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Determinants of STI test frequency and positivity of men who have sex with men in the Netherlands: a 6-year retrospective study

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Word count
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Abstract: 247

Abstract

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 STI positivity.

Methods

Longitudinal data of MSM with at least three consultations at regional Dutch STI clinics between 2008 and 2013 were analysed. MSM whose mean test interval was 6 months or more were grouped as “infrequently tested”, and those with mean test intervals less than 6 months were grouped as “frequently tested”. We used logistic regression to assess the determinants of test frequency and STI positivity in both groups.

Results

953 (59.2%) of the MSM were infrequently tested, and 658 (40.8%) were frequently tested. MSM who had ever had a previous 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. Moreover, in both groups, MSM who had ever been notified by a partner, MSM who had ever had STI symptoms, and MSM who were ever tested HIV positive were more likely to be STI positive.

Conclusions

Among MSM visiting STI clinics, those were ever tested HIV positive were more often STI positive, but did not visit the STI clinic more frequently than HIV-negative MSM. This highlights the necessity of encouraging HIV-positive MSM to have STI tests more frequently. Further insights into the test behaviour of MSM without STIs are needed.

Methodological Strengths and Limitations

- Data from MSM with minimally three consultations at Dutch STI clinics between 2008 and 2013 were grouped for MSM who were frequently or infrequently tested.
- Current study has a long follow-up of 5 years, so that a large number of MSM were included in analyses.
- The MSM population and its test behaviour in this study may differ from the rest of the Netherlands.
- The STI positivity was only available for those who came back for repeat testing; they do not represent the re-infections contracted by all MSM who visit STI clinics.
- Only STI-clinic consultations were available, data from STI tests carried out by general practitioners or other specialists could not be taken into account.

Introduction

Men who have sex with men (MSM) contribute to the worldwide burden of sexually transmitted infections (STIs), including HIV.[1, 2, 3] Some studies have found that MSM reported large proportions of diagnoses of HIV (42%), gonorrhoea (43%), and syphilis (58%).[4,5] In the Netherlands, MSM accounted for the greatest contribution to STI positivity in 2016 at STI clinics; 21% of the tests were positive for one or more STIs.[6]

Early detection and treatment are crucial to reduce the risk of transmitting STIs (including HIV) among MSM.[7] Therefore, the test frequency is important for reducing the transmission of STIs. In Australia, MSM are advised to get a test at least once a year, but one study reports that this advice is poorly adhered to: re-testing rates at 1 year were 35%.[8] A British study estimates that 55% of the MSM were tested once a year where guidelines also recommend HIV tests once a year (and more often for those at "higher risk").[9]

There were only informal guidelines for MSM's test frequency in the Netherlands before 2017. These informal guidelines recommended STI testing for MSM at least twice a year. A formal guideline 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. However, annual testing uptake among MSM in the Netherlands is low. One Dutch study on STI consultations in Amsterdam from 2009 to 2013 reports that 35% of the HIV-negative MSM returned to the STI clinic within 1 year after their initial consultation.[10] Another Dutch study based on national STI clinic data from 2014 to 2015 reports that 48% of the MSM were tested more than once during a 1.5 year follow-up. Only 19% of the MSM were tested consistently every 6 months.[11]

No studies have yet simultaneously investigated the relation between MSM test frequency and STI positivity, with the determinants, in the Netherlands. The aim of this study was to assess the determinants of test frequency and of STI positivity among MSM visiting STI clinics in the Netherlands.

Methods

Study setting and study design

In the Netherlands, general practitioners and STI clinics based in regional public health services (RPHSs) provide primary STI care. The STI clinics are freely accessible and government funded; they aim to reach high-risk groups who might otherwise not seek timely STI care. The STI clinic at the RPHS is always accessible to MSM, while there is a triage system for heterosexuals.[6]

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, and all of them used an online patient-registration system in which sexual preference was a mandatory question. 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.

Study population

We selected all men who reported having sex with men or sex with both women and men, and men who identified themselves as homosexual or bisexual (hereafter referred to as MSM). Only MSM who had three or more consultations were included in the study because three or more consultations were considered to approximate an actual test frequency. We selected MSM who had a minimum of 18 months of follow-up after the first consultation (that took place before June 2012 with a follow-up time extending into 2013) because all the MSM had to have sufficient time to return for two retests. Furthermore, consultations within 35 days of a previous visit were excluded to ensure that no possible test-of-cure consultations were included.

Data description

For each consultation, the following variables were used: age, ethnicity [a combination of two definitions: self-defined ethnicity (a compulsory question until 2010, voluntary from 2011) and ethnicity based on country of birth of the clinic attendee and his parents (voluntary in 2010, compulsory from 2011)], having been notified by a partner, having STI symptoms, socio-economic status (SES, based on postal codes), number of sexual partners in the last 6 months,

being diagnosed with an STI during the study period, being a commercial sex worker, being the client of a commercial sex worker, intravenous drug use, sexual preference (reported as having sex with men or sex with men and women), and HIV status.

Data analysis

The determinants of age, ethnicity, and SES were taken from the first consultation in all analyses, because these determinants are reasonably stable over time. The mean number of partners reported per consultation was used for the determinant of the number of partners in the analysis. All other determinants were assessed on the basis of the occurrence of the event within all an individual's consultations, which resulted in an 'ever' and 'never' occurring categorisation.

MSM were considered to be 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.

Any one of the MSM was considered STI positive if he was 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.

If more than 5% of the values were missing for a variable, these missing values were included in the analysis in a separate category to reduce the loss of data. We performed logistic regression analyses to identify determinants of testing frequency and STI positivity. We used the Enter method with multivariable logistic regression to further analyse determinants with a p-value less than 0.20 in univariable analyses. The multivariable logistic regression was corrected for the number of consultations because the reporting of an event (for example, ever having STI symptoms) is more likely when MSM visit the STI clinic more often. In all analyses, determinants with $p<0.05$ were considered to be statistically significant. We present odds ratios (ORs) and 95% confidence intervals (CIs) to show the associations between the determinants and the outcomes in table 1 and 2. We used IBM SPSS software version 22 for the analyses.

Ethical approval

Ethical approval for the study was not necessary in Dutch law because the study used routinely collected surveillance data that was anonymous.

Results

Study population and test frequency

A total of 5954 MSM visited one of the five participating STI clinics between 2008 and 2013. A total of 1913 MSM had three or more consultations, of whom 1611 also had a minimal follow-up time of 18 months after the first consultation and thus were included. The group “infrequently tested” consisted of 953 MSN (59.2%), and there were 658 MSN (40.8%) in the group “frequently tested”.

Table 1 compares the characteristics of two groups. 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).

Table 1. Characteristics of the frequently and infrequently tested groups and the determinants of the test frequency for MSM who visited an STI clinic in the east of the Netherlands, 2008–2013

	Infrequently tested (n=953) n (%)	Frequently tested (n=658) n (%)	Frequently versus infrequently tested: *Univariable analyses OR (95% CI)*	*Multivariable analysis OR (95% CI)*
Median number of consultations (IQR)	4; 3 to 5	6; 4 to 9		
Age (in years at baseline)				
<26	242 (25.4)	140 (21.3)	ref	ref
≥26	711 (74.6)	518 (78.7)	**1.3 (1.0–1.6)**	0.9 (0.7–1.2)
Ethnicity (baseline)				
Dutch	857 (89.9)	584 (88.8)	ref	nt
Non-western	62 (6.5)	47 (7.1)	1.1 (0.8–1.6)	
Other western	34 (3.6)	27 (4.1)	1.2 (0.7–2.0)	
Socio-economic status (baseline)				
Low	281 (29.5)	183 (27.8)	1.0 (0.7–1.2)	nt
Intermediate	349 (36.6)	256 (38.9)	1.1 (0.9–1.4)	
High	300 (31.5)	203 (30.9)	ref	
Missing	23 (2.4)	16 (2.4)		
Mean number of partners				
<2	122 (12.9)	67 (10.3)	ref	ref
2 to 5	406 (43.0)	227 (35.0)	1.0 (0.7–1.4)	1.0 (0.7–1.5)
≥5	416 (44.1)	354 (54.6)	**1.6 (1.1–2.2)**	1.2 (0.8–1.8)
Missing	9 (0.0)	10 (0.0)		
Notified by a partner				
Never	511 (53.6)	267 (40.6)	ref	ref
Ever	442 (46.4)	391 (59.4)	**1.7 (1.4–2.1)**	1.1 (0.9–1.4)
Diagnosed with an STI				
Never	505 (53.0)	233 (35.4)	ref	ref
Ever	448 (47.0)	425 (64.6)	**2.1 (1.7–2.6)**	**1.4 (1.1–1.7)**
STI-related symptoms				
Never	454 (47.6)	273 (41.5)	ref	ref
Ever	499 (52.4)	385 (58.5)	**1.3 (1.1–1.6)**	**0.8 (0.6–1.0)**
Sexual preference				
Sex with men and women	232 (24.3)	212 (32.2)	ref	ref
Sex with men only	714 (74.9)	442 (67.2)	**0.7 (0.5–0.8)**	**0.6 (0.5–0.8)**
Unknown	7 (0.7)	4 (0.6)		
Known HIV positivity				
Never	860 (90.2)	568 (86.3)	ref	ref
Ever	93 (9.8)	90 (13.7)	**1.5 (1.1–2.0)**	0.8 (0.5-1.2)

IQR, interquartile range
MSM, men who have sex with men
Ref, reference
nt, not tested in multivariable model, since p>0.20 in univariate analysis
In bold: significant (p<0.05)
Regression analysis corrected for number of consultations

STI positivity

Table 2 shows the determinants of STI positivity. The same determinants of STI positivity were identified in both groups: MSM who had ever notified by a partner, MSM who had ever had STI-related symptoms, and MSM who had ever had a HIV-positive test result were more likely to be STI positive. In addition, frequently tested MSM who only had sex with men were more likely to be STI positive.

Table 2. Determinants of STI positivity in infrequently and frequently tested MSM who visited an STI clinic in the east of the Netherlands, 2008–2013

	Infrequently tested		Frequently tested	
	Univariable regression analysis OR (95%CI)	*Multivariable analysis OR (95% CI)**	*Univariable regression analysis OR (95% CI)*	*Multivariable analysis OR (95% CI)*
Age (in years at baseline)	ref	nt	ref	nt
<26	0.8 (0.6–1.1)		0.9 (0.6–1.4)	
≥26				
Ethnicity (baseline)				
Dutch	ref	nt	ref	nt
Non-western	1.4 (0.8–2.3)		1.0 (0.5–1.9)	
Other western	0.8 (0.4–1.7)		1.4 (0.6–3.2)	
SES (baseline)				
Low	1.3 (0.9–1.7)	nt	1.1 (0.7–1.6)	nt
Intermediate	1.2 (0.9–1.6)		0.8 (0.6–1.2)	
High	ref		ref	
Number of partners				
<2	ref	ref	ref	ref
2–5	1.0 (0.7–1.6)	0.9 (0.6–1.4)	**0.8 (0.5–1.4)**	0.9 (0.5–1.7)
≥5	**1.6 (1.1–2.4)**	1.3 (0.8–2.0)	**1.2 (0.7–2.1)**	1.3 (0.7–2.4)
Notified by a partner				
Never	ref	ref	ref	ref
Ever	**2.6 (2.0–3.4)**	**2.2 (1.7–2.9)**	**2.6 (1.9–3.6)**	**2.0 (1.4–2.9)**
STI-related symptoms				
Never	ref	ref	ref	ref
Ever	**2.0 (1.6–2.7)**	**1.6 (1.2–2.1)**	**2.6 (1.9–3.6)**	**1.8 (1.3–2.6)**
Sexual preference				
Sex with men and women	ref	ref	ref	ref
Sex with men	**1.5 (1.1–2.0)**	1.3 (1.0–1.8)	**2.0 (1.4–2.8)**	**1.8 (1.2–2.6)**
Known HIV positivity				
Never	ref	ref	ref	ref
Ever	**4.7 (2.8–7.7)**	**2.7 (1.5–4.6)**	**8.1 (3.7–17.9)**	**6.8 (2.6–17.5)**

nt, not tested in multivariate model, since p>0.20 in univariate analysis
SES, socio-economic status
STI, sexually transmitted infection
In bold: significant (p<0.05)
Regression analysis corrected for number of consultations

Discussion

In this study, we found that 59.2% of the included MSM were infrequently (mean test interval ≥6 months) and 40.8% were frequently tested (mean test interval <6 months). MSM who had had a previous 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. Moreover, we found that the determinants for STI positivity were the same in both groups. MSM who had ever been notified by a partner, MSM who had ever had STI symptoms, and MSM who were ever tested HIV positive were more likely to be STI positive.

This is the first study in the Netherlands that addresses both test frequency and STI positivity among HIV-positive and -negative MSM. Furthermore, our study has a long follow-up of 5 years, so that a large number of MSM were included in analyses. However, the study has several limitations. First, it took place in the east of the Netherlands, which is a more rural area of the Netherlands. The MSM population and its test behaviour may differ from the rest of the Netherlands. Second, the STI positivity was only available for those who came back for repeat testing; they do not represent the re-infections contracted by all MSM who visit STI clinics. Third, in this study, only STI-clinic consultations were available, so that data from STI tests carried out by general practitioners or other specialists could not be taken into account. The number of STI consultations per individual might therefore be an underestimation, and the MSM could have been categorized differently if consultations from other caregivers could have been included.

With the study methods we chose, this study shows that, of all the MSM with at least three consultations, 41% were frequently tested, so that they had mean test intervals of less than 6 months. Current study methods differ widely from other comparable Dutch studies so that comparison is difficult.[10,11] Vriend and colleagues' study found that 16% of HIV-negative MSM returned for repeat tests within 6 months.[10] We only included MSM with at least two subsequent tests and a minimum of 18 months of follow-up, whereas Vriend and colleagues also included MSM only tested once in their analyses, which made a comparison of the proportions of the frequently tested group in their study and our study difficult. However, Vriend and colleagues also looked at consistent 12-month testing among people with at least 3 years

of follow-up (i.e. three or more tests) and found an uptake of 36%, which is more in line with our study.[10]

Our results show that MSM who had ever been diagnosed with an STI are more often frequently tested. However, MSM who had ever been notified by a partner and MSM who had ever had STI-related symptoms are not more likely to be frequently tested. This is in line with another study which finds that MSM who have been notified by a partner or who have reported STI symptoms return to the STI clinic sooner, but are not more likely to be consistently tested every 6 months.[11] 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.

Regarding STI positivity, we show that MSM who had ever been notified by a partner, MSM who had ever had STI symptoms, and MSM who were ever tested HIV positive were more likely to be STI positive. These results are in line with other studies.[12,13,14,15,16] A British analysis using multiple sources of national surveillance data and population survey data concludes that an increasing proportion of STIs are being diagnosed in HIV-positive MSM, with the population rate of STIs rising to four times that of HIV-negative or undiagnosed MSM. Moreover, STI re-infection rates were considerably higher in HIV-positive MSM over a 5-year follow-up period.[17]

By combining the results of the significant determinants of frequent testing and STI positivity, this study demonstrates that MSM who had ever been notified by a partner and MSM who had ever had STI-related symptoms were more likely to be STI positive, but were not more likely to be frequently tested. This means that MSM who had symptoms or who had been notified by a partner appear to find their way to the STI clinics when necessary, but will not come back frequently.

We found that MSM who were ever tested HIV positive were more often STI positive, but did not visit the STI clinic more frequently than MSM who were HIV negative. HIV-positive MSM are not routinely tested for STI in most HIV care centres, except for annual syphilis and HCV screening. Routine screening for STI of HIV-positive MSM is important because regular

screening could help reduce the incidence of STI.[18,19,20] This study therefore highlights the importance of encouraging HIV-positive MSM to be tested for STI frequently.

Acknowledgments

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Conflicts of interest

None declared.

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Key points

- Data from MSM with minimally three consultations at Dutch STI clinics between 2008 and 2013 were grouped for MSM who were frequently or infrequently tested.
- MSM who have ever been notified and who have ever had STI symptoms should be advised to be tested for STIs regularly.
- MSM who are HIV positive should test more often, since they are more likely to test STI positive, but are not frequently tested.

Contributorship statement

- Karlijn Kampman contributed to the statistical analysis, drafted the article, and processed comments made by the other authors.
- Janneke Heijne discussed methodological issues, gave advice about the statistics, and made corrections to the article.

- Nelleke Koedijk drafted the research protocol, collected data, and assisted with the literature search.
- Femke Koedijk contributed to the statistical analysis and commented on the article.
- Maartje Visser discussed methodological issues, gave advice about statistics, and made corrections to the article.
- Jeannine Hautvast commented on the research protocol, helped with the data analysis, and commented on the article.

All authors gave their final approval of the final version of the original article to be published.

Data sharing statement

There are no additional unpublished data from the study available.

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STROBE checklist

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract: The title on the title page (page 1) contains commonly used terms like *Sexually Transmitted Infections* and *Men who have sex with men*. Furthermore, the study design is displayed in the title.
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found: The abstract can be found on page 2 and is providing a balanced summary of what was done and found in this study.
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported: On page 3 the introduction can be found, which also incorporates scientific background an rationale for the current study.
Objectives	3	State specific objectives, including any pre-specified hypotheses: At the end of page 3 the objectives of the study (named 'aims') are described in the last paragraph of the introduction.
Methods		
Study design	4	Present key elements of study design early in the paper: The study designs is described on page 4.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection: The study setting is described on page 4.
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up: On page 4 below the heading 'study population', we have described the eligibility criteria, the selection of participants and the methods of follow-up. *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable: We have defined all outcomes under 'data description' and 'data analysis' on page 4 and 5 .
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group: The sources of data are described under 'study setting and study design' on page 4.
Bias	9	Describe any efforts to address potential sources of bias: In our methods section, starting on page 4, we have addressed the inclusion and exclusion criteria. Also, in the discussion, starting on page 9, we have described potential biases.
Study size	10	Explain how the study size was arrived at: On page 4, the study population is described under the heading 'study population'.
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why: The handling of quantitative variables is described on page 5, under the heading 'data analysis'.
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for

confounding: The statistical methods are described under the heading 'data analysis' on page 5.
(*b*) Describe any methods used to examine subgroups and interactions: Current study doesn't include subgroups.
(*c*) Explain how missing data were addressed: Missing data are addressed op page 5 under 'data analysis': "If more than 5% of the values were missing for a variable, these missing values were included in the analysis in a separate category to reduce the loss of data."
(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed: not applicable. *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
(*e*) Describe any sensitivity analyses: not applicable.

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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

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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

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Abstract

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 STI positivity.

Methods

Longitudinal data of MSM with at least three consultations at regional Dutch STI clinics between 2008 and 2013 were analysed. MSM whose mean test interval was 6 months or more were grouped as “infrequently tested”, and those with mean test intervals less than 6 months were grouped as “frequently tested”. We used logistic regression to assess the determinants of test frequency and STI positivity in both groups.

Results

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. Moreover, in both groups, MSM who had ever been notified by a partner, MSM who had ever had STI symptoms, and MSM who were ever diagnosed with HIV were more likely to be diagnosed with STI.

Conclusions

Among MSM visiting STI clinics, those 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 STI tests more frequently.

Methodological Strengths and Limitations

- Longitudinal data of MSM with at least three consultations at regional Dutch STI clinics between 2008 and 2013 were analysed.
- Current study has a long follow-up of 5 years, so that a large number of MSM were included in analyses.
- The MSM population in the Eastern part of the Netherlands and their test behaviour may differ from the rest of the Netherlands.
- The STI positivity was only available for those who came back for repeat testing; they do not represent the re-infections contracted by all MSM who visit STI clinics.
- Only STI-clinic consultations were available, data from STI tests carried out by general practitioners or other specialists could not be taken into account.

Introduction

Men who have sex with men (MSM) contribute to the worldwide burden of sexually transmitted infections (STIs), including HIV.[1, 2, 3] Some studies have found that MSM reported large proportions of diagnoses of HIV (42%), gonorrhoea (43%), and syphilis (58%).[4,5] In the Netherlands, MSM accounted for the greatest contribution to STI diagnosis in 2016 at STI clinics; 21% of the tests were positive for one or more STIs.[6]

Early detection and treatment are crucial to reduce the risk of transmitting STIs (including HIV) among MSM.[7] Therefore, the test frequency is important for reducing the transmission of STIs. In Australia, MSM are advised to get a test at least once a year, but one study reports that this advice is poorly adhered to: re-testing rates at 1 year were 35%.[8] A British study estimates that 55% of the MSM were tested once a year where guidelines also recommend HIV tests once a year (and more often for those at "higher risk").[9]

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. However, annual testing uptake among MSM in the Netherlands is low. One Dutch study on STI consultations in Amsterdam from 2009 to 2013 reports that 35% of the HIV-negative MSM returned to the STI clinic within 1 year after their initial consultation.[10] Another Dutch study based on national STI clinic data from 2014 to 2015 reports that 48% of the MSM were tested more than once during a 1.5 year follow-up. Only 19% of the MSM were tested consistently every 6 months.[11]

No studies have yet simultaneously investigated the relation between MSM test frequency and STI diagnosis, with the determinants, in the Netherlands. The aim of this study was to assess the determinants of test frequency and of STI diagnosis among MSM visiting STI clinics in the Eastern part of the Netherlands. Study results could provide more insight in the frequency and relevance of testing according to guidelines for certain MSM risk groups.

Methods

Study setting and study design

In the Netherlands, general practitioners and STI clinics based in regional public health services (RPHSs) provide primary STI care. The STI clinics are freely accessible and government funded; they aim to reach high-risk groups who might otherwise not seek timely STI care. 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) [6]

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. All of them used an online patient-registration system in which sexual preference was a mandatory question. 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.

Study population

We selected all men who reported having sex with men or sex with both women and men, and men who identified themselves as homosexual or bisexual (hereafter referred to as MSM). Only MSM who had three or more consultations were included in the study because three or more consultations were considered to approximate an actual test frequency. We selected MSM who had a minimum of 18 months of follow-up after the first consultation (that took place before June 2012 with a follow-up time extending into 2013) because all the MSM had to have sufficient time to return for two retests. Furthermore, consultations within 35 days of a previous visit were excluded to ensure that no possible test-of-cure consultations were included.

Data description

For each consultation, the following variables were used: age (<26 years and ≥26 years, clients younger than 26 years are considered ‘young’ as decided by national STI clinic regulations),

ethnicity (due to a change in 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, other Western and non-Western), having been notified by a partner, having STI symptoms, 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 education), number of sexual partners in the last 6 months, being diagnosed with an STI during the study period, and sexual preference (reported as having sex with men or sex with men and women).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 positive for HIV during the study period or were already known HIV positive before the study period.

Data analysis

The determinants of age, ethnicity, and SES were taken from the first consultation in all analyses, because these determinants are reasonably stable over time. The mean number of partners reported per consultation was used for the determinant of the number of partners in the analysis. All other determinants were assessed on the basis of the occurrence of the event within all an individual's consultations, which resulted in an 'ever' and 'never' occurring categorisation.

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 defined 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.

The outcome of STI diagnosis was defined as follows: any one of the MSM was defined as being diagnosed with an 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.

If more than 5% of the values were missing for a variable, these missing values were included in the analysis in a separate category to reduce the loss of data. We performed logistic regression analyses to identify determinants of testing frequency and STI positivity. Collinearity between variables was checked beforehand. We used the Enter method with multivariable logistic regression to further analyse determinants with a p-value less than 0.20 in univariable analyses. The multivariable logistic regression was corrected for the number of consultations because the reporting of an event (for example, ever having STI symptoms) is more likely when MSM visit the STI clinic more often. In all analyses, determinants with $p<0.05$ were considered to be statistically significant. We present odds ratios (ORs) and 95% confidence intervals (CIs) to show the associations between the determinants and the outcomes in table 1 and 2. We used IBM SPSS software version 22 for the analyses.

Ethical approval

Ethical approval for the study was not necessary in Dutch law because the study used routinely collected surveillance data that was anonymous.

Results

Study population and test frequency

A total of 5954 MSM visited one of the five participating STI clinics between 2008 and 2013. A total of 1913 MSM had three or more consultations, of whom 1611 also had a minimal follow-up time of 18 months after the first consultation and thus were included. The group “infrequently tested” consisted of 953 MSM (59.2%), and there were 658 MSM (40.8%) in the group “frequently tested”.

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. Table 1 also compares the characteristics of two groups. 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.

Table 1. Characteristics of the frequently and infrequently tested groups and the determinants of the test frequency for MSM who visited an STI clinic in the east of the Netherlands, 2008–2013

			Frequently versus infrequently tested	
	Infrequently tested (n=953) n (%)	Frequently tested (n=658) n (%)	*Univariable analyses OR (95% CI)*	*Multivariable analysis OR (95% CI)*
Median number of consultations (IQR)	4; 3 to 5	6; 4 to 9		
Age (in years at baseline)				
<26	242 (25.4)	140 (21.3)	ref	ref
≥26	711 (74.6)	518 (78.7)	**1.3 (1.0–1.6)**	0.9 (0.7–1.2)
Ethnicity (baseline)				
Dutch	857 (89.9)	584 (88.8)	ref	nt
Non-western	62 (6.5)	47 (7.1)	1.1 (0.8–1.6)	
Other western	34 (3.6)	27 (4.1)	1.2 (0.7–2.0)	
Socio-economic status (baseline)				
Low	281 (29.5)	183 (27.8)	1.0 (0.7–1.2)	nt
Intermediate	349 (36.6)	256 (38.9)	1.1 (0.9–1.4)	
High	300 (31.5)	203 (30.9)	ref	
Missing	23 (2.4)	16 (2.4)		
Mean number of partners				
<2	122 (12.9)	67 (10.3)	ref	ref
2 to 5	406 (43.0)	227 (35.0)	1.0 (0.7–1.4)	1.0 (0.7–1.5)
≥5	416 (44.1)	354 (54.6)	**1.6 (1.1–2.2)**	1.2 (0.8–1.8)
Missing	9 (0.0)	10 (0.0)		
Notified by a partner				
Never	511 (53.6)	267 (40.6)	ref	ref
Ever	442 (46.4)	391 (59.4)	**1.7 (1.4–2.1)**	1.1 (0.9–1.4)
Diagnosed with an STI				
Never	505 (53.0)	233 (35.4)	ref	ref
Ever	448 (47.0)	425 (64.6)	**2.1 (1.7–2.6)**	**1.4 (1.1–1.7)**
STI-related symptoms				
Never	454 (47.6)	273 (41.5)	ref	ref
Ever	499 (52.4)	385 (58.5)	**1.3 (1.1–1.6)**	**0.8 (0.6–1.0)**
Sexual preference				
Sex with men and women	232 (24.3)	212 (32.2)	ref	ref
Sex with men only	714 (74.9)	442 (67.2)	**0.7 (0.5–0.8)**	**0.6 (0.5–0.8)**
Unknown	7 (0.7)	4 (0.6)		
Diagnosed with HIV				
Never	860 (90.2)	568 (86.3)	ref	ref
Ever	93 (9.8)	90 (13.7)	**1.5 (1.1–2.0)**	0.8 (0.5-1.2)

IQR, interquartile range
MSM, men who have sex with men
Ref, reference
nt, not tested in multivariable model, since p>0.20 in univariate analysis
In bold: significant (p<0.05); due to rounding into 1 decimal 1.0 is not always significant.
Regression analysis corrected for number of consultations

STI positivity

Table 2 shows the determinants of STI positivity. 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. 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.

Table 2. Determinants of STI diagnosis in infrequently and frequently tested MSM who visited an STI clinic in the east of the Netherlands, 2008–2013

	Infrequently tested		Frequently tested	
	Univariable regression analysis OR (95%CI)	*Multivariable analysis OR (95% CI)**	*Univariable regression analysis OR (95% CI)*	*Multivariable analysis OR (95% CI)*
Age (in years at baseline)	ref	nt	ref	nt
<26	0.8 (0.6–1.1)		0.9 (0.6–1.4)	
≥26				
Ethnicity (baseline)				
Dutch	ref	nt	ref	nt
Non-western	1.4 (0.8–2.3)		1.0 (0.5–1.9)	
Other western	0.8 (0.4–1.7)		1.4 (0.6–3.2)	
SES (baseline)				
Low	1.3 (0.9–1.7)	nt	1.1 (0.7–1.6)	nt
Intermediate	1.2 (0.9–1.6)		0.8 (0.6–1.2)	
High	ref		ref	
Mean number of partners	ref	ref	ref	ref
<2	1.0 (0.7–1.6)	0.9 (0.6–1.4)	**0.8 (0.5–1.4)**	0.9 (0.5–1.7)
2–5	**1.6 (1.1–2.4)**	1.3 (0.8–2.0)	**1.2 (0.7–2.1)**	1.3 (0.7–2.4)
≥5				
Notified by a partner				
Never	ref	ref	ref	ref
Ever	**2.6 (2.0–3.4)**	**2.2 (1.7–2.9)**	**2.6 (1.9–3.6)**	**2.0 (1.4–2.9)**
STI-related symptoms				
Never	ref	ref	ref	ref
Ever	**2.0 (1.6–2.7)**	**1.6 (1.2–2.1)**	**2.6 (1.9–3.6)**	**1.8 (1.3–2.6)**
Sexual preference				
Sex with men and women	ref	ref	ref	ref
Sex with men	**1.5 (1.1–2.0)**	1.3 (1.0–1.8)	**2.0 (1.4–2.8)**	**1.8 (1.2–2.6)**
Diagnosed with HIV				
Never	ref	ref	ref	ref
Ever	**4.7 (2.8–7.7)**	**2.7 (1.5–4.6)**	**8.1 (3.7–17.9)**	**6.8 (2.6–17.5)**

nt, not tested in multivariate model, since p>0.20 in univariate analysis
Ref, reference
SES, socio-economic status
STI, sexually transmitted infection
In bold: significant (p<0.05); due to rounding into 1 decimal 1.0 is not always significant.
Regression analysis corrected for number of consultations

Discussion

In this study, we found that 59.2% of the included MSM were infrequently (mean test interval ≥6 months) and 40.8% were frequently tested (mean test interval <6 months). 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. Moreover, we found that the determinants for STI diagnosis were the same in both groups. MSM who had ever been notified by a partner, MSM who had ever had STI symptoms, and MSM who were ever diagnosed with HIV were more likely to be diagnosed with an STI.

This is the first study in the Netherlands that addresses both test frequency and STI diagnosis among HIV-positive and -negative diagnosed MSM. Furthermore, our study has a long follow-up of 5 years, so that a large number of MSM were included in analyses. However, the study has several limitations. First, it took place in the Eastern part of the Netherlands, which is a semi-rural area of the Netherlands. The study population and their test behaviour may differ from the rest of the Netherlands. Second, STI diagnosis was only available for those who came back for repeat testing; they do not represent the re-infections contracted by all MSM who visit STI clinics. Third, in this study, only STI-clinic consultations were available, so that data from STI tests carried out by general practitioners or other specialists could not be taken into account. The number of STI consultations per individual might therefore be an underestimation, and the MSM could have been categorized differently if consultations from other caregivers could have been included. 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. 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.

With the study methods we chose, this study shows that, of all the MSM with at least three consultations, 41% were frequently tested, so that they had mean test intervals of less than 6 months. Current study methods differ widely from other comparable Dutch studies so

that comparison is difficult.[10,11] Vriend and colleagues' study found that 16% of HIV-negative MSM returned for repeat tests within 6 months.[10] We only included MSM with at least two subsequent tests and a minimum of 18 months of follow-up, whereas Vriend and colleagues also included MSM only tested once in their analyses, which made a comparison of the proportions of the frequently tested group in their study and our study difficult. However, Vriend and colleagues also looked at consistent 12-month testing among people with at least 3 years of follow-up (i.e. three or more tests) and found an uptake of 36%, which is more in line with our study.[10]

Our results show that MSM who had ever been diagnosed with an STI are more often frequently tested. However, MSM who had ever been notified by a partner and MSM who had ever had STI-related symptoms are not more likely to be frequently tested. This is in line with another study which finds that MSM who have been notified by a partner or who have reported STI symptoms return to the STI clinic sooner, but are not more likely to be consistently tested every 6 months.[11] 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.

Regarding STI diagnosis, we show that MSM who had ever been notified by a partner, MSM who had ever had STI symptoms, and MSM who were ever diagnosed with HIV were more likely to have an STI diagnosis. These results are in line with other studies.[12,13,14,15,16] A British analysis using multiple sources of national surveillance data and population survey data concludes that an increasing proportion of STIs are being diagnosed in HIV-positive diagnosed MSM, with the population rate of STIs rising to four times that of HIV-negative or undiagnosed MSM. Moreover, STI re-infection rates were considerably higher in MSM who were diagnosed with HIV over a 5-year follow-up period. 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]

By combining the results of the significant determinants of frequent testing and STI diagnosis, this study demonstrates that MSM who had ever been notified by a partner and MSM who had ever had STI-related symptoms were more likely to have an STI diagnosis, but were not more likely to be frequently tested. This means that MSM who had symptoms or who had been notified by a partner appear to find their way to the STI clinics when necessary, but will not come back frequently. 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.

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.

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Conflicts of interest

None declared.

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Key points

- Data from MSM with minimally three consultations at Dutch STI clinics between 2008 and 2013 were grouped for MSM who were frequently or infrequently tested.
- MSM who have ever been notified and who have ever had STI symptoms should be advised to be tested for STIs regularly.
- MSM who are diagnosed with HIV should test more often, since they are more likely have an STI diagnosis, but are not frequently tested.

Contributorship statement

- Karlijn Kampman contributed to the statistical analysis, drafted the article, and processed comments made by the other authors.
- Janneke Heijne discussed methodological issues, gave advice about the statistics, and made corrections to the article.
- Nelleke Koedijk drafted the research protocol, collected data, and assisted with the literature search.
- Femke Koedijk contributed to the statistical analysis and commented on the article.

- Maartje Visser discussed methodological issues, gave advice about statistics, and made corrections to the article.
- Jeannine Hautvast commented on the research protocol, helped with the data analysis, and commented on the article.

All authors gave their final approval of the final version of the original article to be published.

Data sharing statement

There are no additional unpublished data from the study available.

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STROBE checklist

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract: The title on the title page (page 1) contains commonly used terms like *Sexually Transmitted Infections* and *Men who have sex with men*. Furthermore, the study design is displayed in the title.
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found: The abstract can be found on page 2 and is providing a balanced summary of what was done and found in this study.
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported: On page 3 the introduction can be found, which also incorporates scientific background an rationale for the current study.
Objectives	3	State specific objectives, including any pre-specified hypotheses: At the end of page 3 the objectives of the study (named 'aims') are described in the last paragraph of the introduction.
Methods		
Study design	4	Present key elements of study design early in the paper: The study designs is described on page 4.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection: The study setting is described on page 4.
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up: On page 4 below the heading 'study population', we have described the eligibility criteria, the selection of participants and the methods of follow-up. *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable: We have defined all outcomes under 'data description' and 'data analysis' on page 4 and 5 .
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group: The sources of data are described under 'study setting and study design' on page 4.
Bias	9	Describe any efforts to address potential sources of bias: In our methods section, starting on page 4, we have addressed the inclusion and exclusion criteria. Also, in the discussion, starting on page 9, we have described potential biases.
Study size	10	Explain how the study size was arrived at: On page 4, the study population is described under the heading 'study population'.
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why: The handling of quantitative variables is described on page 5, under the heading 'data analysis'.
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for

confounding: The statistical methods are described under the heading 'data analysis' on page 5.
(*b*) Describe any methods used to examine subgroups and interactions: Current study doesn't include subgroups.
(*c*) Explain how missing data were addressed: Missing data are addressed op page 5 under 'data analysis': "If more than 5% of the values were missing for a variable, these missing values were included in the analysis in a separate category to reduce the loss of data."
(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed: not applicable. *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
(*e*) Describe any sensitivity analyses: not applicable.

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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

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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

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Abstract

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 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.

Strengths and limitations of this study

- Longitudinal data of MSM with at least three consultations at regional Dutch STI clinics between 2008 and 2013 were analysed.
- Current study has a long follow-up of 5 years, so that a large number of MSM were included in analyses.
- The MSM population in the Eastern part of the Netherlands and their test behaviour may differ from the rest of the Netherlands.
- STI diagnosis was only available for those who came back for repeat testing; they do not represent the re-infections contracted by all MSM who visit STI clinics.
- Only STI-clinic consultations were available, data from STI tests carried out by general practitioners or other specialists could not be taken into account.

Introduction

Men who have sex with men (MSM) contribute to the worldwide burden of sexually transmitted infections (STIs), including HIV.[1, 2, 3] Some studies have found that MSM reported large proportions of diagnoses of HIV (42%), gonorrhoea (43%), and syphilis (58%).[4,5] In the Netherlands, MSM accounted for the greatest contribution to STI diagnoses in 2016 at STI clinics; 21% of the tests were positive for one or more STIs.[6]

Early detection and treatment are crucial to reduce the risk of transmitting STIs (including HIV) among MSM.[7] Therefore, the test frequency is important for reducing the transmission of STIs. In Australia, MSM are advised to get a test at least once a year, but one study reports that this advice is poorly adhered to: re-testing rates at 1 year were 35%.[8] A British study estimates that 55% of the MSM were tested once a year where guidelines also recommend HIV tests once a year (and more often for those at "higher risk").[9]

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. MSM who were diagnosed with HIV or MSM who are commercial sex workers), four times a year. However, annual testing uptake among MSM in the Netherlands is low. One Dutch study on STI consultations in Amsterdam from 2009 to 2013 reports that 35% of the HIV-negative MSM returned to the STI clinic within 1 year after their initial consultation.[10] Another Dutch study based on national STI clinic data from 2014 to 2015 reports that 48% of the MSM were tested more than once during a 1.5 year follow-up. Only 19% of the MSM were tested consistently every 6 months.[11]

No studies have yet simultaneously investigated the relation between MSM test frequency and STI diagnosis, with the determinants, in the Netherlands. The aim of this study was to assess the determinants of test frequency and of STI diagnosis among MSM visiting STI clinics in the Eastern part of the Netherlands. Study results could provide more insight in the frequency and relevance of testing according to guidelines for certain MSM risk groups.

Methods

Study setting and study design

In the Netherlands, general practitioners and STI clinics based in regional public health services (RPHSs) provide primary STI care. The STI clinics are freely accessible and government funded; they aim to reach high-risk groups who might otherwise not seek timely STI care. 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) [6]

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. All of them used an online patient-registration system in which sexual preference was a mandatory question. 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.

Study population

We selected all men who reported having sex with men or sex with both women and men, and men who identified themselves as homosexual or bisexual (hereafter referred to as MSM). Only MSM who had three or more consultations were included in the study because three or more consultations were considered to approximate an actual test frequency. We selected MSM who had a minimum of 18 months of follow-up after the first consultation (that took place before June 2012 with a follow-up time extending into 2013) because all the MSM had to have sufficient time to return for two retests. Furthermore, consultations within 35 days of a previous visit were excluded to ensure that no possible test-of-cure consultations were included.

Data description

For each consultation, the following variables were used: age (<26 years and ≥26 years, clients younger than 26 years are considered ‘young’ as decided by national STI clinic regulations),

ethnicity (due to a change in 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, other Western and non-Western), having been notified by a partner, having STI symptoms, 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 education), number of sexual partners in the last 6 months, being diagnosed with an STI during the study period, and sexual preference (reported as having sex with men or sex with men and women). 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 were diagnosed with HIV during the study period or were already diagnosed with HIV before the study period.

Data analysis

The determinants of age, ethnicity, and SES were taken from the first consultation in all analyses, because these determinants are reasonably stable over time. The mean number of partners reported per consultation was used for the determinant of the number of partners in the analysis. All other determinants were assessed on the basis of the occurrence of the event within all an individual's consultations, which resulted in an 'ever' and 'never' occurring categorisation.

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 defined 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.

The outcome of STI diagnosis was defined as follows: any one of the MSM was defined as being diagnosed with an 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.

If more than 5% of the values were missing for a variable, these missing values were included in the analysis in a separate category to reduce the loss of data. We performed logistic regression analyses to identify determinants of testing frequency and STI diagnosis. Collinearity between variables was checked beforehand. We used the Enter method with multivariable logistic regression to further analyse determinants with a p-value less than 0.20 in univariable analyses. The multivariable logistic regression was corrected for the number of consultations because the reporting of an event (for example, ever having STI symptoms) is more likely when MSM visit the STI clinic more often. In all analyses, determinants with $p<0.05$ were considered to be statistically significant. We present odds ratios (ORs) and 95% confidence intervals (CIs) to show the associations between the determinants and the outcomes in table 1 and 2. We used IBM SPSS software version 22 for the analyses.

Ethical approval

Ethical approval for the study was not necessary in Dutch law because the study used routinely collected surveillance data that was anonymous.

Patient and public involvement

The study used routinely collected anonymous surveillance data. Hence, STI clinic visitors were not directly involved in the development or execution of this study. Neither could the results be disseminated to them.

Results

Study population and test frequency

A total of 5954 MSM visited one of the five participating STI clinics between 2008 and 2013. A total of 1913 MSM had three or more consultations, of whom 1611 also had a minimal follow-up time of 18 months after the first consultation and thus were included. The group “infrequently

tested" consisted of 953 MSM (59.2%), and there were 658 MSM (40.8%) in the group "frequently tested".

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. Table 1 also compares the characteristics of two groups. 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.

Table 1. Characteristics of the frequently and infrequently tested groups and the determinants of the test frequency for MSM who visited an STI clinic in the east of the Netherlands, 2008–2013

			Frequently versus infrequently tested	
	Infrequently tested (n=953) n (%)	Frequently tested (n=658) n (%)	*Univariable analyses OR (95% CI)*	*Multivariable analysis OR (95% CI)*
Median number of consultations (IQR)	4; 3 to 5	6; 4 to 9		
Age (in years at baseline)				
<26	242 (25.4)	140 (21.3)	ref	ref
≥26	711 (74.6)	518 (78.7)	**1.3 (1.0–1.6)**	0.9 (0.7–1.2)
Ethnicity (baseline)				
Dutch	857 (89.9)	584 (88.8)	ref	nt
Non-western	62 (6.5)	47 (7.1)	1.1 (0.8–1.6)	
Other western	34 (3.6)	27 (4.1)	1.2 (0.7–2.0)	
Socio-economic status (baseline)				
Low	281 (29.5)	183 (27.8)	1.0 (0.7–1.2)	nt
Intermediate	349 (36.6)	256 (38.9)	1.1 (0.9–1.4)	
High	300 (31.5)	203 (30.9)	ref	
Missing	23 (2.4)	16 (2.4)		
Mean number of partners				
<2	122 (12.9)	67 (10.3)	ref	ref
2 to 5	406 (43.0)	227 (35.0)	1.0 (0.7–1.4)	1.0 (0.7–1.5)
≥5	416 (44.1)	354 (54.6)	**1.6 (1.1–2.2)**	1.2 (0.8–1.8)
Missing	9 (0.0)	10 (0.0)		
Notified by a partner				
Never	511 (53.6)	267 (40.6)	ref	ref
Ever	442 (46.4)	391 (59.4)	**1.7 (1.4–2.1)**	1.1 (0.9–1.4)
Diagnosed with an STI				
Never	505 (53.0)	233 (35.4)	ref	ref
Ever	448 (47.0)	425 (64.6)	**2.1 (1.7–2.6)**	**1.4 (1.1–1.7)**
STI-related symptoms				
Never	454 (47.6)	273 (41.5)	ref	ref
Ever	499 (52.4)	385 (58.5)	**1.3 (1.1–1.6)**	**0.8 (0.6–1.0)**
Sexual preference				
Sex with men and women	232 (24.3)	212 (32.2)	ref	ref
Sex with men only	714 (74.9)	442 (67.2)	**0.7 (0.5–0.8)**	**0.6 (0.5–0.8)**
Unknown	7 (0.7)	4 (0.6)		
Diagnosed with HIV				
Never	860 (90.2)	568 (86.3)	ref	ref
Ever	93 (9.8)	90 (13.7)	**1.5 (1.1–2.0)**	0.8 (0.5-1.2)

IQR, interquartile range
MSM, men who have sex with men
Ref, reference
nt, not tested in multivariable model, since p>0.20 in univariate analysis
In bold: significant (p<0.05); due to rounding into 1 decimal 1.0 is not always significant.
Regression analysis corrected for number of consultations

STI diagnosis

Table 2 shows the determinants of having an STI diagnosis. 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. 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.

Table 2. Determinants of STI diagnosis in infrequently and frequently tested MSM who visited an STI clinic in the east of the Netherlands, 2008–2013

	Infrequently tested		Frequently tested	
	Univariable regression analysis OR (95%CI)	*Multivariable analysis OR (95% CI)**	*Univariable regression analysis OR (95% CI)*	*Multivariable analysis OR (95% CI)*
Age (in years at baseline)	ref	nt	ref	nt
<26	0.8 (0.6–1.1)		0.9 (0.6–1.4)	
≥26				
Ethnicity (baseline)				
Dutch	ref	nt	ref	nt
Non-western	1.4 (0.8–2.3)		1.0 (0.5–1.9)	
Other western	0.8 (0.4–1.7)		1.4 (0.6–3.2)	
SES (baseline)				
Low	1.3 (0.9–1.7)	nt	1.1 (0.7–1.6)	nt
Intermediate	1.2 (0.9–1.6)		0.8 (0.6–1.2)	
High	ref		ref	
Mean number of partners	ref	ref	ref	ref
<2	1.0 (0.7–1.6)	0.9 (0.6–1.4)	**0.8 (0.5–1.4)**	0.9 (0.5–1.7)
2–5	**1.6 (1.1–2.4)**	1.3 (0.8–2.0)	**1.2 (0.7–2.1)**	1.3 (0.7–2.4)
≥5				
Notified by a partner				
Never	ref	ref	ref	ref
Ever	**2.6 (2.0–3.4)**	**2.2 (1.7–2.9)**	**2.6 (1.9–3.6)**	**2.0 (1.4–2.9)**
STI-related symptoms				
Never	ref	ref	ref	ref
Ever	**2.0 (1.6–2.7)**	**1.6 (1.2–2.1)**	**2.6 (1.9–3.6)**	**1.8 (1.3–2.6)**
Sexual preference				
Sex with men and women	ref	ref	ref	ref
Sex with men	**1.5 (1.1–2.0)**	1.3 (1.0–1.8)	**2.0 (1.4–2.8)**	**1.8 (1.2–2.6)**
Diagnosed with HIV				
Never	ref	ref	ref	ref
Ever	**4.7 (2.8–7.7)**	**2.7 (1.5–4.6)**	**8.1 (3.7–17.9)**	**6.8 (2.6–17.5)**

nt, not tested in multivariate model, since p>0.20 in univariate analysis
Ref, reference
SES, socio-economic status
STI, sexually transmitted infection
In bold: significant (p<0.05); due to rounding into 1 decimal 1.0 is not always significant.
Regression analysis corrected for number of consultations

Discussion

In this study, we found that 59.2% of the included MSM were infrequently (mean test interval ≥6 months) and 40.8% were frequently tested (mean test interval <6 months). 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. Moreover, we found that the determinants for STI diagnosis were the same in both groups. MSM who had ever been notified by a partner, MSM who had ever had STI symptoms, and MSM who were ever diagnosed with HIV were more likely to be diagnosed with an STI.

This is the first study in the Netherlands that addresses both test frequency and STI diagnosis among MSM that were and were not diagnosed with HIV. Furthermore, our study has a long follow-up of 5 years, so that a large number of MSM were included in analyses. However, the study has several limitations. First, it took place in the Eastern part of the Netherlands, which is a semi-rural area of the Netherlands. The study population and their test behaviour may differ from the rest of the Netherlands. Second, STI diagnosis was only available for those who came back for repeat testing; they do not represent the re-infections contracted by all MSM who visit STI clinics. Third, in this study, only STI-clinic consultations were available, so that data from STI tests carried out by general practitioners or other specialists could not be taken into account. The number of STI consultations per individual might therefore be an underestimation, and the MSM could have been categorized differently if consultations from other caregivers could have been included. 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. 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.

With the study methods we chose, this study shows that, of all the MSM with at least three consultations, 41% were frequently tested, so that they had mean test intervals of less than 6 months. Current study methods differ widely from other comparable Dutch studies so

that comparison is difficult.[10,11] Vriend and colleagues' study found that 16% of HIV-negative MSM returned for repeat tests within 6 months.[10] We only included MSM with at least two subsequent tests and a minimum of 18 months of follow-up, whereas Vriend and colleagues also included MSM only tested once in their analyses, which made a comparison of the proportions of the frequently tested group in their study and our study difficult. However, Vriend and colleagues also looked at consistent 12-month testing among people with at least 3 years of follow-up (i.e. three or more tests) and found an uptake of 36%, which is more in line with our study.[10]

Our results show that MSM who had ever been diagnosed with an STI are more often frequently tested. However, MSM who had ever been notified by a partner and MSM who had ever had STI-related symptoms are not more likely to be frequently tested. This is in line with another study which finds that MSM who have been notified by a partner or who have reported STI symptoms return to the STI clinic sooner, but are not more likely to be consistently tested every 6 months.[11] 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.

Regarding STI diagnosis, we show that MSM who had ever been notified by a partner, MSM who had ever had STI symptoms, and MSM who were ever diagnosed with HIV were more likely to have an STI diagnosis. These results are in line with other studies.[12,13,14,15,16] A British analysis using multiple sources of national surveillance data and population survey data concludes that an increasing proportion of STIs are being diagnosed in MSM who are diagnosed with HIV, with the population rate of STIs rising to four times that of HIV-negative or undiagnosed MSM. Moreover, STI re-infection rates were considerably higher in MSM who were diagnosed with HIV over a 5-year follow-up period. The authors believe the higher number of bacterial re-infections in MSM who are diagnosed with HIV are indicative of rapid transmission in dense sexual networks.[17] An Italian study assessed risk behaviour before and after being diagnosed with HIV; MSM who are diagnosed with HIV 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 MSM who are diagnosed with HIV may play a role in at risk practices. Among MSM who are diagnosed with HIV, 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]

By combining the results of the significant determinants of frequent testing and STI diagnosis, this study demonstrates that MSM who had ever been notified by a partner and MSM who had ever had STI-related symptoms were more likely to have an STI diagnosis, but were not more likely to be frequently tested. This means that MSM who had symptoms or who had been notified by a partner appear to find their way to the STI clinics when necessary, but will not come back frequently. 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.

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 an 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 diagnoses.[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.

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Conflicts of interest

None declared.

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Key points

- Data from MSM with minimally three consultations at Dutch STI clinics between 2008 and 2013 were grouped for MSM who were frequently or infrequently tested.
- MSM who have ever been notified and who have ever had STI symptoms should be advised to be tested for STIs regularly.
- MSM who are diagnosed with HIV should test more often, since they are more likely have an STI diagnosis, but are not frequently tested.

Contributorship statement

- Karlijn Kampman contributed to the statistical analysis, drafted the article, and processed comments made by the other authors.
- Janneke Heijne discussed methodological issues, gave advice about the statistics, and made corrections to the article.
- Nelleke Koedijk drafted the research protocol, collected data, and assisted with the literature search.
- Femke Koedijk contributed to the statistical analysis and commented on the article.

- Maartje Visser discussed methodological issues, gave advice about statistics, and made corrections to the article.
- Jeannine Hautvast commented on the research protocol, helped with the data analysis, and commented on the article.

All authors gave their final approval of the final version of the original article to be published.

Data sharing statement

There are no additional unpublished data from the study available.

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STROBE checklist

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract: The title on the title page (page 1) contains commonly used terms like *Sexually Transmitted Infections* and *Men who have sex with men*. Furthermore, the study design is displayed in the title.
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found: The abstract can be found on page 2 and is providing a balanced summary of what was done and found in this study.
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported: On page 3 the introduction can be found, which also incorporates scientific background an rationale for the current study.
Objectives	3	State specific objectives, including any pre-specified hypotheses: At the end of page 3 the objectives of the study (named 'aims') are described in the last paragraph of the introduction.
Methods		
Study design	4	Present key elements of study design early in the paper: The study designs is described on page 4.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection: The study setting is described on page 4.
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up: On page 4 below the heading 'study population', we have described the eligibility criteria, the selection of participants and the methods of follow-up. *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable: We have defined all outcomes under 'data description' and 'data analysis' on page 4 and 5 .
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group: The sources of data are described under 'study setting and study design' on page 4.
Bias	9	Describe any efforts to address potential sources of bias: In our methods section, starting on page 4, we have addressed the inclusion and exclusion criteria. Also, in the discussion, starting on page 9, we have described potential biases.
Study size	10	Explain how the study size was arrived at: On page 4, the study population is described under the heading 'study population'.
Quantitative variables	11	Explain how quantitative variables were handled in the

		analyses. If applicable, describe which groupings were chosen and why: The handling of quantitative variables is described on page 5, under the heading 'data analysis'.
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding: The statistical methods are described under the heading 'data analysis' on page 5.
		(*b*) Describe any methods used to examine subgroups and interactions: Current study doesn't include subgroups.
		(*c*) Explain how missing data were addressed: Missing data are addressed op page 5 under 'data analysis': "If more than 5% of the values were missing for a variable, these missing values were included in the analysis in a separate category to reduce the loss of data."
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed: not applicable. *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses: not applicable.
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed: not applicable
		(b) Give reasons for non-participation at each stage: not applicable
		(c) Consider use of a flow diagram: we considered (and made) using a flow diagram, we choose not to uptake a flow diagram in the manuscript.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders: characteristics on study participants are described on page 4 under 'study population'
		(b) Indicate number of participants with missing data for each variable of interest: number of participants and missing data are displayed in table 1 on page 7.
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount): follow up time is described on page 4, under 'study setting and study design'.
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time: Under 'data analysis' on page 5, the outcomes measures are described, the result of these outcome measures are described on page 6 and 7.
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included: The results for multivariable analyses, including 95% confidence in[illegible]57CPOe3V w

		univariable and multivariable analysis were done.
Key results	18	Summarise key results with reference to study objectives: Key results are summoned in 'key points' on page 12.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias: limitations are described under 'discussion' on page 9 (second paragraph).
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence: interpretation of results are described under 'discussion', page 11, last paragraph.
Generalisability	21	Discuss the generalisability (external validity) of the study results: we also have described this under 'discussion', as part of a limitation, on page 11, second paragraph.
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based: not applicable

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.