

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Why don't key populations access HIV testing and counselling centres in Nepal? Findings based on national surveillance survey
AUTHORS	Shrestha, Rachana; Philip, Sairu; Shewade, Hemant; Rawal, Bir; Deuba, Keshab

VERSION 1 – REVIEW

REVIEWER	Hailay Gesesew Jimma University, Ethiopia
REVIEW RETURNED	02-May-2017

GENERAL COMMENTS	<p>Manuscript ID: bmjopen-2017-017408— Why don't key populations access HIV counseling and testing centers in Nepal? Findings based on national surveillance survey is a study on HCT among hard to reach population based on a national surveillance. The paper addresses a neglected population in Nepal, I recommend, the paper is of subject interest and written fairly. I have the following quires. The result has to be re-written if this going to be considered for publication.</p> <ul style="list-style-type: none"> • Abstract—None • Introduction <ul style="list-style-type: none"> o Why this research is conducted (research question) is not clearly stated o The gaps this research fills should also be very clear for the readers o The advantage of early HIV testing may not only be limited to the first 90 of the UNAIDS 90-90-90 treatment targets. It can go for the second and third 90s and this should be included in the introduction. • Methods: <ul style="list-style-type: none"> o The reliability and validity (psychometric values) of the tools listed in the data variables better be explained. • Results; <ul style="list-style-type: none"> o The result is not adequately described and interpreted o The demographic variables should sequentially be described including the response rate o The factors should also be interpreted • Discussion <ul style="list-style-type: none"> o The significant prevalence of non-utilization should be discussed with other countries, and its implication with the UNAIDS 90-90-90 should be linked as described in the introduction o For each variable, the possible comparison and implication for policy and practice should be explicitly written • Reference <ul style="list-style-type: none"> o To be corrected as per the BMJ protocol.
-------------------------	---

REVIEWER	Minh Pham Burnet Institute, Melbourne, Australia Department of Medicine Nursing and Health Science, Monash University, Melbourne, Australia
REVIEW RETURNED	27-May-2017

GENERAL COMMENTS	<p>This manuscript aims to address an interesting research question related to access to and use of HTC services among key populations in Nepal and would be important to publish. However, there are major questions/issues related to statistical method/data analysis, presentation, interpretations and discussion of the results that must be addressed before this manuscript can be proceeded to publication. Detailed comments are below:</p> <p>Abstract: outcome variable "non-utilization of HTC in last year" was not clearly defined: it seems that the authors have it as a binary (Yes/No) outcome variable which beg the question why would Poisson regression model (for count outcome variable) was appropriate to use??? The RDS & RDS analysis for MSM/TG was not mentioned and the conclusion was ambiguous</p> <p>Introduction: reference is needed for statement in page 4 lines 83-84 "different surveillance..... around 50% in FSWs & MSM/TG. Sentences in pages 5 lines 91-94 were not clear & need to be rephrased</p> <p>Method:</p> <ol style="list-style-type: none"> 1. The authors reported RDS was used to recruit MSM/TG (8 seeds and 3 coupons each) then RDS descriptive statistics (e.g. maximum recruitment wave, average number of recruitment wave, recruitment per seed, number of recruitment wave need to reach equilibrium for key outcome variables... as highlighted in the STROBE for RDS study) 2. The authors reported "A self-reported visit to an HTC facility in past year by the FSW and MSM/TG was chosen as the outcome variable" and "not utilizing HTC in last one year" as outcome variable. This need to be clearly defined. Ho was the outcome variable constructed? was it a binary (Y/N) "not use vs. use HTC"? and then WHY/HOW Poisson regression was identified as appropriate model specification in this analysis. 3. The authors reported using RDS-II estimator for RDS analysis of MSM/TG sample: the authors need to report question(s) used to identify personal network size (and also report statistics as part of the RDS descriptive analysis as commented above). 4. How was clustering around the seeds was taken into account/adjusted for in multivariate analysis of the MSM/TG sample? <p>Results:</p> <ol style="list-style-type: none"> 1. The percentages presented in the text (and in Tables 1-2 and web-only Table) appear to be (unadjusted) sample estimates: ALL results on RDS-adjusted estimates were NOT presented??? If RDS analysis (using RDS-II estimator) had been done, then the result must be presented in the Tables 2. There are inconsistencies between data/the presentation of data in Tables 1-2 and the descriptions of statistical analysis in the method: <ul style="list-style-type: none"> - For FSWs (Table 1): adj PRs were presented for "ever inject drug" "physical assault" "forced sex" "having dependent" "police detention"
-------------------------	--

"stigma" BUT these variables were NOT reported to be included in the multivariate model for FSWs (page 9 lines 185-187) while "suicidal thought ever" was reported to be included but results were missing/not presented in the Table

- For MSM/TG (Table 2): similar issues were found with "age", "drinking alcohol" "physical assault" "forced sex" "discrimination in job" and ""education" "depression", respectively.

Discussion:

1. Repeated presentation of the results: page 13 lines 243-248, 260-262

2. Incorrect presentation of the data: "FSWs who had distress or depression (one in two FSWs) had a higher prevalence of non-utilization..." page 13 line 250: The proportion of FSWs who were either depressed or distressed was 44% (268/610) Table 1 NOT "one in two"

3. Presentation of results which were not discussed and/or presented in the Results section?: "Old MSM/TGs were found to use condoms more when compared to younger ones. The median age of first sexual intercourse being 16 years..." page 13 lines 255-256.

4. Unclear messages and/or presentation of data/results which were not discussed in the Result section: "Some factors affecting utilisation of HTC by MSM/TGs were different from that of FSWs. In events like forced sex in last year among FSW, it reduced the utilisation of HTCs among FSWs. Among MSM/TGs, the experience of forced sex led to utilisation of HTC. IBBS survey revealed that the perception of HIV risk by key population was related to condom use, which was higher among MSM/TGs when compared to FSWs.

Three-fourths of MSM/TG believed they were at little or no risk of HIV if condoms were used". e.g. What message does the authors want to convey when stated "forced sex... reduce use of HTC among FSWs"? where the " Three-fourths of MSM/TG believed they were at little or no risk of HIV if condoms were used" came from?

5. Conflicting results and discussion and unclear message page 14 lines 272-286: The authors stated that " in Nepal, major component of a prevention programme is awareness raising activities" and "Hence participation in awareness classes resulted in high condom use and the fact that two-thirds of MSM/TGs and FSWs were tested for HIV at some point in time could have narrowed their risk perception to a low level as well as decreased their felt need to access HTC" Where the two-third of MSM and FSWs tested for HIV... came from and this is conflict with the results presented in this manuscript: 54% & 55% of non-utilization of HTC? also What is the implication for HIV program in Nepal if participation in awareness program lead to increase condom use and reduce use of HTC/HIV testing services???

6. The authors claims related to policy implications of the finding of the study (page 15 lines 290-297) are not strongly supported by the results and remain ambiguous: e.g. "First, psychosocial support needs to be an integral part of programmes for FSW and MSM/TG at all levels. HTC should be developed as an empowerment centre lending psychosocial and treatment support rather than being a centre for testing alone" This is not strongly supported by the results: As it is presented in the Tables (1-2) among psychosocial factors only "depression" was associated with non-utilization of HTC among FSWs, all other factor variables were not NOT significantly associated with the outcome. What is the specific recommendation and/or message the authors want to deliver when stated " HIV prevention programmes in Nepal need to go beyond condom promotion" and similarly for the third point on

	<p>"contextual/demographic differentials between KPs" 5. The statement "Our study adhered to STROBE guidelines for conduct and report of the study" is not fully satisfied: As commented above, the whole RDS analysis results were missing and the current manuscript is not adhered to the STROBE for reporting RDS study!</p>
--	---

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Hailay Gesesew

Institution and Country: Jimma University, Ethiopia

Please state any competing interests: None

Please leave your comments for the authors below

Manuscript ID: bmjopen-2017-017408— Why don't key populations access HIV counseling and testing centers in Nepal? Findings based on national surveillance survey is a study on HCT among hard to reach population based on a national surveillance. The paper addresses a neglected population in Nepal, I recommend, the paper is of subject interest and written fairly. I have the following quires. The result has to be re-written if this going to be considered for publication.

- Abstract—None

- Introduction

- o Why this research is conducted (research question) is not clearly stated

Response: We have updated research question in introduction section of the manuscript.

- o The gaps this research fills should also be very clear for the readers.

Response: We have added about rationale of this study in introduction section of the manuscript.

- o The advantage of early HIV testing may not only be limited to the first 90 of the UNAIDS 90-90-90 treatment targets. It can go for the second and third 90s and this should be included in the introduction.

Response: We agree with the reviewer that the advantage of early HIV testing not only limited for the first 90 but also linked with the second and third 90s. We would like to emphasise that the all three 90s are interdependent and are equally important for treatment and prevention benefits of antiretroviral therapy. We have updated introduction section of manuscript as per the suggestion of the reviewer.

- Methods:

- o The reliability and validity (psychometric values) of the tools listed in the data variables better be explained.

Response: We have added reliability and validity of the tools (depression and social support) used in the manuscript.

- Results;

- o The result is not adequately described and interpreted

Response: We rephrased the interpretation of results in the manuscript.

- o The demographic variables should sequentially be described including the response rate.

Response: We have presented demographic variables of FSW and MSM/TG in separate paragraph. We have also presented response rate in the results section.

o The factors should also be interpreted

Response: We have also updated the interpretation of factors in the results section of the manuscript.

- Discussion

o The significant prevalence of non-utilization should be discussed with other countries, and its implication with the UNAIDS 90-90-90 should be linked as described in the introduction

Response: We have discussed the outcome of interest in comparison with findings from different countries such as India, China and Thailand. Also, discussed its implication in relation to the 90-90-90 targets.

• For each variable, the possible comparison and implication for policy and practice should be explicitly written

Response: We have updated discussion section of manuscript as per the suggestion of the reviewer.

- Reference

o To be corrected as per the BMJ protocol.

Response: We have updated reference as per the BMJ protocol.

Reviewer: 2

Reviewer Name: Minh Pham

Institution and Country: Burnet Institute, Melbourne, Australia, Department of Medicine Nursing and Health Science, Monash University, Melbourne, Australia

Please state any competing interests: None declared

Please leave your comments for the authors below

This manuscript aims to address an interesting research question related to access to and use of HTC services among key populations in Nepal and would be important to publish. However, there are major questions/issues related to statistical method/data analysis, presentation, interpretations and discussion of the results that must be addressed before this manuscript can be proceeded to publication. Detailed comments are below:

Abstract: outcome variable "non-utilization of HTC in last year" was not clearly defined: it seems that the authors have it as a binary (Yes/No) outcome variable which beg the question why would Poisson regression model (for count outcome variable) was appropriate to use??? The RDS & RDS analysis for MSM/TG was not mentioned, and the conclusion was ambiguous

Response: Initially we have used the log-binomial model to assess the association between independent and outcome variable of interest. However, our model fails to converge. To overcome the effects of failed convergence we have used the Poisson regression with robust variance estimates as mentioned in the article of Tyler et al¹. We would like to emphasise that the Poisson regression with robust variance can be used as an alternative of logistic regression and also provides accurate estimates in the cross-sectional study with binary outcome of interest². We have calculated the prevalence ratio because it is easy to interpret than the odds ratio. We also mentioned this issue in the methods section of the manuscript.

Introduction: the reference is needed for the statement in page 4 lines 83-84 "different surveillance..... around 50% in FSWs & MSM/TG. Sentences in pages 5 lines 91-94 were not clear & need to be rephrased

Response: We have added a reference in the lines 83-84 and also rephrased the unclear sentences.

Method:

1. The authors reported RDS was used to recruit MSM/TG (8 seeds and 3 coupons each) then RDS descriptive statistics (e.g. maximum recruitment wave, average number of recruitment wave, recruitment per seed, number of recruitment wave need to reach equilibrium for key outcome variables... as highlighted in the STROBE for RDS study)

Response: We have added additional RDS related information in the web-only table 2. Regarding equilibrium of outcome variable of interest, we have calculated seed dependence through convergence. The convergence of outcome variable of interest is presented in web-only figure 1. The convergence plot indicated stabilization for estimate for outcome variable after recruiting 200 samples (for detail refer to web-only figure 1).

2. The authors reported "A self-reported visit to an HTC facility in past year by the FSW and MSM/TG was chosen as the outcome variable" and "not utilizing HTC in last one year" as the outcome variable. This need to be clearly defined. How was the outcome variable constructed? was it a binary (Y/N) "not use vs. use HTC"? and then WHY/HOW Poisson regression was identified as an appropriate model specification in this analysis.

Response: We have rephrased the outcome variable of interest. Regarding the use of Poisson regression, please refer to our response to comment of the abstract section.

3. The authors reported using RDS-II estimator for RDS analysis of MSM/TG sample: the authors need to report question(s) used to identify personal network size (and also report statistics as part of the RDS descriptive analysis as commented above).

Response: We have added questions to identify the network size in the methods section of the manuscript. Also presented RDS adjusted values in the web-only table 2.

4. How was clustering around the seeds was taken into account/adjusted for in multivariate analysis of the MSM/TG sample?

Response: Only descriptive statistics were computed using RDS II estimator. But we used unweighted values for the multivariate analysis because performing regression analysis on RDS data is not yet sufficiently developed.

Results:

1. The percentages presented in the text (and in Tables 1-2 and web-only Table) appear to be (unadjusted) sample estimates: ALL results on RDS-adjusted estimates were NOT presented??? If RDS analysis (using RDS-II estimator) had been done, then the result must be presented in the Tables

Response: We have presented separately RDS weighted descriptive statistics in the web-only table 2. But all the data presented in the prevalence ratios were unadjusted ones. We have mentioned this information in the manuscript.

2. There are inconsistencies between data/the presentation of data in Tables 1-2 and the descriptions of statistical analysis in the method:

- For FSWs (Table 1): adj PRs were presented for "ever inject drug" "physical assault" "forced sex" "having dependent" "police detention" "stigma" BUT these variables were NOT reported to be included in the multivariate model for FSWs (page 9 lines 185-187) while "suicidal thought ever" was reported to be included but results were missing/not presented in the Table

- For MSM/TG (Table 2): similar issues were found with "age", "drinking alcohol" "physical assault" "forced sex" "discrimination in job" and ""education" "depression", respectively.

Response: Thank you for pointing this out. The lines described above have been revised in the manuscript as follows. The variables included for FSW were age, educational status, condom use at last sex, ever inject drugs, participated (ever) in HIV awareness programmes, physical assault in last year, forced sex in last year, having dependents, police detention in last six months, stigma towards HIV and depression. The variables included for MSM/TG were age, condom use at last sex, participated (ever) in HIV awareness programmes, physical assault in last year, forced sex in last year, discrimination in job and suicidal thoughts (ever).

The variables which did not found a significant association in bivariate analysis were not included in the final multivariate model, but their frequencies were presented in the table.

Discussion:

1. Repeated presentation of the results: page 13 lines 243-248, 260-262

Response: We have rephrased the interpretation in results section so the lines 243-248 are different from the results section. However, for lines 260-262, we rephrased the sentences in the discussion section.

2. Incorrect presentation of the data: "FSWs who had distress or depression (one in two FSWs) had a higher prevalence of non-utilization..." page 13 line 250: The proportion of FSWs who were either depressed or distressed was 44% (268/610) Table 1 NOT "one in two."

Response: We would like to thank the reviewer for noticing the typo. We have corrected the sentence in the manuscript.

3. Presentation of results which were not discussed and/or presented in the Results section?: "Old MSM/TGs were found to use condoms more when compared to younger ones. The median age of first sexual intercourse being 16 years..." page 13 lines 255-256.

Response: We presented this information from the IBBS report published by the NCASC in Nepal. But to clarify we rephrased the sentence in the manuscript.

4. Unclear messages and/or presentation of data/results which were not discussed in the Result section: "Some factors affecting utilisation of HTC by MSM/TGs were different from that of FSWs. In events like forced sex in last year among FSW, it reduced the utilisation of HTCs among FSWs. Among MSM/TGs, the experience of forced sex led to utilisation of HTC. IBBS survey revealed that the perception of HIV risk by key population was related to condom use, which was higher among MSM/TGs when compared to FSWs. Three-fourths of MSM/TG believed they were at little or no risk of HIV if condoms were used". e.g. What message does the authors want to convey when stated "forced sex... reduce use of HTC among FSWs"? where the " Three-fourths of MSM/TG believed they were at little or no risk of HIV if condoms were used" came from?

Response: We have added new explanations for this association and removed the previously explained reasons. In updated version of the manuscript we have presented information more clearly and to the point.

5. Conflicting results and discussion and unclear message page 14 lines 272-286: The authors stated that " in Nepal, major component of a prevention programme is awareness raising activities" and "Hence participation in awareness classes resulted in high condom use and the fact that two-thirds of MSM/TGs and FSWs were tested for HIV at some point in time could have narrowed their risk perception to a low level as well as decreased their felt need to access HTC" Where the two-third of MSM and FSWs tested for HIV... came from and this is conflict with the results presented in this manuscript: 54% & 55% of non-utilization of HTC? also What is the implication for HIV program in Nepal if participation in awareness program lead to increase condom use and reduce use of HTC/HIV testing services???

Response: We have rephrased the interpretation in the results and discussion section of the manuscript and removed the not clear sentences from the manuscript.

6. The authors claims related to policy implications of the finding of the study (page 15 lines 290-297) are not strongly supported by the results and remain ambiguous: e.g. "First, psychosocial support needs to be an integral part of programmes for FSW and MSM/TG at all levels. HTC should be developed as an empowerment centre lending psychosocial and treatment support rather than being a centre for testing alone" This is not strongly supported by the results: As it is presented in the Tables (1-2) among psychosocial factors only "depression" was associated with non-utilization of HTC among FSWs, all other factor variables were not NOT significantly associated with the outcome. What is the specific recommendation and/or message the authors want to deliver when stated" HIV prevention programmes in Nepal need to go beyond condom promotion" and similarly for the third point on "contextual/demographic differentials between KPs."

Response: We have rephrased the policy implications and made it more accurate to the findings.

7. The statement "Our study adhered to STROBE guidelines for conduct and report of the study" is not fully satisfied: As commented above, the whole RDS analysis results were missing and the current manuscript is not adhered to the STROBE for reporting RDS study!

Response: We have provided RDS-weighted values and other RDS related information on the web only table 2 and web-only figure 1.

References

1. Williamson T, Eliasziw M, Fick GH. Log-binomial models: exploring failed convergence. *Emerg Themes Epidemiol* 2013;10(1):14. doi: 10.1186/1742-7622-10-14 [published Online First: 2013/12/13]
2. Barros AJ, Hirkata VN. Alternatives for logistic regression in cross-sectional studies: an empirical comparison of models that directly estimate the prevalence ratio. *BMC Med Res Methodol* 2003;3:21. doi: 10.1186/1471-2288-3-21 [published Online First: 2003/10/20]
3. Tyldum G, Johnston L. *Applying Respondent Driven Sampling to Migrant Populations: Lessons from the Field*. Palgrave Macmillan; 2014.

VERSION 2 – REVIEW

REVIEWER	Hailay Gesesew Jimma University, Ethiopia Flinders University, Australia
REVIEW RETURNED	04-Jul-2017

GENERAL COMMENTS	Once the paper polished for language edition, it is suitable for publication.
-------------------------	---

REVIEWER	Minh Pham Burnet Institute, Australia
REVIEW RETURNED	14-Jul-2017

GENERAL COMMENTS	<p>1. Author's responses/justification for the use of Poisson regression is acceptable.</p> <p>2. For regression analysis with RDS data, even though no consensus has been reached, I would recommend the authors to perform both unweighted and weighted analysis and report on weighted analysis if there is significant difference in the results</p> <p>*How was clustering around the seeds was taken into account/adjusted for in multivariate analysis of the MSM/TG sample?</p> <p>Response: Only descriptive statistics were computed using RDS II estimator. But we used unweighted values for the multivariate analysis because performing regression analysis on RDS data is not yet sufficiently developed</p>
-------------------------	---

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Hailay Gesesew

Institution and Country: Jimma University, Ethiopia, Flinders University, Australia

Please state any competing interests: None

Please leave your comments for the authors below

Once the paper polished for language edition, it is suitable for publication.

Response: We have revised the manuscript.

Reviewer: 2

Reviewer Name: Minh Pham

Institution and Country: Burnet Institute, Australia

Please state any competing interests: None declared

Please leave your comments for the authors below

1. Author's responses/justification for the use of Poisson regression is acceptable.

Response: Thanks.

2. For regression analysis with RDS data, even though no consensus has been reached, I would recommend the authors to perform both unweighted and weighted analysis and report on weighted analysis if there is significant difference in the results

*How was clustering around the seeds was taken into account/adjusted for in the multivariate analysis of the MSM/TG sample?

Response: Only descriptive statistics were computed using RDS II estimator. But we used unweighted values for the multivariate analysis because performing regression analysis on RDS data is not yet sufficiently developed.

Response:

As per the request of reviewer 2 we have also included a web-only table 1 that includes the results of associations between outcome and independent variables via Poisson model using individualised RDS weights (web-only table 1). Though the results are almost same (except the result of a physical assault in last year) we stick to the unweighted Poisson regression in results section due to following reasons:

- The weighted analysis in Poisson model did not allow us to calculate robust variance estimate of glm with the svy prefix. So the results are not comparable to unweighted and weighted analysis.
- Since RDS is designed only to predict parameter using weights and the use of a complex model to assess associations using weights is in infancy. We also provided our reason with reference in our previous response.

One of the co-authors (KD) also associated with the reputed European university and he consulted with the statistician and got the same recommendation to avoid using RDS weights in a complex model that aim to assess associations. However, we are aware that that some researchers used regression model using RDS weights.

VERSION 3 – REVIEW

REVIEWER	Minh Pham Burnet Institute Australia
REVIEW RETURNED	21-Aug-2017
GENERAL COMMENTS	Please add & discuss the results of weighted regression analysis in the results (no significant differences from unweighted analysis?)

VERSION 3 – AUTHOR RESPONSE

Reviewer: 2

Reviewer Name: Minh Pham

Institution and Country: Burnet Institute Australia

Please state any competing interests: None

Please leave your comments for the authors below

Please add & discuss the results of weighted regression analysis in the results (no significant differences from unweighted analysis?)

Response: We have discussed the results of weighted and unweighted analysis in the results section of the manuscript.