensive tweaking and the manuscript can benefit from extensive editing and proofing. Best wishes.

#### Abstract

Please follow the journal’s guidelines.

**Response: Thank you. We followed the journal guidelines to write the abstract. However, we are happy to receive advice from the editorial team.**

See applicable comments below

#### Background

1. HIV should be written in full first. See also how UDHS, SSA, STI etc have been used throughout the manuscript.

**Response: We had fully defined HIV on line #68 as human immunodeficiency virus (HIV). The same applies to UDHS as Uganda DHS (UDHS) since DHS was earlier defined as Demographic Health Survey. SSA and STI were fully defined as well. In this submission, we have cross-checked the entire manuscript and made sure all abbreviations are fully defined at the first mention.**

2. Add a sentence of two about incidences of HIV infection in Uganda- between line 68 and 69

**Response: Agreed. We have added the sentence:**

**“The 2020 Uganda Population-Based HIV Impact Assessment<sup>3</sup> reports a 5.5% HIV prevalence among people aged 15-49 years (7.1% females, 3.8% males). However, new HIV infections among adults (≥15 years) progressively declined from 71,000 in 2010 to 48,000 in 2020, a 32% drop.”**

3. Did you mean HIV uninfected partner?

**Response: Yes, we meant partner that had no HIV. We have revised the sentence to read as follows: “..... having just one faithful partner without HIV can reduce the chances of getting HIV.”**

4. Reference are needed for lines 76 to 79. Which DHS data (year) is being referred to in this section?

**Response: The data analyzed are from the DHS dataset for 15 countries in SSA so the years are varied. We have included all the 15 countries and the respective years of the dataset. The sentence reads as follows:**

**“The 15 countries included Burundi (2016/17), Ethiopia (2016), Rwanda (2015), Uganda (2016), Zambia (2018/19), Benin (2017/18), Gambia (2019/20), Guinea (2018), Liberia (2019/20), Mali (2018), Nigeria (2018), Sierra Leone (2019), Cameroon (2018/19), and Chad (2015).”**

5. Reference needed for line 92

**Response: Agreed. This was the Uganda DHS data referenced earlier but we have re-inserted the reference.**

6. Would the authors cite studies mentioned in line 94?

**Response: The studies were conducted by Teshale, et al (2022) and Frimpong et al (2022). We have inserted the reference citations as needed.**

7. A lot of information in this section needs references. Please revise accordingly

**Response: We have provided the needed reference citations but are happy to add for unaddressed areas.**

8. There is a great deal of literature reporting correlations between HIV knowledge and sexual behaviours with results pointing to the direction of findings from this study. Some examples can be found in the links below. Would the authors justify the relevance of this study? Why this study after over 3 decades of HIV health educational campaigns in SSA?

<https://iussp2009.princeton.edu/papers/91553>

<https://riviste.unimi.it/index.php/ebph/article/view/17457>

<https://aphrc.org/wp-content/uploads/2019/07/Kadengye-DT-and-Shona-D-2018.-Social-intolerance-and-association-with-HIV-knowledge-among-Ugandan-adults.pdf>

**Response: Thank you for the resources.**

The first study by Nambatya and Ntozi focused on HIV knowledge but did not examine its causal effect on the outcomes that we examined. The focus of the study was on factors associated with willingness to test for HIV. Although we noticed that the study found a relatively high HIV knowledge among the youth in northern Uganda, overall, the research question, setting, design, and population were different from our study.

The second study by Nuwasiima et al (2017) focused on HIV prevention knowledge and sexual behavior among university students. The data analyzed are not nationally representative and the population was different from the current study. The findings are limiting to generalized due to differences in the study population and study setting. The research question was different from the question we addressed in the current study.

The third study by Damazo, one of the co-authors listed in the current manuscript, focused on social intolerance, risky sexual behaviors, and their association with HIV knowledge among Ugandan adults. The study used the 2011 AIDS Indicator Survey data, which is relatively obsolete compared to the data the 2016 DHS data that we analyzed. We note that although the study focused on HIV knowledge, the outcomes of interest were different when compared to the present study. Lastly, the analytic

approach employed (multivariable logistic regression) has limitations when it comes to answering questions about causality.

Overall, although it appears a great deal literature does exist in relation to the topic, previous studies have addressed different research questions compared to the current study.

9. It is good that knowledge of HIV and correlates have been discussed in this background, readers can also benefit from learning what is already known about the impact of knowledge on HIV risk behaviours. I would recommend streamlining the introduction to sexual risky behaviours in married couples to be more focused. What is known about married couples and HIV risk behaviours? This will be your problem statement which will justify why you are interested in married couples only.

**Response: We have added sentences on risky sexual behaviors among married/cohabiting couples in Uganda:**

**“Between 2016 and 2019, the prevalence of HIV among married or cohabiting couples in Uganda was 6.6%, exceeding the 6.0% prevalence among adults aged 15-49 years. Low condom use among married/cohabiting couples in extramarital sexual relationship is a risk for HIV infection. The 2016 UDHS9 reports condom use at the last sexual intercourse among married/cohabiting couples with  $\geq 2$  sexual partners in the past 12 months is higher among men (9.7%) than women (7.9%).”**

10. I am not sure how the first and secondary objectives differ from each other considering that this study was conducted among men and women. Kindly review and provide more clear objectives

**Response: The 2 objectives are different. The primary objective focused on establishing the effect of comprehensive knowledge of HIV on extramarital sexual relationships and consistent use of condom among married or cohabiting couples in the general population. The secondary objective examined the same effects by sex (separately for men and women) to highlight sex-differences. We propose to maintain both objectives as it has different implications for gender and HIV programming.**

11. In general, HIV knowledge has been discussed at length in the introduction, but nothing is mentioned on condoms use. Kindly review the introduction to highlight the magnitude on the problem.

**Response: We have addressed this comment under response to comment #9 above.**

Methods

12. The authors state that they used data from DHS database. This data is from surveys. Kindly confirm that this report is based on DHS data and not RCT?

**Response: Yes, our manuscript is based on the analysis of the Uganda DHS data. The data are from a survey. We had described the source of data under the section “Description of data source”.**

**Yes, this report is not an RCT. However, we used the data to emulate an RCT using a statistical approach described in the data analysis section.**

13. Survey questionnaire should be explained in more detail

**Response: Previously, we described the 2 components of the women’s questionnaire that were related to the focus on the study. We have attempted to add the other components of the questionnaire as detailed below. However, this would be in excess of the required word**

count. We deem that excluding the other questions would not substantially flaw the description of the data source as people can always read the UDHS report for additional information. We wish to exclude the details. Should this remain a big concern, we would defer to the handling academic editor.

**“The women’s questionnaire collected information from all eligible women aged 15-49 and they were asked the questions on the following: 1) Husbands’ background characteristics and women’s work: husbands’ age, level of education, and occupation and women’s occupation and sources of earnings; 2) sexually transmitted infections (STIs) and HIV/AIDS: knowledge of STIs and AIDS and methods of transmission, sources of information, behaviors to avoid STIs and HIV, and stigma; 3) Questions on reproduction included the number of children ever born, birth history, and current pregnancy; 4) Family planning questions included knowledge and use of contraception, the sources of contraceptive methods, and information on family planning; 5) Questions on maternal and child health, breastfeeding, and nutrition included prenatal care, delivery, postnatal care, practices of breastfeeding and complementary feeding, coverage of vaccination, diarrhea prevalence and treatment, symptoms of acute respiratory infection (ARI), fever, knowledge of oral rehydration salts and use of oral rehydration therapy; 6) Questions on fertility preferences included desire for more children, the ideal number of children, gender preferences, and the intention to use a family planning method; 7) Questions were asked regarding knowledge, attitudes, and behaviors related to injections and smoking; 7) Additional questions focused on adult and maternal mortality, domestic violence, and early childhood development.”**

14. Who collected the data and how? How many people were interviewed per household?

**Response: We have indicated that the survey was conducted by the Uganda Bureau of Statistic (UBOS), and the revised sentence reads:**

**“We analyzed data from a nationally representative population-based household survey, the 2016 UDHS, conducted by the Uganda Bureau of Statistics (UBOS).**

Regarding who collected the data, we have added the sentence:

**“The 2016 UDHS data were collected by 21 trained research teams, with each consisting of a team leader, field manager, 3 female interviewers, 1 male interviewer, 1 health technician, and 1 driver.”** For the number of people interviewed per household, we had described the selectin of households and the number of people interviewed per household. Also, please note that the survey was a huge undertaking and describing the entire process of the survey would lead to lots of inappropriate information for the readers. As much as we would like to include a detailed information, we felt it would not be a good idea to bombard the readers with too much information. We request that you allow us keep the description of the data source more focused.

15. If this is RCT, there is a lot of missing information including control group, duration of interventions, type of intervention etc

**Response:** This is not an RCT, but rather a quasi-experimental study. We used observational data to mimic an RCT through statistical means – propensity score matching. The motivation for approximating an RCT from an observational data was described in-depth under the section “study design”.

16. The variables are overlapping in this section. Kindly present them in a clearer pattern. What measurements were carried out to assess outcomes?

**Response:** Under the variables and measurement section, we had defined the primary and secondary outcomes. In the revised manuscript, we have included sub-headings for the exposure, outcomes, and covariates used for matching.

The exposure reads as follows:

**“Exposure: Comprehensive knowledge of HIV was the exposure of interest, measured on a binary scale (yes versus no) using five indicators, namely 1) knowing that consistent use of condoms during sexual intercourse can reduce the chance of getting HIV; 2) knowing that having just one faithful partner without HIV can reduce the chance of getting HIV; 3) knowing that a healthy-looking person can have HIV; 4) rejecting that HIV can be transmitted through mosquitoes; and 5) rejecting that HIV can be transmitted by sharing of food. Indicators 4-5 are the two most common local misconceptions about HIV transmission or prevention in Uganda. Participants with correct responses to all the five indicators were considered having comprehensive knowledge of HIV otherwise no. The exposed group consisted of participants with comprehensive knowledge of HIV while the unexposed (comparison) group consisted of those without comprehensive knowledge of HIV.”**

The description of the outcome is:

**“Outcomes: The primary outcome was extramarital sexual relationships measured on a binary scale (yes or no). Participants in sexual relations with another sexual partner other than the spouse or cohabiting partner were considered to have indulged in extramarital sexual relationships in the 12 months preceding the survey. The secondary outcome was the consistent use of condoms measured on a binary scale, computed as the percentage of respondents who had used a condom every time they had sex with any non-spouse or non-cohabiting partner over the past 12 months.”**

The description for the covariates used for matching is:

**“Matching covariates: These included sex (male or female), age group (15 to 19, 20 to 24, 25 to 29, 30 to 34, 35 to 39, 40 to 44, 45 to 49, and 50 to 54), level of education (none/no education, primary, secondary, and higher), marital status (never in a union, currently in a union, and formerly in a union), number of living children, wealth index (poorest, poorer, middle, richer, and richest), religion (no religion, Anglican, Catholic, Muslim, Seventh Day Adventist, Pentecostal, and others), and the 15 regions in Uganda (Kampala, Central 1, Central 2, Busoga, Bukedi, Bugishu, Teso, Karamoja, Lango, Acholi, West Nile, Bunyoro, Tooro, Ankole, and Kigezi)”**

17. How were the interventions applied in this RCT .....and what are they?

**Response:** Our study is not RCT as explained earlier in responses to comments #15 and #16. Although we examined the effect of comprehensive knowledge of HIV, we used observational data to do so and the exposed and unexposed groups are explicitly described in response to comment #16.

18. How did the authors re-identify DHS survey participants and follow them up for 12 months?

**Response: This was not an RCT so there was not follow-up. Please refer to responses to previous comments (15, 16, and 17).**

19. line 186 How were the outcomes measured?

**Response: Thank you. We have already responded to this comment in response to comment #16.**

20. Propensity score matching cannot be used where there is no control group. Please revise your data analysis methods to match you collected data

**Response: In a quasi-experimental study (non-randomized studies), the focus is to compare outcomes between the exposed and the unexposed group. Participants who had comprehensive knowledge of HIV comprised the exposed group, while those without comprehensive knowledge of HIV formed the unexposed group. Sometimes, these 2 groups are technically termed as treated and untreated. In our manuscript, we clearly defined these 2 groups as exposed versus unexposed as already mentioned in response to comments #16. Also, in quasi-experimental studies, we are careful not to use the word “control”, rather “comparison” to ensure departure from an experimental study.**

21. If it is an RCT ethical approval is a must

**Response: This was not an RCT. No ethical approval is needed since we analyzed publicly available data.**

## **Discussion**

22. See my comments under the introduction section. What new conclusion are the authors making from this study? Health education has been there since the inception of HIV. What change or new approach can this study findings suggest to the society?

**Response: We thank you for this comment. Our conclusion is guided by the study findings but we are happy to receive further guidance. Although we have revised the conclusion along the results, we recognize that health education is not a one-time event, rather a continuous process due to ever evolving knowledge. So, providing consistent and correct knowledge about HIV prevention improves self-efficacy and results in effective control over the social determinants of health, especially behaviors that put people at risk for HIV infection like extramarital sexual relationships, alcohol drinking, and drug abuse amongst others.**

23. Line 395- clarify what other approached or environmental determinants mean in this context

**Response: The social and environmental determinants are behaviors that increase the risk for HIV acquisition and they include factors like alcohol drinking, cigarette smoking, and drug abuse. These factors are known to influence sexual behavior. We have revised the sentence to read as follows:**

**“There is a need to complement existing behaviour change communication strategies with other approaches that lessen the influence of social and environmental determinants (alcohol consumption and smoking, for example) that places the population at risk for HIV infection.”**



24. The ‘what next’ is missing in this discussion. What do you recommend? Making sense out of your findings should be your main focus considering that there are other studies with similar findings.

**Response: This comment is important to us. We have revised the discussion to highlight the implications of the findings for practice, policy, and further research.**

25. A conclusion should highlight the take-home message from the study and not just summaries of the narrations in the report.

**Response: We revised the conclusion with a clear take home message and it reads:**

**“Comprehensive knowledge of HIV has no effect on extramarital sexual relationships among married or cohabiting couples in Uganda. However, it increases consistent use of condoms in extramarital relationships among married or cohabiting men but not in the married or cohabiting women. Our findings emphasize a need to continue providing consistent and correct HIV prevention health education messages.”**

#### **Reviewer: 2**

It is an interesting study where authors investigated association between comprehensive knowledge of HIV on risky sexual behaviors among Ugandans. Impact of knowledge on behavior could be limited but worthy of assessment. However, some technical issues could limit publication of this work as following:

1. Although authors used PSM, the nature of study is still observational. So it is inappropriate to say that “Since no true randomization was employed, the study design is a non-randomized, quasi-experimental study”. moreover, the title should be also changed because just association was investigated.

**Response: Thank you for reviewing our manuscript. Yes, we used observational data and employed propensity-score matching to overcome the limitations of observational data, namely selection bias and confounding. While we agree that the data are observational, the removal of selection bias helps to ensure that the groups being compared are balanced on all measured characteristics thus mimicking a randomized control trial (RCT). Therefore, the relationship between the exposure and the outcome is unbiased hence a true effect. For these reasons, we propose that you allow us maintain the title.**

2. It is unclear about exposure, what is group with comprehensive knowledge of HIV? Knowing any one knowledge among three or all of them?

**Response: The measurement of comprehensive knowledge of HIV was based on 5 indicators, and all of them were considered in the computation. In the variables and measurement section, we had earlier indicated that “Comprehensive knowledge of HIV was defined as knowing that consistent use of condoms during sexual intercourse and having just one uninfected faithful partner can reduce the chance of getting HIV, knowing that a healthy-looking person can have HIV, and rejecting the two most common local misconceptions about transmission or prevention of HIV. The two most common local misconceptions about HIV transmission in Uganda we examined included: HIV can be transmitted through mosquitoes and sharing of food.”.**

**In the revised manuscript, we have added a sub-title “exposure” to ensure clarity and we have revised the description to read as follows:**

**“Exposure: Comprehensive knowledge of HIV was the exposure of interest, measured on a binary scale (yes versus no) using five indicators, namely 1) knowing that consistent use**

of condoms during sexual intercourse can reduce the chance of getting HIV; 2) knowing that having just one faithful partner without HIV can reduce the chance of getting HIV; 3) knowing that a healthy-looking person can have HIV; 4) rejecting that HIV can be transmitted through mosquitoes; and 5) rejecting that HIV can be transmitted by sharing of food. Indicators 4-5 are the two most common local misconceptions about HIV transmission or prevention in Uganda. Participants with correct responses to all the five indicators were considered having comprehensive knowledge of HIV otherwise no. The exposed group consisted of participants with comprehensive knowledge of HIV while the unexposed (comparison) group consisted of those without comprehensive knowledge of HIV.”

3. In PSM, it is little confusing about matching. What variables were used for matching? Generally, they are covariates but not outcome variables.

**Response:** Yes, they are covariates but not outcomes. We had describe the covariates earlier bit to ensure clarity, we have added a sub-title “Matching covariates” and it reads:

“Matching covariates: These included sex (male or female), age group (15 to 19, 20 to 24, 25 to 29, 30 to 34, 35 to 39, 40 to 44, 45 to 49, and 50 to 54), level of education (none/no education, primary, secondary, and higher), marital status (never in a union, currently in a union, and formerly in a union), number of living children, wealth index (poorest, poorer, middle, richer, and richest), religion (no religion, Anglican, Catholic, Muslim, Seventh Day Adventist, Pentecostal, and others), and the 15 regions in Uganda (Kampala, Central 1, Central 2, Busoga, Bukedi, Bugishu, Teso, Karamoja, Lango, Acholi, West Nile, Bunyoro, Tooro, Ankole, and Kigezi)”.

4. Why did authors present table 2? It means that authors used outcome variables as matching variables? Or outcome variable are balanced between two groups with and without knowledge? Authors should check them carefully.

**Response:** We did not use the outcomes for matching. In Table 2, we demonstrate the distribution of the outcomes before and after PSM. Th aim was to show if there are differences in the outcomes before and after matching. We propose to maintain the table but are happy to receive further guidance, whether to delete or not.

5. For table 3, what covariates were adjusted in adjusted analysis?

**Response:** We adjusted for all the matching covariates. We have revised the sentence to include the description of the variables included in the adjusted analysis. The revised sentence reads as follows:

“We fitted a binary logistic regression model for the unadjusted and adjusted analysis, with the latter model adjusted for all the matching covariates.”

6. If authors conducted 1:1 PS matching, conditional Logistic regression should be used for PSM data.

**Response:** Yes, we used a conditional logistic regression for the PSM dataset and took nto consideration the matched pairs. We have made this correction so the sentence now reads:

“For the PSM dataset, we fitted a conditional logistic regression taking into consideration the matched pairs.”