

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) | Determinants of frequent and infrequent STI testing and STI diagnosis related to test frequency among men who have sex with men in the Eastern part of the Netherlands: a 6-year retrospective study |
| AUTHORS | Kampman, Carolina; Heijne, Janneke; Koedijk, Petronella; Koedijk, Femke; Visser, Maartje; Hautvast, Jeannine L. A. |

VERSION 1 – REVIEW

| | |
|------------------------|---|
| REVIEWER | A. J. Schmidt London School of Hygiene and Tropical Medicine, United Kingdom |
| REVIEW RETURNED | 22-Nov-2017 |

| | |
|-------------------------|--|
| GENERAL COMMENTS | <p>While the topic - how often should MSM get tested for STIs, and how can we better adapt test frequency according to risk - is important, I recommend to reject the paper for the following reasons:</p> <ul style="list-style-type: none"> - The title and the introduction suggest the paper looks at test frequency and rates of STI diagnoses among MSM in the Netherlands, but it turns out that STI diagnoses rates are not at all reported, and that it is not about the Netherlands but about a rural region within the Netherlands. - The introduction is highly incoherent, and it does neither try to explain the rationale for the current Dutch recommendation for MSM to test for STIs twice a year, nor how this study could contribute to confirm or modify the current recommendations. - The methods part fails to explain how STI diagnoses (called "STI positivity") were measured in this study, and if and what kind of screening was performed in the absence of symptoms. As clinical data bases are used, one might ASSUME that diagnoses are based on clinical records, but even that is unclear - a paragraph in the discussion suggests that it might be self-reported. It is therefore impossible for the reader to interpret any of the findings. - Low frequency testers are a priori excluded from the analysis, introducing a large bias which is not addressed in the section on limitations. - Most variables, including one of the two outcome variables, are not described. In the two occasions descriptions are given, the definitions are highly problematic - defining individual ethnicity by country of birth, or individual socio-economic status by the residential postal code. |
|-------------------------|--|

| | |
|--|--|
| | <ul style="list-style-type: none"> - There is no indication that the variables were checked for collinearity prior to performing logistic regression analysis. - Some central variables such as transactional sex are mentioned as available, but were not included in the analysis. - The results part fails to show the main outcomes, in particular which STIs were found and at what rate. - The discussion part fails draw valid conclusion from the results, or to make use of the existing literature in an adequate way. - The level of English is fine, but both language and conclusions are highly stigmatising towards people with HIV. |
|--|--|

| | |
|------------------------|---|
| REVIEWER | Kristina I Persson Karolinska Institutet, Sweden |
| REVIEW RETURNED | 30-Nov-2017 |

| | |
|-------------------------|--|
| GENERAL COMMENTS | <p>General comments</p> <ul style="list-style-type: none"> - The paper is of great value for healthcare professionals & planners. - Some revisions may improve the manuscript further and make it clearer. - Large sample and long follow-up time are among the benefits of the study design. - The term "STI positivity" is used in the title, as key word and throughout the text. I do not find it clear or established. I would suggest rephrasing to STI frequency, STI diagnosis, STI rate, STI incidence, STI prevalence or similar. - HIV positive could be rephrased to MSM living with HIV. - It is not necessary to write MSM throughout the text. When it is clear that you refer to the men in your study you can write respondents, participants or even men to not repeat the MSM abbreviation. <p>Abstract Page 2 Line 4. Advised by whom? Line 38. Unclear who is "the rest". "Rest of" MSM in other parts of the Netherlands or do you mean compared to the general population?</p> <p>Introduction Page 3 In the introduction you mention STIs including HIV. Later, you exclude HIV (e.g. page 5 line 31-34). A sentence or paragraph declaring your STI definition and how and why HIV is excluded would be of value. Line 18, Why compare with Australia? European recommendations and test rates would be more interesting when comparing with the Netherlands. EMIS 2010 survey data may provide this.</p> <p>Results Page 6 Line 24, says MSN instead of MSM. Line 27 and on. More often than whom? You need to also declare which is the comparison group so that one can grasp it without seeing the table.</p> |
|-------------------------|--|

| | |
|-------------------------|---|
| | <p>Tables 1 and 2 (and possibly methods section)</p> <ul style="list-style-type: none"> - What are the reasons for the age division <26 and > 26? - How were western and non-western defined and why is this a good/useful categorization? - Were all participants recently HIV tested? If not, some of them may not know their HIV status, right? - Suggestion: rephrase Known HIV positivity to HIV status, Living with HIV/Not living with HIV/Unsure of HIV status. - In Table 1 OR 1.0 is bold/assessed significant (STI related symptoms) but the same is not applied in table 2 (sexual preference). Why is that? <p>Discussion</p> <ul style="list-style-type: none"> - Is it possible to compare results with rural MSM studies in other countries/contexts in the discussion? - Were there any sexual practice/sexual behavior questions in the questionnaire? If so, can you see whether this differs between the two groups? May the frequent testers/MSM subgroup with higher STI occurrence be a group of MSM with broader sexual practice? If so, please, discuss this and maybe add references to previous studies on this. - What are the STI prevention implications of your results? Please, elaborate on this. <p>Page 9</p> <p>Line 25. Here it is mentioned that it is a rural area. Please, describe this earlier in the manuscript. The reader who is not familiar with Dutch geography may not grasp that otherwise.</p> <p>Line 27. The STUDY population, not the MSM population, right?</p> <p>Page 10</p> <p>Line 16-22. References to studies on bridge populations may be useful and can deepen the discussions here. E.g. Behaviourally bisexual men as a bridge population for HIV and sexually transmitted infections? Evidence from a national probability survey. Mercer CH, Hart GJ, Johnson AM, Cassell JA. Int J STD AIDS. 2009 Feb;20(2):87-94.</p> <p>Line 25-36. STI among MSM living with HIV. Discuss in more detail. Behaviour/sexual practice differences?</p> <p>Line 44-46. What about legislation on partner notification/communicable disease act in in the Netherlands? Are you obliged to seek care/test if you've been notified by a sex partner who was diagnosed with STIs? If so, this may explain the association between partner notification and seeking care. Please, clarify.</p> |
| REVIEWER | Associate Professor Stephen Neville Auckland University of Technology New Zealand |
| REVIEW RETURNED | 04-Dec-2017 |
| GENERAL COMMENTS | <p>Thank you for providing me the opportunity to read and comment on your manuscript. The topic is interesting and contemporary considering some western countries are experiencing an increase in HIV infection rates in MSM. There are some issues that require attention and these include:</p> <ol style="list-style-type: none"> 1. The data is dated and while the author/s attempt to explain this what is provided is insufficient. A more convincing argument needs to be presented. If the manuscript is accepted for publication data will be between 5 and 10 years old. I therefore question the usefulness of reporting these data. |

| | |
|--|---|
| | <p>2. Page 2 section "Methodological Strengths and Limitations", the sentence "Data from MSM with minimally three consultations ..." doesn't make sense.</p> <p>3. The word "ever" needs to be replaced with "never".</p> <p>4. In the discussion section make sure similar international studies that have looked at test frequency and STI positivity are included.</p> <p>5. There is a heavy reliance on "Vriend and colleagues". A wider range of literature needs to be included in the discussion section.</p> <p>6. Study limitations related to the age of the data need to be strengthened.</p> |
|--|---|

VERSION 1 – AUTHOR RESPONSE

Editors comments

We appreciate that one of the reviewers' comments are quite negative; however, in light of the positive comments from the other two reviewers, we felt we should give you the opportunity to respond to the negative criticisms and revise your manuscript appropriately. We felt that many of the criticisms could be addressed by clearly outlining the limitations of your study design. Please note that we may ask any or all of the reviewers to assess your revised manuscript so urge you address all comments as thoroughly as possible.

Thank you very much for the opportunity to revise our manuscript, we will do so accordingly. We will also outline the limitations of our study design more clearly. Below you will find our response to the reviewers' comments point by point in blue.

Reviewer: 1

Reviewer Name: A. J. Schmidt

Institution and Country: London School of Hygiene and Tropical Medicine, United Kingdom

Please state any competing interests or state 'None declared': None declared.

While the topic - how often should MSM get tested for STIs, and how can we better adapt test frequency according to risk - is important, I recommend to reject the paper for the following reasons:

Thank you very much for taking the time to carefully read our manuscript and for your comments. We are given the chance by the editors of BMJ Open to correct our manuscript and carefully address all of the comments. We hope that we have improved the manuscript in such manner, that it will be worth publishing.

- The title and the introduction suggest the paper looks at test frequency and rates of STI diagnoses among MSM in the Netherlands, but it turns out that STI diagnoses rates are not at all reported, and that it is not about the Netherlands but about a rural region within the Netherlands.

We have adjusted the title as follows:

"Determinants of frequent and infrequent STI testing and STI diagnosis related to test frequency among men who have sex with men in the Eastern part of the Netherlands: a 6 year retrospective study"

We have also added the STI diagnoses rates in our results, as well as in our table 1, as follows;

“Table 1 shows that among infrequently tested MSM, 47.0% were ever diagnosed with an STI, compared to 64.6% of the frequently tested MSM.”

- The introduction is highly incoherent, and it does neither try to explain the rationale for the current Dutch recommendation for MSM to test for STIs twice a year, nor how this study could contribute to confirm or modify the current recommendations.

We have clarified the rationale for the current guidelines with the following additions (in *italic*);

“There were only informal guidelines, for MSM’s test frequency in the Netherlands before 2017, based on expert opinion. These informal guidelines recommended STI testing for MSM at least twice a year. A formal guideline, based on Dutch epidemiological findings, has now (2017) been drafted, and it advises MSM to be tested at least twice a year; and high-risk MSM (e.g. HIV-positive MSM or MSM who are commercial sex workers), four times a year.”

Furthermore, we have added how the results of this study could be linked with the guidelines;

“Study results could provide more insight in the frequency and relevance of testing according to guidelines for certain MSM risk groups.”

- The methods part fails to explain how STI diagnoses (called “STI positivity”) were measured in this study, and if and what kind of screening was performed in the absence of symptoms. As clinical data bases are used, one might ASSUME that diagnoses are based on clinical records, but even that is unclear - a paragraph in the discussion suggests that it might be self-reported. It is therefore impossible for the reader to interpret any of the findings.

To make clear how screening is performed in the absence of symptoms, we have added the following (in *italic*) in the methods-section:

“The STI clinic at the RPHS is always accessible to MSM, whether or not reporting STI –related symptoms, while there is a triage system for heterosexuals. Furthermore, MSM are always tested on 5 STIs; chlamydia, gonorrhoea, syphilis, HIV (unless clients opt out) and hepatitis B (when not successfully vaccinated against hepatitis B).”

About being STI positive there is a clear description in the method-section, we tried to make it clearer (in *italic*):

“The outcome of STI diagnoses was defined as follows: any one of the MSM was defined as being diagnosed with one or more STIs, including chlamydia, gonorrhoea, syphilis, and/or infectious hepatitis B, at one or more body locations (oral, genital, or anal) at one or more consultations during the study period.”

We have adjusted the discussion and tried to make it clear that being STI positive is not based on self-reports (in *italic*):

“MSM who were ever diagnosed with an STI, MSM who had never had STI symptoms, and MSM who had ever had sex with men as well as women were more often frequently tested.”

We also changed this in our abstract (in *italic*):

“953 (59.2%) of the MSM were infrequently tested, and 658 (40.8%) were frequently tested. MSM who were ever diagnosed with an STI, MSM who had never had STI symptoms, and MSM who had ever had sex with both men and women were more often frequently tested.

- Low frequency testers are a priori excluded from the analysis, introducing a large bias which is not addressed in the section on limitations.

We did indeed exclude the group of MSM with only one consultation. As we assume that you mean MSM with only one consultation by ‘low frequency testers’, we made an addition in the ‘limitation section’:

“Fifth, we excluded MSM with only one consultation. We reasoned that leaving them out would provide us with a more valid overview of test frequency in those who appear to be a regular client of the STI clinics.”

- Most variables, including one of the two outcome variables, are not described. In the two occasions descriptions are given, the definitions are highly problematic - defining individual ethnicity by country of birth, or individual socio-economic status by the residential postal code.

Although the two outcome variables were already described in the current methods-section, it appears not to be clear enough for a reader. We therefore adjusted the description as follows (in italic):

1. Test frequency: “The outcome of test frequency was defined as follows: MSM were defined infrequently tested if their mean test intervals were 6 months or more. They were labelled as frequently tested if their mean test intervals were less than 6 months. A 1-month margin was taken into account to ensure that a person would not be regarded as infrequently tested if the mean test interval was only slightly more than 6 months.”

2. STI positivity: “The outcome of STI diagnosis was defined as follows: any one of the MSM was defined as being diagnosed with one or more STIs, including chlamydia, gonorrhoea, syphilis, and/or infectious hepatitis B, at one or more body locations (oral, genital, or anal) at one or more consultations during the study period.”

Concerning the other two unclear variables (changes in italic):

1. Ethnicity: “ethnicity (due to a change in the registration, ethnicity was a combination variable that consisted of self-defined ethnicity (from 2006 until 2010) and ethnicity based on (parental) country of birth (from 2011 until 2013), MSM were subsequently categorized under Dutch, Western and non-Western”).

Unfortunately, two definitions concerning ethnicity were used during the study period; self-declared and based on country of birth. This is due to National Institute for Public Health and the Environment that sets up the registration rules. Ethnicity and its two definitions has been investigated in 2012, study outcome (being chlamydia positive) did not differ:

Haasnoot A, Koedijk FD, Op De Coul, et al. Comparing two definitions of ethnicity for identifying young persons at risk for chlamydia. *Epidemiol Infect.* 2012 May;140(5):951-8

2. Socio-economic status: “based on postal codes.”

Socio-economic status in a certain postal code area is induced by a number of factors derived from the inhabitants: education, income and their position on the job market. To clarify this, we have added the following (in italic); “socio-economic status (SES, based on postal codes (four digits). This measure of SES was deduced by postal code-associated data from the Netherlands Institute for

Social Research and is a composed measure of four variables: average income per household; percentage of households with low incomes; percentage of residents without a paid job; and percentage of households with an average to low educations developed by the Netherlands institute for social research and is an average of, for example, income and employment status of the inhabitants of each postal code area)”

- There is no indication that the variables were checked for collinearity prior to performing logistic regression analysis.

The data were checked for multicollinearity, using tolerance and the variance inflation factor (VIF). VIF-values greater than 10 and tolerance-values smaller than .10 may indicate multicollinearity. There were no signs of multicollinearity in any of the regression models.

We added this in our ‘methods’ section (in italic):

“We performed logistic regression analyses to identify determinants of testing frequency and STI positivity. Collinearity between variables was checked beforehand.”

- Some central variables such as transactional sex are mentioned as available, but were not included in the analysis.

There are 3 variables that aren’t included in analysis: being a commercial sex worker, being the client of a commercial sex worker and intravenous drug use. We wanted to include these variables initially, but we decided to exclude them, because the group sizes were too small for analysis, as shown in the table below;

| Infrequent testers | Frequent testers |
|---------------------------------|------------------|
| Client of commercial sex worker | |
| Never | |
| Ever | |
| 916(96.1%) | |
| 37(3.9%) | |
| 629(95.6%) | |
| 29(4.4%) | |
| Commercial sex worker | |
| Never | |
| Ever | |
| 939(98.5%) | |
| 14(1.5%) | |
| 641(97.4%) | |
| 17(2.6%) | |
| Intravenous drug use | |
| Never | |
| Ever | |
| 900(94.4%) | |
| 53(5.6%) | |
| 590(89.7%) | |
| 68(10.3%) | |

To avoid any confusion, we have now deleted the mentioning of these variables in the ‘methods’ section.

- The results part fails to show the main outcomes, in particular which STIs were found and at what rate.

Table 1 shows that 47.0% of the infrequent testers were ever tested STI positive, whereas 64.6% of the frequent testers were ever tested STI positive. We have added these numbers in our results-section, as follows;

“Table 1 shows that among infrequently tested MSM, 47.0% were ever diagnosed with an STI, compared to 64.6% of the frequently teste MSM.”

We choose not to make a distinction between the different STI in particular, because the aim of our study was to establish the relationship between test frequency and STI positivity. HIV status was considered a separate variable, based on existing literature that indicates that MSM who are diagnosed with HIV are more likely to be diagnosed with an STI. MSM were defined as diagnosed with HIV when they tested HIV positive during study period or were already known HIV positive before study period.

- The discussion part fails draw valid conclusion from the results, or to make use of the existing literature in an adequate way.

Unfortunately the reviewer did not specifically indicate which conclusions he did not judge to be valid. We were therefore not able to improve the manuscript accordingly. As the two other reviewers did not come up with a similar comment, we as well did not consider it useful to alter the manuscript by ourselves without specific directions.

With regards to the use of existing literature; we did search thoroughly, but did not find other studies that investigate the relations between test frequency and STI positivity in MSM using comparable study methods to ours. Studies on this topic focus on repeated testing, compared to MSM with a single consultations, and its importance, while we specifically studied STI positivity among frequent testers (not compared to single testers). Where possible, we did include the relevant literature in our discussion.

- The level of English is fine, but both language and conclusions are highly stigmatising towards people with HIV.

It is not our intention that our article appears stigmatizing towards people with HIV. We have decided to change 'HIV positive' in to 'diagnosed with HIV', and we have changed this throughout our manuscript.

As it is our goal to prevent the further spread of STI, by testing certain high risk groups regularly, we decided to make MSM who were diagnosed with HIV a separate variable. This is based on existing literature, which indicates that MSM who are diagnosed with HIV are more likely to be STI positive. This is also experienced by the STI-clinic workers and epidemiologically determined in the Netherlands. As our study shows that MSM who were diagnosed with HIV more likely to be STI positive, but do test less frequently, we concluded that MSM who were diagnosed with HIV should be motivated to test (more) frequently, or according to guideline (four times a year).

Reviewer: 2

Reviewer Name: Kristina I. Persson

Institution and Country: Karolinska Institutet, Sweden

Please state any competing interests or state 'None declared': None declared

General comments

- The paper is of great value for healthcare professionals & planners.
- Some revisions may improve the manuscript further and make it clearer.
- Large sample and long follow-up time are among the benefits of the study design.

Thank you very much for your kind remarks. We value your comments very much and thank you for carefully reading our manuscript.

- The term "STI positivity" is used in the title, as key word and throughout the text. I do not find it clear or established. I would suggest rephrasing to STI frequency, STI diagnosis, STI rate, STI incidence, STI prevalence or similar.

We did, improve the definition of being STI positive in the 'methods' sections, as follows:

"The outcome of STI diagnosis was defined as follows: any one of the MSM was defined as being diagnosed with one or more STIs, including chlamydia, gonorrhoea, syphilis, and/or infectious hepatitis B, at one or more body locations (oral, genital, or anal) at one or more consultations during the study period."

We have considered your rephrasings carefully, and decided to use the term 'diagnosed with STI' and 'STI diagnosis'. We have changed this throughout our manuscript.

- HIV positive could be rephrased to MSM living with HIV.

Thank you for your suggestion. We have decided to rephrase HIV positive with 'being diagnosed with HIV' throughout the manuscript. We did not provide a clear definition of being HIV positive in the 'methods' section. Therefore, we have added the following sentence:

"MSM were defined as diagnosed with HIV when they tested positive for HIV during study the period or were already known HIV positive before the study period."

- It is not necessary to write MSM throughout the text. When it is clear that you refer to the men in your study you can write respondents, participants or even men to not repeat the MSM abbreviation.

Because our study is retrospective, one cannot speak of 'respondents' or 'participate', because they did not respond or participate in our study. Also, if we replace MSM with only the word 'men', we fear that one will also interpret 'men' as being heterosexual as well.

- Abstract, Page 2, Line 4. Advised by whom?

To not exceed the word count in the abstract, we have elaborated on this in the 'introduction' section as follows:

"There were only informal guidelines for MSM's test frequency in the Netherlands before 2017, based on expert opinion. These informal guidelines recommended STI testing for MSM at least twice a year."

- Abstract, Line 38. Unclear who is "the rest". "Rest of" MSM in other parts of the Netherlands or do you mean compared to the general population?

This is indeed unclear. We have adjusted the title to make clear our study concerns the Eastern part of the Netherlands:

“Determinants of frequent and infrequent STI testing and STI diagnosis related to test frequency among men who have sex with men in the Eastern part of the Netherlands: a 6 year retrospective study”

And adjusted this sentence in the methodological strengths and limitations as follows (in italic):

“The MSM population in the Eastern part of the Netherlands and their test behaviour may differ from the rest of the Netherlands.”

We have also checked this addition in our ‘discussion’ section, which was already according your suggestion.

-Introduction, Page 3, In the introduction you mention STIs including HIV. Later, you exclude HIV (e.g. page 5 line 31-34). A sentence or paragraph declaring your STI definition and how and why HIV is excluded would be of value.

In our ‘methods’ section we have improved the description of the definition used in this study for ‘STI diagnosis’ and for ‘diagnosed with HIV’ (see reply to your comment above). But we did not make clear why we regarded HIV status as a separate variable. We have therefore added the following sentence on this in our ‘methods’ section:

“HIV status was considered a separate variable, based on existing literature that indicates that MSM who are diagnosed with HIV are more likely to be diagnosed with an STI.^{12,13,14,15} MSM were defined as diagnosed with HIV when they tested HIV positive during study period or were already known HIV positive before study period.”

-Introduction, Line 18, Why compare with Australia? European recommendations and test rates would be more interesting when comparing with the Netherlands. EMIS 2010 survey data may provide this.

Yes, we have carefully read the ‘EMIS’ results. Reference number 14 is an EMIS-study. However, in this part in the introduction, we describe guidelines concerning test frequencies for MSM. The EMIS does unfortunately not provide guidelines on test frequency for MSM.

-Results, Page 6, Line 24, says MSN instead of MSM.

We have corrected this accordingly.

-Results, Line 27 and on. More often than whom? You need to also declare which is the comparison group so that one can grasp it without seeing the table.

We have adjusted this accordingly (in italic):

“Multivariable analysis showed that the frequently tested had more often been diagnosed with an STI (OR 1.4, 95% CI 1.1–1.7), were less likely to ever have reported STI-related symptoms (OR 0.8, 95% CI 0.6–1.0) and had less often ever had sex with men only (OR 0.6, 95% CI 0.5–0.8) than the infrequently tested.”

And,

“The same determinants of STI diagnosis were identified in both groups: MSM who had ever been notified by a partner, MSM who had ever had STI-related symptoms, and MSM who were ever diagnosed with HIV were more likely to have an STI diagnosis.”

And,

“In addition, frequently tested MSM who only had sex with men were more likely to have an STI diagnosis, which was not seen among infrequently tested MSM.”

-Tables 1 and 2 (and possibly methods section), What are the reasons for the age division <26 and > 26?

We have adjusted this in the ‘methods’ section in the following way (in italic):

“age (<26 years and ≥26 years, clients younger than 26 years are considered ‘young’ as decided by national STI clinic regulations)”

-Tables, How were western and non-western defined and why is this a good/useful categorization?

We have addressed this as follows in the ‘methods’ section (in italic):

“ethnicity (due to a change in the registration, ethnicity was a combination variable that consisted of self-defined ethnicity (from 2006 until 2010) and ethnicity based on (parental) country of birth (from 2011 until 2013), MSM were subsequently categorized under Dutch, Western and non-Western)

We have chosen this categorization because non-Western clients have different risk profile in STI than Western/Dutch clients.

-Tables, Were all participants recently HIV tested? If not, some of them may not know their HIV status, right?

In the Netherlands all MSM are tested for the ‘big five’ (chlamydia, gonorrhoea, syphilis, hepatitis B and HIV) at every consultation. Though testing on HIV is not mandatory, more than 99% does test on HIV. In our analysis only 3 of the 1611 MSM opted out for testing on HIV. Of course, MSM who are already HIV positive, are not tested on HIV repeatedly.

-Tables, Suggestion: rephrase Known HIV positivity to HIV status, Living with HIV/Not living with HIV/Unsure of HIV status.

We have rephrased this into ‘diagnosed with HIV’ throughout the manuscript.

-Tables, In Table 1 OR 1.0 is bold/assessed significant (STI related symptoms) but the same is not applied in table 2 (sexual preference). Why is that?

We think you refer to the confidence intervals: this is due to rounding issues. Significance was based on the p-value.

We have added a footnote under table 2 (in italic):

“In bold: significant ($p < 0.05$); due to rounding into 1 decimal 1.0 is not always significant.”

-Discussion, Is it possible to compare results with rural MSM studies in other countries/contexts in the discussion?

Unfortunately, we could not find any such results, since literature on this specific topic is scarce. Also, we did find in existing literature that study methods differ significantly, which makes our study difficult to compare to other studies.

-Discussion, Were there any sexual practice/sexual behaviour questions in the questionnaire? If so, can you see whether this differs between the two groups? May the frequent testers/MSM subgroup with higher STI occurrence be a group of MSM with broader sexual practice? If so, please, discuss this and maybe add references to previous studies on this.

There were indeed sexual behaviour questions in the questionnaire (which is the patient registration system). Of those the following two were used in the analysis: number of partners and sexual preference. Table 1 shows that MSM who ever had sex with men only were more likely to be frequent testers. Table 2 shows that frequently tested MSM who only had sex with men were more likely to have an STI diagnosis in multivariable analysis. Number of partners wasn't significant in multivariable analysis on the two outcome measures. We have elaborated on these study findings in the discussion, where we compare our study findings to existing literature.

The other sexual behaviour questions were; drug use, transactional sex and condom use with last sexual contact. Unfortunately, these questions were poorly replied to and numbers were too low to enter these variables into analysis.

-Discussion, What are the STI prevention implications of your results? Please, elaborate on this.

We have highlighted this in the final paragraph of our 'discussion' section;

"We also found that MSM who were ever diagnosed with HIV were more often diagnosed with an STI, but did not visit the STI clinic more frequently than MSM who tested HIV negative. Other studies also show that MSM who are diagnosed with HIV are more likely have another STI diagnosis.^{12,13,14,15} Routine screening for STI of MSM who were diagnosed with HIV is important because regular screening could help reduce the incidence of STI.^{22,23,24} MSM diagnosed with HIV are not routinely tested for STI in most HIV care centres, except for annual syphilis and HCV screening. Dutch STI clinics put great efforts in motivating MSM to test for STIs by outreach activities at MSM events and providing anonymous online test facilities. This study highlights the importance of ongoing efforts done by STI clinics in encouraging MSM who were diagnosed with HIV to be tested for STI frequently."

-Discussion, Page 9, Line 25. Here it is mentioned that it is a rural area. Please, describe this earlier in the manuscript. The reader who is not familiar with Dutch geography may not grasp that otherwise.

We have adjusted the title accordingly and described this in the 'methods' section;

"We performed a 6-year retrospective study (2008–2013), utilising data from 5 of the 25 Dutch STI clinics. The participating clinics were in the east of the Netherlands, which is a semi-rural area."

-Discussion, Line 27. The STUDY population, not the MSM population, right?

Yes, you are correct, we have adjusted this accordingly.

-Discussion, Page 10, Line 16-22. References to studies on bridge populations may be useful and can deepen the discussions here. E.g. Behaviourally bisexual men as a bridge population for HIV and

sexually transmitted infections? Evidence from a national probability survey. Mercer CH, Hart GJ, Johnson AM, Cassell JA. Int J STD AIDS. 2009 Feb;20(2):87-94.

About bisexual men we have written the following in our manuscript;

“Furthermore, our study shows that MSM who had ever had sex with men as well as women were more often frequently tested. In two other Dutch studies, men who had sex with both genders less often had repeat tests.^{10,11} We do not have a clear explanation for this discrepancy, but a reporting bias in sexual preference could be a possible explanation. Further research is needed to gain more insight into this.”

By reporting bias we mean that men who had sex with men could self-report in what category they felt they belonged (e.g. ‘sex with men only’ or ‘sex with men and women’), this was not scored on sexual behaviour. We felt that this reporting bias has such a large impact, that we cannot draw any solid conclusions on this matter. Therefore, we have decided not to elaborate on this matter that much.

-Discussion, Line 25-36. STI among MSM living with HIV. Discuss in more detail. Behaviour/sexual practice differences?

We have discussed this in more detail in our ‘discussion’ section, the following way:

“The authors believe the higher number of bacterial re-infections in HIV positive diagnosed MSM are indicative of rapid transmission in dense sexual networks.¹⁷ An Italian study assessed risk behaviour before and after being diagnosed with HIV; HIV positive diagnosed MSM continue to engage in at risk practices: one fourth of them did not use a condom during STI-episodes, 12.5% of the participants had engaged in sex for money, and 8.4% had paid for sex.¹⁸ Also, serosorting (selecting sex partners of the same HIV status) or assumed serosorting among HIV positive diagnosed MSM may play a role in at risk practices. Among HIV-positive diagnosed men, the likelihood of unprotected anal intercourse (UAI) is higher when a partner's status was known. Furthermore, assumed seroconcordant UAI is associated with increased STI prevalence.^{19,20,21}”

-Discussion, Line 44-46. What about legislation on partner notification/communicable disease act in the Netherlands? Are you obliged to seek care/test if you've been notified by a sex partner who was diagnosed with STIs? If so, this may explain the association between partner notification and seeking care. Please, clarify.

We have added the following sentence to this paragraph;

“There is no legislation on partner notification in the Netherlands. Also, partner notification is performed anonymously, the STI clinic doesn't know to full extend who is being notified.”

Reviewer: 3

Reviewer Name: Associate Professor Stephen Neville

Institution and Country: Auckland University of Technology, New Zealand

Please state any competing interests or state ‘None declared’: None declared.

Thank you for providing me the opportunity to read and comment on your manuscript. The topic is interesting and contemporary considering some western countries are experiencing an increase in HIV infection rates in MSM.

Thank you very much for taking the time and interest to read our manuscript. We value your comments and will take great care in addressing them point by point below. Thank you for making our manuscript better by your comments.

There are some issues that require attention and these include:

1. The data is dated and while the author/s attempt to explain this what is provided is insufficient. A more convincing argument needs to be presented. If the manuscript is accepted for publication data will be between 5 and 10 years old. I therefore question the usefulness of reporting these data.

In our 'methods' section, we have provided our reasoning;

"Data from 2013 onwards were not included due to changes in the patient-registration system of the STI clinics. The definitions of database variables could not be matched."

We believe, however, our study data are still of importance for today's practice, we have elaborated on this limitation in the 'discussion' section the following way:

"Fourth, due to changes in the patient registration system, we could not include data beyond the year 2013. The STI clinic has, however, always been freely accessible to MSM over the years. We do not think there has been any sudden changes in risk behaviour and/or test frequency among MSM, therefore we think current study data is still of importance to STI care nowadays."

2. Page 2 section "Methodological Strengths and Limitations", the sentence "Data from MSM with minimally three consultations ..." doesn't make sense.

We have replaced this with the following sentence;

"Longitudinal data of MSM with at least three consultations at regional Dutch STI clinics between 2008 and 2013 were analysed."

3. The word "ever" needs to be replaced with "never".

We have chosen to use the word 'ever', to refer to the occurrence of the event within an individual's consultations (for example, being STI positive, being notified of having had STI related symptoms), instead of reporting the absence of the event. We think that by displaying our result this way, the manuscript is easier to understand.

4. In the discussion section make sure similar international studies that have looked at test frequency and STI positivity are included.

Unfortunately, there are no other studies that study the relations between test frequency and STI positivity in MSM using comparable study methods to ours. Studies on this topic focus on repeated testing, compared to MSM with a single consultations, and its importance, while we specifically studied STI positivity among frequent testers (not compared to single testers).

5. There is a heavy reliance on "Vriend and colleagues". A wider range of literature needs to be included in the discussion section.

Please see our response at the comment above.

6. Study limitations related to the age of the data need to be strengthened.

We would like to refer you to our response on your first comment.

VERSION 2 – REVIEW

| | |
|------------------------|---|
| REVIEWER | Kristina I Persson Karolinska Institutet, Sweden |
| REVIEW RETURNED | 01-Feb-2018 |

| | |
|-------------------------|--|
| GENERAL COMMENTS | <p>Thanks for letting me review the revised manuscript. I appreciate the changes made and as far as I can see you have catered for the needs of clarification and revision.</p> <p>I previously suggested that HIV positive could be rephrased to MSM living with HIV and also another reviewer commented on how MSM living with HIV were described.</p> <p>You answered that "We have decided to rephrase HIV positive with 'being diagnosed with HIV' throughout the manuscript." and that you added "MSM were defined as diagnosed with HIV when they tested positive for HIV during study the period or were already known HIV positive before the study period."</p> <p>This means that you did not omit 'HIV positive' in the manuscript. It even says 'HIV positive diagnosed' on page 10 and 11 now. Please, rephrase.</p> <p>Some small formatting and language needs remain.</p> |
|-------------------------|--|

| | |
|------------------------|---|
| REVIEWER | Stephen Neville Auckland University of Technology New Zealand |
| REVIEW RETURNED | 04-Feb-2018 |

| | |
|-------------------------|---|
| GENERAL COMMENTS | Thank you for considering reviewer feedback. The manuscript is much improved. |
|-------------------------|---|

VERSION 2 – AUTHOR RESPONSE

Editors comments

We have answered your questions and adjusted the text of the manuscript accordingly.

- Please ensure that your abstract is formatted according to our Instructions for Authors:
http://bmjopen.bmj.com/pages/authors/#research_articles

We have adjusted the abstract according your formatting requests below:

“Objectives

Men who have sex with men (MSM) remain vulnerable to STIs and are advised to be tested at least twice a year. The aim of this study was to assess the determinants of test frequency and their associations with an STI diagnosis.

Design

A 6-year retrospective study.

Setting

5 STI clinics in the Eastern part of the Netherlands.

Participants

MSM whose mean test interval was 6 months or more were grouped as "infrequently tested" (n=953), and those with mean test intervals less than 6 months were grouped as "frequently tested" (n=658).

Primary and secondary outcome measures

Test frequency and STI diagnosis and its determinants.

Results

MSM who were ever diagnosed with an STI (OR=1.4; 95% CI 1.1 to 1.7), MSM who had never had STI symptoms (OR=0.8;95%CI 0.6 to 1.0), and MSM who had ever had sex with both men and women (OR=0.6;95%CI 0.5 to 0.8) were more often frequently tested. Moreover, in both groups, MSM who had ever been notified by a partner (OR=2.2;95%CI 1.7 to 2.9 infrequently tested, OR=2.0;95%CI 1.4 to 2.9 frequently tested), MSM who had ever had STI symptoms (OR=1.6;95%CI 1.2 to 2.1 infrequently tested, OR=1.8;95%CI 1.3 to 2.6 frequently tested) , and MSM who were ever diagnosed with HIV (OR=2.7;95%CI 1.5 to 4.6 infrequently tested, OR=6.8;95%CI 2.6 to 17.5 frequently tested) were more likely to be diagnosed with an STI.

Conclusions

Among MSM visiting STI clinics, those who were ever diagnosed with HIV were more often diagnosed with an STI, but did not visit the STI clinic more frequently than HIV-negative MSM. This highlights the necessity of encouraging MSM who are diagnosed with HIV to have an STI tests more frequently."

- Please improve the reporting of the statistics throughout your abstract by including OR and 95% CI.

We have done so accordingly;

"MSM who were ever diagnosed with an STI (OR=1.4; 95% CI 1.1 to 1.7), MSM who had never had STI symptoms (OR=0.8;95%CI 0.6 to 1.0), and MSM who had ever had sex with both men and women (OR=0.6;95%CI 0.5 to 0.8) were more often frequently tested. Moreover, in both groups, MSM who had ever been notified by a partner (OR=2.2;95%CI 1.7 to 2.9 infrequently tested, OR=2.0;95%CI 1.4 to 2.9 frequently tested), MSM who had ever had STI symptoms (OR=1.6;95%CI 1.2 to 2.1 infrequently tested, OR=1.8;95%CI 1.3 to 2.6 frequently tested) , and MSM who were ever diagnosed with HIV (OR=2.7;95%CI 1.5 to 4.6 infrequently tested, OR=6.8;95%CI 2.6 to 17.5 frequently tested) were more likely to be diagnosed with an STI."

- Please ensure that the terminology is revised to be consistent throughout your manuscript. For example, you use the terminology "STI positivity" and "STI diagnosis" interchangeably throughout the rest of the manuscript.

Thank you for pointing this out. We have changed this where applicable; STI positivity into STI diagnosis.

- Along with your revised manuscript, please include a complete copy of the STROBE checklist indicating the page/line numbers of your manuscript where the relevant information can be found (<https://strobe-statement.org/index.php?id=strobe-home>). We noted the the STROBE checklist

currently provided includes only contains the first 12 items (the first page) of the STROBE checklist, and is missing the second page of the checklist which contains items 13-22.

Sorry for not uploading the complete document, with our second revision we have uploaded the complete STROBE-checklist, please see 'files'.

Reviewer: 2

Reviewer Name: Kristina I Persson

Institution and Country: Karolinska Institutet, Sweden

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

Thanks for letting me review the revised manuscript. I appreciate the changes made and as far as I can see you have catered for the needs of clarification and revision.

I previously suggested that HIV positive could be rephrased to MSM living with HIV and also another reviewer commented on how MSM living with HIV were described.

You answered that "We have decided to rephrase HIV positive with 'being diagnosed with HIV' throughout the manuscript." and that you added "MSM were defined as diagnosed with HIV when they tested positive for HIV during study the period or were already known HIV positive before the study period."

This means that you did not omit 'HIV positive' in the manuscript. It even says 'HIV positive diagnosed' on page 10 and 11 now. Please, rephrase.

Some small formatting and language needs remain.

Thank you very much for your comment and your second review. We weren't consistent in changing 'HIV positive' into 'being diagnosed with HIV'. We have made changes accordingly throughout the manuscript.

Reviewer: 3

Reviewer Name: Stephen Neville

Institution and Country: Auckland University of Technology, New Zealand

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

Thank you for considering reviewer feedback. The manuscript is much improved.

Thank you very much.