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Regional differences in chlamydia and gonorrhoea positivity rate among heterosexual STI clinic visitors in the Netherlands: contribution of client and regional characteristics

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ABSTRACT

Objectives

To assess to what extent triage criteria, client and regional characteristics explain regional differences in Chlamydia trachomatis (Ct) and Neisseria gonorrhoeae (Ng) positivity

Design

Retrospective cross-sectional study in the Dutch national STI surveillance of STI clinic visits at 24 STI clinics in 2015

Participants

All STI clinic visits of heterosexual persons in 2015 with a Ct (N=101,495) and/or Ng test (N=101,081)

Primary outcome measure

Two-level logistic regression analyses were performed to calculate the median odds ratio (MOR) and the percentage change in regional variance (PCV) after adding triage criteria (model 1), other client characteristics (model 2) and regional characteristics (model 3) to the empty model. The contribution of single characteristics was determined after removing them from model 3.

Results

There was a statistically significant regional variance in Ct (MOR=1.14) and Ng (MOR=1.44). For Ct, the PCV was 11.7% in model 1, 32.2 % in model 2 and 59.3% in model 3. Age, notified for Ct, level of education and regional degree of urbanisation explained variance most. For Ng, the PCV was 38.7% in model 1, 61.2% in model 2 and 69.1% in model 3. Ethnicity, partner in risk group, level of education and neighbourhood and regional socioeconomic status (SES) explained variance most. A significant part of regional variance remained unexplained.

Conclusions

One-third of regional variance in Ct and two-thirds of regional variance in Ng was explained by differences in client characteristics among heterosexuals, suggesting Ng is more concentrated in high-risk persons, while Ct is endemic. Clustering of Ng in low SES regions additionally explained regional variance in Ng; targeted interventions in low SES regions may assist Ng control. Including educational level as triage criterion is recommended, given the high Ct/Ng risk among lower-educated visitors. Studies incorporating prevalence data are needed to assess whether regional clustering underlies unexplained regional variance.

Strengths and limitations

- We assess regional differences in Ct and Ng positivity among heterosexual STI clinic visitors between the 24 Dutch STI clinic regions.
- The nationwide database covering all STI clinic consultations of heterosexuals with a large set of demographic and behavioural characteristics enabled us to study a range of explanatory variables for Ct and Ng positivity.
- By using a multilevel approach, it was possible to quantify the contribution of characteristics of STI clinic visitors to the regional variance in positivity.
- The study is limited as 15% of consultations data was incomplete for some variables of interest. Missing data were incorporated as a separate group, which could have distorted results.
- Our study is limited to STI clinic visitors, since there is no national database covering all STI related consultations at both GP and STI clinics in the Netherlands.

INTRODUCTION

Chlamydia trachomatis (Ct) and Neisseria gonorrhoeae (Ng) are the most common bacterial sexually transmitted infections (STI) among heterosexual men and women in Europe.(1) In the Netherlands, Ct and Ng diagnostic tests are mainly performed by general practitioners and STI clinics at Public Health Services resulting is an estimated total number of 400,000 STI consultations nationwide. Online testing accounts for an additional 50,000 STI test in 2015. (2, 3) In 2016, it was estimated that approximately 20,000 Ct infections were diagnosed at the STI clinics and 35,000 at the GP. For Ng infections these number are 6,000 and 8,000 respectively.(4) The GP is accessible to everyone in society and offers Ct and Ng testing on request. A drawback of STI tests at the GP is that laboratory tests are subject to the obligatory own risk of health insurance and therefore not always reimbursed. STI clinics have been introduced in 1976 to provide confidential and free of charge STI testing and treatment for high-risk groups with the aim to support individual and public health. MSM are eligible for regular testing at STI clinics and MSM consultations are disproportionally high at STI clinics. Heterosexuals are eligible to the STI clinic when they fulfil at least one of the high-risk triage criteria: notified by a partner for STI, STI-related symptoms, aged below 25 years of age, having a high risk for STI (e.g. originating from or having a partner from an STI-endemic country or working as a commercial sex worker (CSW)) and/or victims of sexual violence. All STI clinic visitors are routinely tested for chlamydia and gonorrhoeae, syphilis, HIV (with the possibility to opt-out) and hepatitis B/C (on indication). Since 2015, testing of persons younger than 25 years of age without another indication is limited to Ct and Ng.(5) Despite this national control policy there are regional differences in the number of consultations and in Ct and Ng positivity among heterosexual STI clinic visitors. Explanations might be found in variations in the proportion of certain high-risk characteristics of STI clinic visitors and in variations in regional characteristics related to positivity. Knowledge about these underlying factors might inform STI policy optimisation. In this study, we assess regional differences in Ct and Ng positivity among heterosexual STI clinic visitors between the 24 Dutch STI clinic regions. Furthermore, we study into what extent these regional differences are explained by variations in client and regional characteristics.

METHODS

Data collection

Data on STI clinic consultations and diagnoses were obtained from the national STI surveillance database (SOAP), in which a predefined set of characteristics (including STI risk factors, diagnostic tests performed and outcomes measured) of all consultations at the 24 Dutch STI clinics is mandatory and routinely collected on an anonymous basis. The 24 STI clinics are spread throughout the Netherlands. In the SOAP database all consultations of heterosexual STI clinic visitors in 2015 were selected (N=101,710). This database was merged with demographic data for each four-digit zip code (degree of urbanisation, socioeconomic status (SES)) and for each STI clinic region (distribution of age, gender, STI-endemic ethnicity, degree of urbanisation, SES). Demographic data on age, gender, STI-endemic ethnicity and degree of urbanisation were obtained from 'Statline', an open-access platform providing freely downloadable data of Statistics Netherlands (CBS).(6) Demographic data on SES was requested at the Netherlands Institute for Social Research (SCP). In this merged dataset, only consultations with a Ct test were selected for Ct analyses (101,495) and only consultations with an Ng test were selected for Ng analyses (N=101,081). Because the data was routinely and anonymously collected for surveillance purposes, no ethical approval was needed.

Explanatory variables

Triage criteria

All triage criteria were included in the analyses: age, notified by a sexpartner for Ct (in Ct analyses), notified for Ng (in Ng analyses), STI-related symptoms, commercial sex worker (CSW), originating from an STI-endemic country, partner from risk group and Ct/Ng/syphilis infection in the previous year.(5)

The continuous variable age was categorised in the age groups <20, 20-24, 25-29, 30-34, ≥35 for Ct analyses and <20, 20-24, 25-39, ≥39 years for Ng analyses. The presence of STI-related symptoms was unknown in 0.6% of consultations. We assumed that these persons did not have symptoms and

were therefore included in the category 'no symptoms'. Ethnicity was based on the definition of CBS and was categorised into persons originating from a non STI-endemic country, first generation STI-endemic migrants and second generation STI-endemic migrants.(7) STI-endemic countries include Turkey and all countries in Africa, Asia, Eastern Europe and Latin-America.(8) A partner from risk group was defined as having a partner originating from an STI-endemic country or in women as having a partner with MSM contacts. Missing data were incorporated in a separate category.

Other client characteristics

The following other client characteristics were included in the analyses: gender, level of education, number of sex partners in past six months, condom use in last sexual contact, Ng infection (for Ct analyses), Ct infection (for Ng analyses), infection with HIV/hepatitis B/syphilis, repeated consultation at the same STI clinic, living in the region of the STI clinic consulted, neighbourhood SES and degree of urbanisation.

The continuous variable number of sex partners was categorised in the groups 0-1, 2-3, 4-9, and ≥10. CSW who had an unknown number of partners were allocated to the group ≥10. A consultation was assigned 'repeated' when the person had a previous STI clinic consultation in 2015. Degree of urbanisation was obtained from CBS per four-digit zip code and categorised in three groups. Neighbourhood SES was obtained from SCP providing a continuous 'statusscore' per four-digit zip code in 2014, based on level of education, employment and income of inhabitants. The statusscores were transformed into tertiles, with tertile one representing the lowest SES. Missing data were incorporated in a separate category.

Regional characteristics of STI clinic regions

Regional characteristics included the percentage of males, 15-44 year olds (the age group to which the majority of heterosexual STI clinic visitors belong), persons originating from an STI-endemic country (first and second generation), persons with a high degree of urbanisation and persons with a low SES

within each of the 24 STI clinic regions. The median of these 24 percentages was used to construct dichotomized variables (percentage in region <median, percentage in region ≥median).

Outcome variables

Outcome variables were a Ct or Ng infection as indicated by a positive NAAT test at one or more anatomic locations. All analyses were performed for Ct and Ng separately.

Statistical analyses

Main analyses

Ct and Ng positivity rates were estimated by region with corresponding 95% confidence intervals (95%CI) using one-sample t-tests and were depicted with forest plots. Two-level logistic regression was used to analyse explanatory factors of regional differences in positivity, with consultations (level 1) nested within regions (level 2). First, a random intercept model (model 0) without any explanatory variables was conducted to obtain baseline regional variance (Vr) and to calculate the median odds ratio (MOR).

$$MOR = \exp(0.95 * \sqrt{Vr})$$

The MOR is the median value of the odds ratio between the region at highest and lowest risk when randomly picking out two regions.(9) A MOR of 1 reflects an absent regional variance; the regional variance increases with higher values above 1. Besides model 0, three extended models were conducted: model 1 included triage criteria, model 2 additionally included other individual level characteristics and model 3 additionally included regional characteristics. For every model, the association between characteristics and outcomes were computed as adjusted odds ratio's (aOR) with 95%CI. Furthermore, the regional variance was noted and the MOR calculated. The proportional change in variance (PCV) was calculated to assess the extent to which the characteristics in the model explained regional variance.(10)

$$PCV = \frac{Vr_0 - Vr_1}{Vr_0} * 100\%$$

Vr_0=regional variance of model 0.

Vr_1=regional variance of one of the subsequent models.

To investigate which characteristics contributed most to regional variance, the percentage of contribution was computed for each variable separately.

$$\%\ contribution = \frac{Vr_4 - Vr_3}{Vr_4}$$

Vr_4=regional variance of model 3 without the one characteristic of which the percentage contribution is calculated.

Vr_3=regional variance of model 3.

Cleaning and merging of datasets and calculation of positivity rates were performed with SPSS 24.0. Two-level logistic regression analyses were performed with SAS 9.4. Forest plots were produced with Microsoft Excel 2010.

Additional analyses

It was examined whether the association between client characteristics and the outcomes differed between regions. Therefore, model 3 was extended with random slopes for all client characteristics. With a backward selection procedure, only statistically significant ($p<0.05$) random slopes were included in the model. Subsequently, the MOR and PCV were calculated to investigate into what extent random slopes additionally explained regional variance.

RESULTS

Chlamydia

Ct positivity ranged from 12.6% (11.6%-13.6%) to 20.0% (18.1%-21.9%) (Figure 1). The MOR, reflecting regional variance, was 1.14 (p=0.001) (Table 1). After including triage criteria, 11.7% of regional variance was explained. In this model, almost all triage criteria were statistically significantly associated with Ct, except for CSW and partner in risk group. After including other client characteristics, 32.2% of regional variance was explained. The triage criteria CSW and partner in risk group also became independently associated with Ct: CSW and those with a partner in risk group had lower Ct positivity. Other client characteristics associated with Ct were level of education, number of partners in past six months, condom use in last sexual contact, Ng infection, repeated consultation, neighbourhood SES and degree of urbanisation. After including regional characteristics, 59.3% of regional variance was explained. The MOR of this final model was 1.09 (p=0.003). The only regional characteristic independently associated with Ct was degree of urbanisation: those living in highly urbanised regions had lower Ct positivity when visiting the STI clinic.

The variables age, being notified for Ct , level of education and regional degree of urbanisation contributed most to regional variance, respectively -38.2%, -15.0%, -15.4% and -24.0% (Table 2). On the other hand, STI-related symptoms, number of partners in past six months and repeated consultation increased regional variance after including them in the model, respectively +44.8%, +15.0% and 18.0%.

There were significant random slopes for age, notified, STI-related symptoms, partner in risk group, gender and repeated consultation. After adding these random slopes to model 3, the PCV increased to 100% (Table 1).

Gonorrhoea

Ng positivity ranged from 0.8% (0.5%-1.1%) to 3.8% (3.4%-4.2%) (Figure 1). The MOR, reflecting regional variance, was 1.44 (p=0.002) (Table 3). After including triage criteria, 38.7% of regional variance was explained. In this model, all triage criteria were statistically significantly associated with Ng. After adding other client characteristics, 61.2% of regional variance was explained. Other client characteristics associated with Ng were level of education, number of partners in past six months, Ct

infection, repeated consultation, neighbourhood SES and living in region of STI clinic consultation. After adding regional characteristics, 69.1% of regional variance was explained, leaving a MOR of 1.23 (p=0.013). The only regional characteristic independently associated with Ng was SES: those living in low SES regions had a borderline statistically significant higher Ng positivity when visiting the STI clinic.

The variables STI-endemic migrant, partner in risk group, level of education and SES on neighbourhood and regional level contributed most to regional variance, respectively -17.2%, -11.3%, -16.1%, -9.4% and -18.6% (Table 2). On the other hand, STI-related symptoms increased regional variance after including it in the model (+30.7%).

There was a significant random slope for age. After adding this random slope to model 3, the PCV increased from 69.1% to 87.2%, with no statistically significant regional variance left (Table 3).

DISCUSSION

Main findings

Our study showed moderate statistically significant regional variance in Ct and Ng positivity among Dutch heterosexual STI clinic visitors, with most regional variance seen for Ng positivity (MOR 1.44). For Ct, about one-third of regional variance was explained by differences in client characteristics (mainly age, being notified for Ct and level of education), and about 20% by differences in regional characteristics (mainly low degree of urbanisation)), confirming the endemic character of Ct among heterosexual men and women. For Ng, about two-thirds of regional variance was explained by differences in client characteristics (mainly STI-endemic migrant, partner from risk group, level of education and neighbourhood SES), and about 8% by differences in regional characteristics (mainly low SES). This is in line with the occurrence of Ng in high risk groups.

Strengths and limitations

The analyses were performed in a nationwide database covering all STI clinic consultations of heterosexuals with a large set of demographic and behavioural characteristics. This enabled us to study a range of explanatory variables. By using a multilevel approach, it was possible to quantify the contribution of characteristics of STI clinic visitors to the regional variance in positivity. To the best of our knowledge, this has not been done before. There are also some limitations to address. First, in 15% of consultations data was incomplete for some variables of interest, varying between 0.1% and 6.7%. Missing data were incorporated as a separate group, which could have distorted results. However, missing data were imputed using multiple imputation, and results remained robust (not shown). Second, the contribution to the regional variance was determined for each variable separately. It should be kept in mind that these 'contributions' do not add up to the total PCV. Third, our study is limited to STI clinic visitors, since there is no national database covering all STI related consultations at both GP and STI clinics in the Netherlands. Information on sexual behaviour of patients diagnosed at the GP is not available, therefore we are unable to compare sexual behaviour of GP patients with that of STI clinic visitors. The demographic composition of the STI clinic visitors does not necessarily reflect the demographic composition of the entire Dutch population, affecting associations. Those visiting are at high risk, partially due to self-selection and due to triage prioritising those at highest risks.(11, 12) Fourth, although a large set of characteristics was available, residual confounding remains possible.

Regional variance explained by triage criteria and other individual level characteristics

For Ct about one-third and for Ng about two-thirds of regional variance was explained by differences in client characteristics. The larger contribution of client characteristics to regional variance in Ng as compared to Ct indicates that Ng is more concentrated in high-risk persons/networks, while Ct is endemic among young heterosexual men and women.(13) This is also reflected in the overall higher positivity rate for Ct as compared to Ng, and the higher regional variation of Ng positivity as compared to Ct positivity in all models presented in the study. The contribution to regional variance was calculated for each client characteristic separately. In order to contribute to regional variance, a characteristic has to fulfil the following conditions:

1) The characteristic has to be related to the outcome.
2) The proportion of the characteristic has to vary between regions.
3) The prevalence of the characteristic has to be sufficiently high.

For Ct, age, being notified for Ct and level of education reduced regional variance most. For Ng, STI-endemic migrant, partner in risk group, level of education and neighbourhood SES reduced regional variance most. These characteristics are strongly associated with Ct/Ng positivity, which has also been found previously.(14-21) Furthermore, the proportion of visitors with these characteristics is higher in regions with higher positivity. Consequently, correcting for these variables decreased regional variance. Some characteristics increased regional variance when included in the model, mainly STI-related symptoms. This indicates that there are fewer visitors with STI-related symptoms in regions with higher positivity. Correcting for this characteristic therefore increased regional variance. The reasons behind different proportions of client characteristics between regions might be related to:

1) differences in location of STI clinics, resulting in the attraction of certain groups;
2) differences in familiarity with and accessibility of STI clinics;
3) differences in balance between consultation requests versus availability of consultations, influencing the degree of prioritising at the gate;
4) differences in demography between STI clinic regions (e.g. urbanisations and ethnicity).

The characteristics contributing most to regional variance differed between Ct and Ng, mainly because of varying associations between these characteristics and the two outcomes. For example, STI-endemic migrant, partner in risk group and neighbourhood SES were more strongly related to Ng positivity than to Ct positivity. Furthermore, although being notified for Ng was strongly associated with Ng positivity, the prevalence of Ng notifications was too low to influence regional variance.

Our results showed that some other client characteristics, not included as triage criteria, were independently associated with Ct and/or Ng positivity and contributed importantly to regional variance, especially low/intermediate level of education. Previous Ct and Ng prevalence studies also showed that low/intermediate level of education was associated with higher Ct and Ng risk.(20, 22)

Low/intermediate educated persons are underrepresented at STI clinics: only 33% of STI clinic visitors had a low/intermediate level of education, while this was 70% in the general Dutch population.(23)

Regional variance explained by regional characteristics

Regional SES explained part of regional variance in Ng positivity. Living in a low SES region increased Ng positivity independent of neighbourhood SES and level of education. This suggests that there is clustering of Ng among heterosexuals within low SES neighbourhoods and regions. Previous studies also found clustering of Ng within low SES regions and among migrant populations.(14-16, 21, 24) Neighbourhood and regional SES had no influence on regional variance in Ct positivity, as is also described previously.(25) However, regional degree of urbanisation was an important contributor to regional variance in Ct. Living in urbanised regions decreased Ct positivity at STI clinics. This is in contrast to previous Dutch studies in which a high degree of urbanisation was related to higher Ct prevalence.(22, 26) However, our study is limited to STI clinic visitors and results may be affected by self-selection of inhabitants to visit the STI clinic. Indeed, additional analyses showed that high urbanised regions had lower Ct positivity rates among those notified for Ct and among those with STI-related symptoms than low urbanised regions (not shown). Possibly, inhabitants of urbanised regions are more familiar with and have easier access to STI clinics, lowering the threshold of an STI clinic visit. The population at these STI clinics may therefore be at lower risk, even when being notified by a partner or experiencing STI-related symptoms.

Unexplained regional variance

Part of regional variance remained unexplained. After including significant random slopes in model 3 (age, notified, STI-related symptoms, partner in risk group, gender, and repeated consultation for Ct and age for Ng) all regional variance was explained. The differential association between these characteristics and infection between regions explained all remaining regional variance. This implies that Ct/Ng risk of an STI clinic visitor differs between regions, even when client characteristics are similar. This may be caused by differences in the self-selection of persons visiting the STI clinic and

in prioritising practices at STI clinics between regions, but it may also reflect real regional differences. Previous studies reported strong evidence for spatial Ng clustering in the UK and the USA, independent of sociodemographic regional factors.(15, 24, 27-30) Also regional Ct clusters have been reported, although they were less strong and more diffuse compared to Ng clusters.(31) Studies incorporating prevalence data are needed to assess whether regional clustering of Ct and Ng is present in the Netherlands.

CONCLUSION AND RECOMMENDATIONS

We found statistically significant regional variance in Ct and Ng positivity among Dutch heterosexual STI clinic visitors. Although moderate, this regional variance was stronger for Ng than for Ct. For Ct about one-third and for Ng about two-thirds of regional variance was explained by differences in client characteristics, suggesting that Ng is more concentrated in high-risk persons while Ct is endemic. Furthermore, results indicate Ng clustering among heterosexuals within low SES neighbourhoods and regions; targeted interventions in low SES regions may therefore be valuable for Ng control. About one-third of regional variance in Ct and Ng positivity remained unexplained. Studies incorporating prevalence data are needed to assess whether this may be caused by regional clustering. The strong association between low/intermediate level of education and positivity implies that, besides triage criteria, the lower educated visitors could be prioritised, especially at STI clinics facing time/financial constraints. Furthermore, each STI clinic should investigate the characteristics of their clients at highest risk to develop targeted prioritising practices and ideally combine this information with data from GP patients to get a complete regional picture.

COMPETING INTERESTS

The authors declare that they have no competing interests.

CONTRIBUTORSHIP

AO initiated the study, analysed and interpreted the data and drafted the manuscript. HG initiated the study, helped interpreting the data and revised the manuscript draft. BvB and CH helped interpreting the data and revised the manuscript draft. All authors read and approved the final manuscript.

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DATA SHARING STATEMENT STI

Results of analyses on the imputed datasets are available upon request from the corresponding author after permission of the registration committee for the Dutch STI clinic database. "The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non-exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd to permit this article (if accepted) to be published in BMJ open and any other BMJPGL products and sub-licences such use and exploit all subsidiary rights, as set out in our licence http://group.bmj.com/products/journals/instructions-for-author

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Competing interests statement.

The authors declare no competing interests.

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TABLES

Table 1 Measures of association between triage criteria, other client characteristics and regional characteristics and Ct positivity and measures of variation in Ct positivity between regions in the Netherlands, 2015, obtained from two-level logistic regression

		N (% of total)	Model 0*	Model 1**	Model 2#	Model 3†
MEASURES OF ASSOCIATION – AOR (95% CI)						
Triage criteria						
Age	<20	10,208 (10.1)		**1.00**	**1.00**	**1.00**
	20-24	55,508 (54.2)		0.73 (0.70;0.78)	0.78 (0.73;0.82)	0.78 (0.73;0.82)
	25-29	19,482 (19.2)		0.47 (0.44;0.51)	0.51 (0.47;0.54)	0.51 (0.47;0.54)
	30-34	6,852 (6.8)		0.38 (0.34;0.41)	0.40 (0.36;0.44)	0.40 (0.36;0.44)
	≥35	9,945 (9.8)		0.29 (0.26;0.32)	0.28 (0.25;0.31)	0.28 (0.25;0.31)
Notified for chlamydia	No	80,862 (79.7)		**1.00**	**1.00**	**1.00**
	Yes	15,507 (14.8)		4.52 (4.33;4.71)	4.52 (4.33;4.72)	4.51 (4.32;4.71)
	Yes, other/unknown STI	5,159 (5.1)		1.52 (1.39;1.65)	1.37 (1.26;1.49)	1.37 (1.26;1.49)
	Unknown	417 (0.4)		0.86 (0.61;1.21)	0.85 (0.60;1.21)	0.86 (0.60;1.21)
STI-related symptoms	No	65,555 (64.6)		**1.00**	**1.00**	**1.00**
	Yes	35,940 (35.4)		1.72 (1.66;1.79)	1.65 (1.59;1.72)	1.65 (1.59;1.72)
CSW	No or unknown	95,484 (94.1)		**1.00**	**1.00**	**1.00**
	Yes	6,011 (5.9)		0.88 (0.79;0.98)	0.66 (0.58;0.76)	0.66 (0.58;0.76)
STI-endemic migrant	No	74,990 (73.9)		**1.00**	**1.00**	**1.00**
	Yes, first generation	11,376 (11.2)		1.25 (1.17;1.33)	1.13 (1.06;1.21)	1.13 (1.06;1.21)
	Yes, second generation	14,978 (14.8)		1.27 (1.21;1.34)	1.13 (1.07;1.19)	1.14 (1.08;1.20)
	Unknown	151 (0.1)		0.68 (0.37;1.24)	0.68 (0.37;1.24)	0.67 (0.37;1.23)
Partner in risk group	No	74,816 (73.7)		**1.00**	**1.00**	**1.00**
	Yes	25,408 (25.0)		0.96 (0.91;1.00)	0.90 (0.86;0.95)	0.90 (0.86;0.95)
	Unknown	1,271 (1.3)		0.84 (0.69;1.03)	0.81 (0.66;0.99)	0.80 (0.65;0.98)
Chlamydia, gonorrhoea or syphilis in past year	No	90,009 (88.7)		**1.00**	**1.00**	**1.00**
	Yes	11,486 (11.3)		1.25 (1.19;1.32)	1.14 (1.08;1.21)	1.14 (1.08;1.21)
Other client characteristics						
Gender	Men	35,628 (35.1)			**1.00**	**1.00**
	Women	65,867 (64.9)			0.97 (0.93;1.01)	0.96 (0.93;1.00)
Level of education^	Low or intermediate	33,387 (32.9)			**1.00**	**1.00**
	High	61,591 (60.7)			0.75 (0.72;0.78)	0.75 (0.72;0.78)
	Unknown	6,517 (6.4)			0.90 (0.82;0.99)	0.90 (0.82;0.99)

		N (% of total)	Model 0*	Model 1**	Model 2#	Model 3†
Number of partners in past 6 months	0-1	25,718 (25.3)			**1.00**	**1.00**
	2-3	41,843 (41.2)			1.20 (1.14;1.26)	1.20 (1.14;1.25)
	4-9	23,908 (23.6)			1.32 (1.25;1.39)	1.32 (1.25;1.39)
	≥10	9,332 (9.2)			1.48 (1.35;1.62)	1.47 (1.34;1.62)
	Unknown	694 (0.7)			1.08 (0.86;1.36)	1.09 (0.87;1.38)
Condom use in last sexual contact	No	74,028 (72.9)			**1.00**	**1.00**
	Yes	23,695 (23.3)			0.77 (0.73;0.81)	0.77 (0.73;0.81)
	Unknown	3,772 (3.7)			0.95 (0.86;1.05)	0.96 (0.86;1.06)
Gonorrhoea infection	No	99,796 (98.3)			**1.00**	**1.00**
	Yes	1,699 (1.7)			3.75 (3.37;4.17)	3.74 (3.36;4.17)
HIV/HBV/Syphilis infection	No	101,358 (99.9)			**1.00**	**1.00**
	Yes	137 (0.1)			1.15 (0.69;1.90)	1.13 (0.68;1.88)
Repeated consultation	No	89,948 (88.6)			**1.00**	**1.00**
	Yes	11,547 (11.4)			1.87 (1.78;1.97)	1.87 (1.77;1.97)
SES on neighbourhood level	Low	43,012 (42.4)			**1.00**	**1.00**
	Medium	21,453 (21.1)			0.97 (0.92;1.02)	0.97 (0.92;1.02)
	High	30,274 (29.8)			0.91 (0.86;0.95)	0.91 (0.87;0.95)
	Unknown	6,756 (6.7)			0.93 (0.60;1.45)	0.94 (0.61;1.47)
Degree of urbanisation$	Very high	52,094 (51.3)			**1.00**	**1.00**
	High or intermediate	30,877 (30.4)			1.09 (1.04;1.14)	1.08 (1.04;1.14)
	Low or very low	11,948 (11.8)			1.07 (1.00;1.15)	1.06 (0.99;1.14)
	Unknown	6,567 (6.5)			1.24 (0.77;1.99)	1.22 (0.76;1.96)
STI consultation in region of living	No	10,947 (10.8)			**1.00**	**1.00**
	Yes	85,306 (84.0)			0.95 (0.89;1.01)	0.95 (0.89;1.01)
	Unknown	5,242 (5.2)			0.79 (0.65;0.97)	0.79 (0.65;0.97)
Regional characteristics						
Percentage men	<median	69,367 (68.3)				**1.00**
	≥median	32,128 (31.7)				0.99 (0.88;1.11)
Percentage 15-45 years	<median	24,320 (24.0)				**1.00**
	≥median	77,175 (76.0)				1.04 (0.94;1.14)
Percentage non-Western migrants	<median	33,950 (33.4)				**1.00**
	≥median	67,545 (66.6)				1.11 (0.94;1.31)
Percentage with high degree of urbanisation	<median	31,407 (30.9)				**1.00**
	≥median	70,088 (69.1)				0.79 (0.66;0.94)
Percentage with low SES	<median	38,057 (37.5)				**1.00**
	≥median	63,438 (62.5)				1.01 (0.92;1.11)

		N (% of total)	Model 0*	Model 1**	Model 2#	Model 3†
MEASURES OF VARIATION – RANDOM INTERCEPT ONLY						
Area level variance (95% CI)			0.01919	0.01695	0.01301	0.007810
P-value			0.0010	0.0013	0.0018	0.0029
PCV			-	-11.7%	-32.2%	-59.3%
MOR			1.14	1.13	1.11	1.09
AIC			85118	78623	77018	77018
MEASURES OF VARIATION – RANDOM INTERCEPT AND SIGNIFICANT RANDOM SLOPES‡						
Area level variance (95% CI)						0
P-value						-
PCV						-100%
MOR (95% CI)						1
AIC						76842

**Empty model*

***Model with all triage criteria*

#Model with all triage criteria and other client characteristics

†Model with all triage criteria, individual level characteristics and regional characteristics

‡Significant random slopes included: age, gender, notified, STI-related symptoms, partner in risk group and repeated consultation.

^Low/intermediate level of education: everyone who did not have education at all or who enrolled in or completed elementary school, preparatory secondary vocational education or lower general secondary education; high level of education: everyone enrolled in or who completed the school of higher general secondary education, the pre-university education, university of applied sciences or university.

$Very high degree of urbanisation: those living in neighbourhoods with more than 2,500 addresses per km^2; high or intermediate level of education: those living in neighbourhoods with 1,000 to 2,500 addresses per km^2; low or very low degree of urbanisation: those living in neighbourhoods with less than 1,000 addresses per km^2.

Table 2 Contribution of triage criteria, other client characteristics and regional characteristics to the regional variation in Ct and Ng positivity in the Netherlands, 2015, obtained from two-level logistic regression

	% contribution of variable to variance*	
	Ct	Ng
TRIAGE CRITERIA		
Age	-38.2%	-4.3%
Notified for chlamydia/gonorrhoea	-15.0%	+3.1%
STI-related symptoms	+44.8%	+30.7%
CSW	+1.4%	+4.2%
STI-endemic migrant	+2.6%	-17.2%
Partner in risk group	+8.2%	-11.3%
Chlamydia, gonorrhoea or syphilis in past year	+0.8%	-3.0%
OTHER CLIENT CHARACTERISTICS		
Gender	-0.4%	-2.0%
Level of education	-15.4%	-16.1%
Number of partners in past 6 months	+15.0%	+2.6%
Condom use in last sexual contact	+2.2%	-1.0%
Gonorrhoea/chlamydia infection	-5.0%	-0.1%
HIV/HBV/Syphilis infection	+1.1%	-0.1%
Repeated consultation	+18.0%	+2.1%
SES on neighbourhood level	-2.9%	-9.4%
Degree of urbanisation	+1.4%	1.1%
STI consultation in region of living	-1.1%	-1.4%
REGIONAL CHARACTERISTICS		
Percentage men	0.0%	-0.2%
Percentage between 15-45 years	-1.1%	+0.2%
Percentage non-Western migrants	-5.8%	-0.5%
Percentage with high degree of urbanisation	-24.0%	-1.5%
Percentage with low SES	+1.2%	-18.6%

**Percentage contribution of variable to regional variance. Separate variables are deleted from full model and variance is compared to variance in full model. Percentage contribution=-((variance full model without 1 variable – variance full model)/variance full model without 1 variable)*100%. This is a different measure than the PCV; therefore, these percentages do not add up to the total PCV of the full model.*

Table 3 Measures of association between triage criteria, other client characteristics and regional characteristics and Ng positivity and measures of variation in Ng positivity between regions in the Netherlands, 2015, obtained from two-level logistic regression

		N (% of total)	Model 0*	Model 1**	Model 2#	Model 3†
MEASURES OF ASSOCIATION – AOR (95% CI)						
Triage criteria						
Age	<20	10,093 (10.0)		**1.00**	**1.00**	**1.00**
	20-24	54,734 (54.1)		0.47 (0.41;0.54)	0.59 (0.50;0.69)	0.59 (0.50;0.69)
	25-39	29,538 (29.2)		0.46 (0.39;0.54)	0.65 (0.55;0.77)	0.65 (0.55;0.77)
	≥40	6,716 (6.6)		0.74 (0.61;0.91)	1.07 (0.87;1.32)	1.07 (0.87;1.32)
Notified for gonorrhoea	No	80,547 (79.7)		**1.00**	**1.00**	**1.00**
	Yes	1,452 (1.4)		18.51 (15.95;21.48)	15.36 (13.15;17.94)	15.35 (13.14;17.93)
	Yes, other/unknown STI	18,755 (18.6)		1.09 (0.94;1.26)	0.78 (0.67;0.91)	0.78 (0.67;0.91)
	Unknown	327 (0.3)		0.61 (0.19;1.97)	0.63 (0.19;2.06)	0.61 (0.19;2.01)
STI-related symptoms	No	65,195 (64.5)		**1.00**	**1.00**	**1.00**
	Yes	35,886 (35.5)		2.24 (2.02;2.48)	1.91 (1.72;2.13)	1.91 (1.72;2.13)
CSW	No or unknown	95,069 (94.1)		**1.00**	**1.00**	**1.00**
	Yes	6.012 (5.9)		1.95 (1.62;2.34)	1.44 (1.11;1.86)	1.44 (1.12;1.87)
STI-endemic migrant	No	74,584 (73.8)		**1.00**	**1.00**	**1.00**
	Yes, first generation	11,374 (11.3)		2.47 (2.15;2.84)	1.88 (1.62;2.18)	1.88 (1.62;2.18)
	Yes, second generation	14,972 (14.8)		2.47 (2.18;2.79)	1.86 (1.63;2.13)	1.86 (1.63;2.12)
	Unknown	151 (0.1)		0.70 (0.09;5.73)	0.72 (0.09;5.50)	0.73 (0.10;5.53)
Partner in risk group	No	74,528 (73.7)		**1.00**	**1.00**	**1.00**
	Yes	25,383 (25.1)		1.31 (1.16;1.46)	1.24 (1.10;1.39)	1.23 (1.10;1.39)
	Unknown	1,170 (1.2)		1.64 (1.10;2.44)	1.63 (1.09;2.43)	1.63 (1.09;2.44)
Chlamydia, gonorrhoea or syphilis in past year	No	89,611 (88.7)		**1.00**	**1.00**	**1.00**
	Yes	11,470 (11.3)		1.71 (1.51;1.94)	1.49 (1.32;1.70)	1.49 (1.31;1.69)
Other individual level characteristics						
Gender	Men	35,516 (35.1)			**1.00**	**1.00**

		N (% of total)	Model 0*	Model 1**	Model 2#	Model 3†
	Women	65,565 (64.9)			0.90 (0.80;1.01)	0.90 (0.80;1.01)
Level of education^	Low or intermediate	33,184 (32.8)			**1.00**	**1.00**
	High	61,406 (60.7)			0.44 (0.39;0.49)	0.44 (0.39;0.49)
	Unknown	6,491 (6.4)			0.73 (0.59;0.89)	0.73 (0.59;0.89)
Number of partners in past 6 months	0-1	25,535 (25.3)			**1.00**	**1.00**
	2-3	41,669 (41.2)			1.09 (0.96;1.25)	1.09 (0.96;1.25)
	4-9	23,873 (23.6)			1.03 (0.88;1.21)	1.03 (0.88;1.21)
	≥10	9,331 (9.2)			1.38 (1.11;1.71)	1.38 (1.11;1.71)
	Unknown	673 (0.7)			1.27 (0.75;2.15)	1.27 (0.75;2.16)
Condom use in last sexual contact	No	73,755 (73.0)			**1.00**	**1.00**
	Yes	23,645 (23.4)			0.92 (0.81;1.04)	0.92 (0.81;1.04)
	Unknown	3,681 (3.6)			0.98 (0.75;1.27)	1.00 (0.77;1.29)
Chlamydia infection	No	86,009 (85.1)			**1.00**	**1.00**
	Yes	15,072 (14.9)			3.88 (3.48;4.33)	3.88 (3.48;4.33)
HIV/HBV/Syphilis infection	No	100,944 (99.9)			**1.00**	**1.00**
	Yes	137 (0.1)			1.28 (0.49;3.35)	1.30 (0.50;3.38)
Repeated consultation	No	89,578 (88.6)			**1.00**	**1.00**
	Yes	11,503 (11.4)			1.51 (1.33;1.72)	1.51 (1.33;1.72)
SES on neighbourhood level	Low	42,802 (52.3)			**1.00**	**1.00**
	Medium	21,340 (21.1)			0.77 (0.67;0.90)	0.78 (0.67;0.91)
	High	30,215 (29.9)			0.74 (0.64;0.85)	0.74 (0.64;0.86)
	Unknown	6,724 (6.7)			1.02 (0.31;3.41)	1.01 (0.30;3.39)
Degree of urbanisation$	Very high	51,942 (51.4)			**1.00**	**1.00**
	High or intermediate	30,756 (30.4)			1.01 (0.89;1.15)	1.02 (0.89;1.16)
	Low or very low	11,839 (11.7)			0.89 (0.73;1.10)	0.90 (0.73;1.11)
	Unknown	6,544 (6.5)			0.83 (0.23;2.96)	0.83 (0.23;3.00)
STI consultation in region of living	No	10,886 (10.8)			**1.00**	**1.00**
	Yes	84,973 (84.1)			0.79 (0.67;0.92)	0.79 (0.67;0.93)
	Unknown	5,222 (5.2)			0.92 (0.58;1.45)	0.94 (0.59;1.48)
Regional characteristics						
Percentage men	<median	69,194 (68.5)				**1.00**

		N (% of total)	Model 0*	Model 1**	Model 2#	Model 3†
	≥median	31,887 (31.5)				1.02 (0.75;1.38)
Percentage 15-45 years	<median	24,153 (23.9)				**1.00**
	≥median	76,928 (76.1)				1.02 (0.79;1.32)
Percentage non-Western migrants	<median	33,581 (33.2)				**1.00**
	≥median	67,500 (66.8)				1.04 (0.69;1.58)
Percentage with high degree of urbanisation	<median	31,038 (30.7)				**1.00**
	≥median	70,043 (69.3)				1.10 (0.70;1.73)
Percentage with low SES	<median	38,008 (37.6)				**1.00**
	≥median	63,073 (62.4)				1.26 (0.99;1.59)
MEASURES OF VARIATION – RANDOM INTERCEPT						
Area level variance (95% CI)			0.1497	0.09182	0.05812	0.04624
P-value			0.0016	0.0046	0.0095	0.0127
PCV			-	-38.7%	-61.2%	-69.1%
MOR			1.44	1.33	1.26	1.23
AIC			17021	15032	14157	14164
MEASURES OF VARIATION – RANDOM INTERCEPT PLUS SIGNIFICANT RANSOM SLOPE‡						
Area level variance (95% CI)						0.01914
P-value						0.1666
PCV						-87.2%
MOR						1.14
AIC						14146

**Empty model*

***Model with all triage criteria*

#Model with all triage criteria and other client characteristics

†Model with all triage criteria, other clients' characteristics and regional characteristics

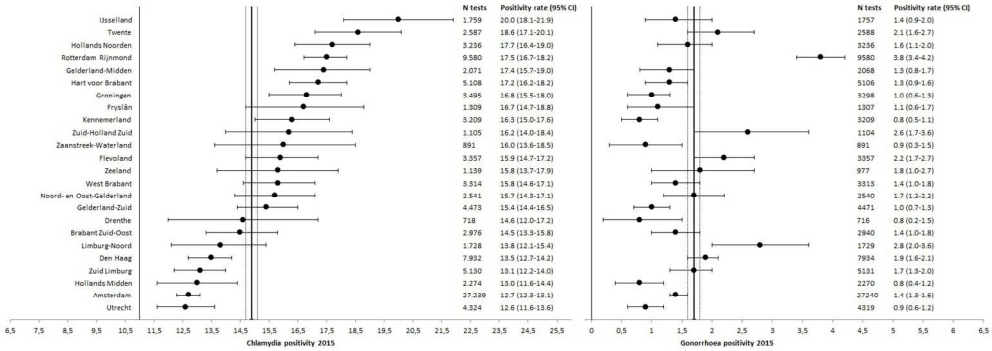
‡Significant random slope for age included

^Low/intermediate level of education: everyone who did not have education at all or who enrolled in or completed elementary school, preparatory secondary vocational education or lower general secondary education; high level of education: everyone enrolled in or who completed the school of higher general secondary education, the pre-university education, university of applied sciences or university.

$Very high degree of urbanisation: those living in neighbourhoods with more than 2,500 addresses per km^2; high or intermediate level of education: those living in neighbourhoods with 1,000 to 2,500 addresses per km^2; low or very low degree of urbanisation: those living in neighbourhoods with less than 1,000 addresses per km^2.

Figure legends

Figure 1 Ct and Ng positivity rate by STI clinic region in the Netherlands, 2015



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STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1/2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1-2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
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	7-8
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	7-8
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	n.a.
		(*e*) Describe any sensitivity analyses	n.a.
Results			
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	9
		(b) Give reasons for non-participation at each stage	n.a.
		(c) Consider use of a flow diagram	n.a.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	22-28
Outcome data	15*	Report numbers of outcome events or summary measures	11, 22-28
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	11, 22-28

		(*b*) Report category boundaries when continuous variables were categorized	11, 22-28
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n.a.
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
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	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
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	17

*Give information separately for exposed and unexposed groups.

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.

BMJ Open

Regional differences in chlamydia and gonorrhoea positivity rate among heterosexual STI clinic visitors in the Netherlands: contribution of client and regional characteristics as assessed by cross-sectional surveillance data

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Regional differences in chlamydia and gonorrhoea positivity rate among heterosexual STI clinic visitors in the Netherlands: contribution of client and regional characteristics as assessed by cross-sectional surveillance data

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ABSTRACT

Objectives

To assess to what extent triage criteria, client and regional characteristics explain regional differences in *Chlamydia trachomatis* (Ct) and *Neisseria gonorrhoeae* (Ng) positivity

Design

Retrospective cross-sectional study on the Dutch national STI surveillance database of all 24 STI clinics

Participants

All STI clinic visits of heterosexual persons in 2015 with a Ct (N=101,495) and/or Ng test (N=101,081)

Primary outcome measure

Two-level logistic regression analyses were performed to calculate the median odds ratio (MOR) and the percentage change in regional variance (PCV) after adding triage criteria (model 1), other client characteristics (model 2) and regional characteristics (model 3) to the empty model. The contribution of single characteristics was determined after removing them from model 3.

Results

There was a statistically significant regional variance in Ct (MOR=1.14) and Ng (MOR=1.44). For Ct, the PCV was 11.7% in model 1, 32.2 % in model 2 and 59.3% in model 3. Age, notified for Ct, level of education and regional degree of urbanisation explained variance most. For Ng, the PCV was 38.7% in model 1, 61.2% in model 2 and 69.1% in

model 3. Ethnicity, partner in risk group, level of education and neighbourhood, and regional socioeconomic status (SES) explained variance most. A significant part of regional variance remained unexplained.

Conclusions

One-third of regional variance in Ct and two-thirds of regional variance in Ng was explained by differences in client characteristics among heterosexuals, indicating that triage and self-selection influence positivity rates in the surveillance data.

Clustering of Ng in low SES regions additionally explained regional variance in Ng; targeted interventions in low SES regions may assist Ng control. Including educational level as triage criterion is recommended, given the high Ct/Ng risk among lower-educated visitors. Studies incorporating prevalence data are needed to assess whether regional clustering underlies unexplained regional variance.

Strengths and limitations

- The large nationwide database covering all STI clinic consultations of heterosexuals with a large set of demographic and behavioural characteristics enabled us to study a range of explanatory variables for regional Ct and Ng positivity differences.
- By using a multilevel approach, it was possible to quantify the contribution of characteristics of STI clinic visitors to the regional variance in positivity.
- Some consultation data was incomplete for some variables of interest (15%) which limited the generalisability of our results although a separate analysis did not show distortion of our results.
- As we studied only STI clinic visitors our results are not generalizable to all STI patients as we did not include patients from GP practices.

INTRODUCTION

Chlamydia trachomatis (Ct) and *Neisseria gonorrhoeae* (Ng) are the most common bacterial sexually transmitted infections (STI) among heterosexual men and women in Europe.(1) In the Netherlands, Ct and Ng diagnostic tests are mainly performed by general practitioners (GP) and STI clinics at Public Health Services, resulting in an estimated total number of 400,000 STI consultations nationwide. In 2016, it was estimated that approximately 20,000 Ct infections were diagnosed at the STI clinics and 35,000 at the GP. For Ng infections these number are 6,000 and 8,000 respectively.(2) The GP is accessible to everyone in society and offers Ct and Ng testing on request. Laboratory tests at the GP are reimbursed by the insurance. However, a drawback is that the first few hundred Euros of health care costs are not deductible, and consequently STI tests are not always reimbursed. Public health oriented STI clinics have been introduced nationwide in 2006 to provide confidential and free of charge STI testing and treatment for high-risk groups. Men who have sex with men (MSM) are eligible for regular testing at STI clinics and MSM consultations are disproportionally high at STI clinics. Heterosexuals are eligible to the STI clinic testing and treatment when they fulfil at least one of the high-risk triage criteria: notified by a partner for STI, STI-related symptoms, aged below 25 years of age, having a high risk for STI (e.g. originating from or having a partner from an STI-endemic country or working as a commercial sex worker (CSW)) and/or victims of sexual violence. All STI clinic visitors are routinely tested for chlamydia and gonorrhoeae, syphilis, HIV (with the possibility to opt-out) and hepatitis B/C (on indication). Previously all of the STI clinics got fully tested for Ct and Ng and for HIV and syphilis. Since 2015, those younger than 25 years are all tested for Ct ánd Ng and on indication for HIV and syphilis. (3) Despite national triage criteria and test policy, there are regional differences in the number of consultations and in Ct and Ng positivity among heterosexual STI clinic visitors. Explanations might be found in variations in the proportion

of certain high-risk characteristics of STI clinic visitors and in variations in regional characteristics related to positivity. Knowledge about these underlying factors might improve our understanding of the surveillance data and may possibly inform priority setting for STI clinics. In this study, we assess regional differences in Ct and Ng positivity among heterosexual STI clinic visitors between the 24 Dutch public health STI clinic regions. Our main objective is to identify explanatory factors of regional variance in Ct and Ng positivity, especially client and regional characteristics. client

METHODS

Data collection

Data on STI clinic consultations and diagnoses in 2015 were obtained from the Dutch national STI surveillance database (SOAP), in which a predefined set of characteristics (including STI risk factors, diagnostic tests performed and outcomes measured) of all consultations at the 24 Dutch Public Health STI clinics is mandatory and routinely collected on a pseudonymous basis (numerical identifier per person which is not traceable to a person).(4) The 24 STI clinics are scattered throughout the country. See fFigure 1. In the SOAP database all consultations of heterosexual STI clinic visitors in 2015 were selected (N=101,710). This database was merged with demographic data for each four-digit zip code (degree of urbanisation, socioeconomic status (SES)) and for each STI clinic region (distribution of age, gender, STI-endemic ethnicity, degree of urbanisation, SES). Demographic data on age, gender, STI-endemic ethnicity and degree of urbanisation in 2015 were obtained from 'Statline' (statline.cbs.nl), an open-access platform providing freely downloadable data of Statistics Netherlands (CBS). Demographic data on SES in 2014 was requested at the Netherlands Institute for Social Research (SCP). In this merged dataset, only consultations

with a Ct test were selected for Ct analyses (101,495) and only consultations with an Ng test were selected for Ng analyses (N=101,081). For an overview of all variables see Table 1.

The data was routinely and pseudonymously collected for surveillance purposes and therefore the study was exempt from formal medical ethical approval under prevailing laws in the Netherlands.

Explanatory variables

Triage criteria

All triage criteria were included in the analyses: age, being notified by a sex partner for chlamydia (in Ct analyses), notified for gonorrhoea (in Ng analyses), STI-related symptoms, commercial sex worker (CSW), originating from an STI-endemic country, partner from risk group and Ct/Ng/syphilis infection in the previous year.(3)

The continuous variable age was categorised in age groups because of the non-linear relation between age and the log odds of the outcomes chlamydia and gonorrhoea. The categories were based on the relation between age and the outcomes on a log odds scale. We chose <20, 20-24, 25-29, 30-34, ≥35 for Ct analyses and <20, 20-24, 25-39, ≥40 years for Ng analyses. The presence of STI-related symptoms was unknown in 0.6% of consultations. We assumed that these persons did not have symptoms and were therefore included in the category 'no symptoms'. Ethnicity was based on the definition of Statistics Netherlands, which is based on country of birth of the person, mother and father. STI-endemic countries include Turkey and all countries in Africa, Asia, Eastern Europe and Latin-America.(5) Categories include persons with a first generation migratory background (person born in an STI endemic country), and second generation migratory background (mother or father born in an STI endemic country) and persons originating from a non STI-endemic country.(6)

A partner from risk group was defined as having a partner originating from an STI-endemic country or in women as having a partner with MSM contacts. Missing data were incorporated in a separate category.

Other individual level client characteristics

The following other client characteristics were also included in the analyses: gender, level of education, number of sex partners in past six months, condom use in last sexual contact, infections diagnosed in the current consultation (Ng infection (for Ct analyses), Ct infection (for Ng analyses), infection with HIV/hepatitis B/syphilis), repeated consultation at the same STI clinic during 2015, living in the region of the STI clinic consulted, neighbourhood SES and degree of urbanisation. The continuous variable number of sex partners was categorised in the groups 0-1, 2-3, 4-9, and ≥10 based on the relation between number of sex partners and the outcomes on a log odds scale. CSW who had an unknown number of partners were allocated to the group ≥10. A consultation was assigned 'repeated' when the person had a previous STI clinic consultation in 2015.

Client characteristics on neighbourhood level

Degree of urbanisation was obtained from CBS per four-digit zip code and categorised in three groups (1,000 to 2,500 addresses per km^2 and less or more than this range). Neighbourhood SES was obtained from SCP providing a continuous 'statusscore' per four-digit zip code in 2014, based on level of education, employment and income of inhabitants.(7) The statusscores were transformed into tertiles, with tertile one representing the lowest SES. Missing data were incorporated in a separate category.

Regional characteristics of STI clinic regions

Regional characteristics included the percentage of men, 15-44 year olds (the age group to whom the majority of heterosexual STI clinic visitors belong), persons originating from an STI-endemic country (first and second generation), persons with a high degree of urbanisation and persons with a low SES within each of the 24 STI clinic regions. The median of these 24 percentages was used to construct dichotomized variables (percentage in region <median, percentage in region ≥median).

Outcome variables

Outcome variables were binary (positive/negative) for either Ct or Ng infection as indicated by a positive NAAT test at one or more anatomic locations. All analyses were performed for Ct and Ng separately.

Statistical analyses

Main analyses For each region, the Ct and Ng positivity was calculated by dividing the number of positives by the number of tests performed. The corresponding 95% confidence interval (95%CI) was calculated with the following formula: $\hat{p} \pm z\sqrt{\frac{\hat{p}(1-\hat{p})}{n}}$, where P=proportion with positive test, Z=1,96, z-value for a 95% confidence interval, N=number of tests performed. 95% CI were depicted with forest plots.

Two-level logistic regression was used to analyse explanatory factors of regional differences in positivity, with consultations (level 1) nested within regions (level 2).s First, a random intercept model (model 0) without any explanatory variables was conducted to obtain baseline regional variance (Vr) and to calculate the median odds ratio (MOR):$MOR = \exp(0.95 * \sqrt{Vr})$

The MOR is the median value of the odds ratio between the region at highest and lowest risk when randomly picking out two regions.(8) A MOR of 1 reflects an absent regional variance; the regional variance increases with higher values above 1. Besides model 0, three extended models were conducted with random intercepts and fixed slopes: model 1 included triage criteria, model 2 triage criteria and other individual level characteristics and model 3 triage criteria, other individual level characteristics and regional characteristics. For every model, the association between characteristics and outcomes were computed as adjusted odds ratio's (aOR) with 95%CI. Furthermore, the regional variance was noted and the MOR calculated. The proportional change in variance (PCV) was calculated to assess the extent to which the characteristics in the model explained regional variance.(9)

$$PCV = \frac{Vr_0 - Vr_1}{Vr_0} * 100\%$$

Vr_0=regional variance of model 0.

Vr_1=regional variance of one of the subsequent models.

To investigate which characteristics contributed most to regional variance, the percentage of contribution was computed for each variable separately.

$$\%\ contribution = \frac{Vr_4 - Vr_3}{Vr_4}$$

Vr_4=regional variance of model 3 without the one characteristic of which the percentage contribution is calculated.

Vr_3=regional variance of model 3.

Cleaning and merging of datasets and calculation of positivity rates were performed with SPSS 24.0. Two-level logistic regression analyses were performed with SAS 9.4. Forest plots were produced with Microsoft Excel 2010.

Additional analyses

To examine whether the associations between client characteristics and the outcomes differ between regions, model 3 was extended with random slopes for all client characteristics. With a backward selection procedure, only statistically significant ($p<0.05$) random slopes were included in the model. Subsequently, the MOR and PCV were calculated to investigate into what extent random slopes additionally explained regional variance. Furthermore, all analyses were repeated after missing values were imputed using multiple imputation (data not shown).

'Patient and Public Involvement'.

Patients and or public were not involved in this retrospective study based on STI surveillance data.

RESULTS

The characteristics of the study population are shown in Table 2.

Ct positivity

Ct positivity was 14.9% (95% CI 14.7% -15.1%) and ranged from 12.6% (95%CI 11.6%-13.6%) to 20.0% (95%CI 18.1%-21.9%) regionally (Figure 2). The MOR, reflecting regional variance, was 1.14 (p=0.001) (Table 3). After including triage criteria, 11.7% of regional variance was explained. In this model, almost all triage criteria were statistically significantly associated with Ct, except for CSW and partner in risk group. After including other client characteristics, 32.2% of regional variance was explained. The triage criteria CSW and

partner in risk group also became independently associated with Ct: CSW and those with a partner in risk group had lower Ct positivity. Other patient characteristics associated with Ct were level of education, number of partners in past six months, condom use in last sexual contact, Ng co-infection, repeated consultation, neighbourhood SES and degree of urbanisation. After including regional characteristics, 59.3% of regional variance was explained. The MOR of this final model was 1.09 (p=0.003). The only regional characteristic independently associated with Ct was degree of urbanisation: those living in highly urbanised regions had lower Ct positivity when visiting the STI clinic.

The variables age, being notified for Ct, level of education and regional degree of urbanisation contributed most to regional variance, respectively -38.2%, -15.0%, -15.4% and -24.0% (Table 4). On the other hand, STI-related symptoms, number of partners in past six months and repeated consultation increased regional variance after including them in the model, respectively +44.8%, +15.0% and 18.0%.

There were significant random slopes for age, notified, STI-related symptoms, partner in risk group, gender and repeated consultation. After adding these random slopes to model 3, the PCV increased to 100% (Table 3).

Ng positivity

Ng positivity was 1.7% (95% CI 1.6 %-1.8%) and ranged from 0.8% (95% CI 0.5%-1.1%) to 3.8% (95% CI 3.4%-4.2%) regionally (Figure 3). The MOR, reflecting regional variance, was 1.44 (p=0.002) (Table 5. After including triage criteria, 38.7% of regional variance was explained. In this model, all triage criteria were statistically significantly associated with Ng. After adding other client characteristics, 61.2% of regional variance was explained. Other client characteristics associated with Ng were level of education, number of partners in past six months, Ct infection, repeated consultation, neighbourhood SES and living in region of

STI clinic consultation. After adding regional characteristics, 69.1% of regional variance was explained, leaving a MOR of 1.23 (p=0.013). The only regional characteristic independently associated with Ng was SES: those living in low SES regions had a borderline statistically significant higher Ng positivity when visiting the STI clinic.

The variables STI-endemic migrant, partner in risk group, level of education and SES on neighbourhood and regional level contributed most to regional variance, respectively -17.2%, -11.3%, -16.1%, -9.4% and -18.6% (Table 4). On the other hand, STI-related symptoms increased regional variance after including it in the model (+30.7%).

There was a significant random slope for age. After adding this random slope to model 3, the PCV increased from 69.1% to 87.2%, with no statistically significant regional variance left (Table 5).

DISCUSSION

Main findings

Our study showed moderate statistically significant regional variance in Ct and Ng positivity among Dutch heterosexual STI clinic visitors, with most regional variance seen for Ng positivity (MOR 1.44). For Ct, about one-third of regional variance was explained by differences in client characteristics (mainly age, being notified for Ct and level of education), and about 27% by differences in regional characteristics (mainly low degree of urbanisation)). For Ng, about two-thirds of regional variance was explained by differences in client characteristics (mainly STI-endemic migrant, partner from risk group, level of education and neighbourhood SES), and about 8% by differences in regional characteristics (mainly low SES). Although we do not have a clear cut-off, these results are in line with the endemic

nature of Ct among heterosexual men and women, and with the higher positivity rate of Ng in risk groups.(10)

Strengths and limitations

The analyses were performed in a large nationwide database with a large set of demographic and behavioural characteristics. This enabled us to study a range of explanatory variables. By using a multilevel approach, it was possible to quantify the contribution of characteristics of STI clinic visitors to the regional variance in positivity. To the best of our knowledge, this has not been done before. There are also some limitations to address. First, in 15% of consultations data was incomplete for some variables of interest, varying between 0.1% and 6.7%. Missing data were incorporated as a separate group, which could have distorted results. However, missing data were imputed using multiple imputation, and results remained robust (not shown).(11) Secondly our study is limited to STI clinic visitors, and did not account for STI related consultations at GP practices. STI visitors are at high risk, partially due to self-selection and due to triage, and therefore do not reflect the Dutch population.(12, 13) As our aim was to explain regional variance within the STI clinic data and not to investigate the real positivity, this is in fact not limiting the results of our study. Third, prevalence studies of the two pathogens would help to clarify what the policy implications are. Fourth, although a large set of characteristics was available, residual confounding remains possible.

Regional variance explained by client level characteristics

For Ct about one-third and for Ng about two-thirds of regional variance was explained by differences in client characteristics. In order to contribute to regional variance, a client characteristic has to fulfil the following conditions:

1) The characteristic has to be related to the outcome.

2) The proportion of the characteristic has to vary between regions.

3) The prevalence of the characteristic has to be sufficiently high.

For Ct, client characteristics age, being notified for Ct and level of education reduced regional variance most. For Ng, client characteristics STI-endemic migrant, partner in risk group, level of education and neighbourhood SES reduced regional variance most. These characteristics are strongly associated with Ct and Ng positivity, which has also been found previously.(14-21) Furthermore, the proportion of visitors with these characteristics is higher in regions with higher positivity. Consequently, correcting for these variables decreased regional variance. Some client characteristics increased regional variance when included in the model, mainly STI-related symptoms. This indicates that the proportion of visitors with STI-related symptoms in regions with higher positivity is lower. Correcting for this characteristic therefore increased regional variance. The reasons behind different proportions of client characteristics between regions might be related to STI clinic location by familiarity with and accessibility of STI clinics, balance between availability of consultations and requests and subsequent stringent triage application, and differences in demography of STI clinics adherence area like urbanisation and ethnicity.

The characteristics contributing most to regional variance differed between Ct and Ng, mainly because of varying associations between these characteristics and the two outcomes. For example, STI-endemic migrant, partner in risk group and neighbourhood SES were more strongly related to Ng positivity than to Ct positivity. Furthermore, although being notified for Ng was strongly associated with Ng positivity, the prevalence of Ng notifications was too low to influence regional variance.

Our results showed client characteristics, which are not included as triage criteria in our STI clinic access policy. , Low/intermediate level of education was independently associated with

Ct and/or Ng positivity and contributed strongly to regional variance .which confirms previous studies.(20, 22) We advise to include low/intermediate education as a triage criterion in the future as these persons are underrepresented at STI clinics as only 33% of STI clinic visitors had a low/intermediate level of education, while this is 70% in the general Dutch population.(4)

Regional variance explained by regional characteristics

Regional SES explained part of regional variance in Ng positivity. Living in a low SES region increased Ng positivity independent of neighbourhood SES and level of education. This suggests that there is clustering of Ng among heterosexuals within low SES neighbourhoods and regions. Previous studies also found clustering of Ng within low SES regions and among migrant populations.(14-16, 21, 23) Neighbourhood and regional SES had no influence on regional variance in Ct positivity, as is also described previously.(24) However, regional degree of urbanisation was an important contributor to regional variance in Ct. Living in urbanised regions decreased Ct positivity at STI clinics. This is apparently in contrast to previous Dutch studies in which a high degree of urbanisation was related to higher Ct prevalence.(22, 25) However, our study is limited to STI clinic visitors and a large proportion of visitors is from urbanised areas where most STI clinics are located. These results show that those from low urbanised areas visit STI clinics less frequently but those that do visit the STI clinic have a higher Ct positivity rate possibly due to effective self-selection. Additional analyses showed that high urbanised regions had lower Ct positivity rates among those notified for Ct and among those with STI-related symptoms than low urbanised regions (not shown). Possibly, inhabitants of urbanised regions are more familiar with and have easier access to STI clinics.

Unexplained regional variance

Part of regional variance remained unexplained. After including significant random slopes in model 3 (age, notified, STI-related symptoms, partner in risk group, gender, and repeated consultation for Ct and age for Ng) all regional variance was explained. The differential association between these characteristics and infection between regions explained all remaining regional variance. This implies that Ct/Ng risk of an STI clinic visitor differs between regions, even when client characteristics are similar. This may be caused by differences in the self-selection of persons visiting the STI clinic and in prioritising practices at STI clinics between regions, but it may also reflect real regional differences. Previous studies reported strong evidence for spatial Ng clustering in the UK and the USA, independent of sociodemographic regional factors.(15, 23, 26-29) Also regional Ct clusters have been reported, although they were less strong and more diffuse compared to Ng clusters.(30) Studies incorporating prevalence data are needed to assess whether regional clustering of Ct and Ng is present in the Netherlands.

CONCLUSION AND RECOMMENDATIONS

We found statistically significant regional variance in Ct and Ng positivity among Dutch heterosexual STI clinic visitors. Although moderate, this regional variance was stronger for Ng than for Ct. For Ct about one-third and for Ng about two-thirds of regional variance was explained by differences in client characteristics, confirming that Ng is more concentrated in high-risk persons while Ct is more endemic. Furthermore, results indicate Ng clustering among heterosexuals within low SES neighbourhoods and regions; targeted interventions in low SES regions may therefore be valuable for Ng control. STI clinics might strengthen their efforts to include young heterosexuals from low education to improve Ct control, and also increase their efforts in reaching more low educated persons from low SES and/or migrant origin in case of Ng control. Although prevalence studies are known to have methodological and practical challenges and are scarce , they are needed to assess whether regional real

regional differences appear, The strong association between low/intermediate level of education and positivity implies that, besides introduction of a new triage criterion, the lower educated visitors should be prioritised,. Furthermore, each STI clinic should investigate the characteristics of their clients at highest risk to develop targeted prioritising policy and ideally combine this information with data from GP patients to get a complete regional perspective.

COMPETING INTERESTS

The authors declare that they have no competing interests.

CONTRIBUTORSHIP

HG initiated the study, helped interpreting the data and drafted and revised the manuscript. LvO initiated the study, analysed and interpreted the data and drafted the manuscript. BvB and CH helped interpreting the data and revised the manuscript draft. All authors read and approved the final manuscript.

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DATA SHARING STATEMENT STI

Results of analyses on the imputed datasets are available upon request from the corresponding author after permission of the registration committee for the Dutch STI clinic database. "The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non-exclusive for government employees) on a

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Competing interests statement.

The authors declare no competing interests.

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TABLES

Table 1: Overview source of data collection& level of analysis

	SOAP	Statistics Netherlands	Institute for Social Research	categories
Triage criteria				
Age Chlamydia	x	x		<20, 20-24, 25-29, 30-34, ≥35
Age Gonorrhoea				<20, 20-24, 25-39, ≥40
Notified for chlamydia / Ng	x			Yes, other/unknown STI, unknown
STI-related symptoms	x			No, yes
CSW	x			No or unknown, yes
Originating from an STI-endemic country	x	x		No, first generation, second generation, unknown
Partner in risk group	x			No, yes, unknown
Chlamydia, gonorrhoea or syphilis in past year	x			No, yes
Other client characteristics				
Gender	x	x		Men, women
Level of education ^	x			Low or intermediate, high, unknown
Number of partners in past 6 months	x			0-1, 2-3, 4-9, ≥10, unknown
Condom use in last sexual contact	x			No, yes, unknown
Ct/Ng infection	x			No, yes
HIV/HBV/Syphilis infection	x			No, yes
Repeated consultation	x			No, yes
SES on neighbourhood level (4zip code) #			x	Low, medium, high, unknown
Degree of urbanization $ (4zip code)		x		Very high, high or intermediate, low or very low, unknown
STI consultation in region of living (4zip code)	x			No, yes, unknown
Regional characteristics				
Percentage men		x		< median, ≥ median
Percentage 15-45 years		x		< median, ≥ median
Percentage non-Western migrants		x		< median, ≥ median
Percentage with high degree of urbanisation		x		< median, ≥ median
Percentage with low SES		x	x	< median, ≥ median

Legend : light grey: Individual level, medium grey: Neighbourhood level; dark grey Regional level ^Low/intermediate level of education: everyone who did not have education at all or who enrolled in or completed elementary school, preparatory secondary vocational education or lower general secondary education; high level of education: everyone enrolled in or who completed the school of higher general secondary education, the pre-university education, university of applied sciences or university.

SES was obtained from the SCP providing a continuous 'statusscore' per four-digit zip code of the entire Netherlands in 2014. This statusscore was based on level of education, employment and income of the inhabitants of the four-digit zip codes. The status scores were transformed into tertiles, with tertile one representing the lowest SES and tertile three representing the highest SES.

$Very high degree of urbanisation: those living in neighbourhoods with more than 2,500 addresses per km2; high or intermediate level of education: those living in neighbourhoods with 1,000 to 2,500 addresses per km2; low or very low degree of urbanisation: those living in neighbourhoods with less than 1,000 addresses per km2.

Table 2: Descriptive analyses of the Study population

		Male	%	Female	%	Total	%
Agegroup							
	<20	2175	6%	8054	12%	10229	10%
	20-24	17748	50%	37339	57%	55087	54%
	25-29	8245	23%	11276	17%	19521	19%
	30-34	3231	9%	3639	6%	6870	7%
	>34	4320	12%	5683	9%	10003	10%
Total		35719	100%	65991	100%	101710	100%
Notified STI		9501	27%	10749	16%	20250	20%
Notified chlamydia		*7147*	20%	*7924*	12%	*15071*	15%
Notified gonorrhoea		*630*	2%	*824*	1%	*1454*	1%
Not notified		26075	73%	54962	83%	81037	80%
Missing		143	0%	280	0%	423	0%
Total		35719	100%	65991	100%	101710	100%
STI-related symptoms	Yes	12972	36%	23052	35%	36024	35%
	No	22747	64%	42939	65%	65686	65%
Total		35719	100%	65991	100%	101710	100%
Originating from an STI-endemic country							
	No	24337	68%	50799	77%	75136	74%
	Yes 1st generation	4630	13%	6788	10%	11418	11%
	Yes 2nd generation	6695	19%	8307	13%	15002	15%
	missing	57	0%	97	0%	154	0%
Total		35719	100%	65991	100%	101710	100%
Partner in risk group		8888	25%	16592	25%	25480	25%
Commercial sex worker		198	1%	5829	9%	6027	6%

Chlamydia, gonorrhea or syphilis in past year		3550	10%	7960	12%	11510	11%
Level of education	Low/intermediate	12583	35%	20885	32%	33468	33%
	High	21175	59%	40504	61%	61679	61%
	Unkwown	1961	5%	4602	7%	6563	6%
Total		35719	100%	65991	100%	101710	100%

Table 3 Measures of association between triage criteria, other client characteristics and regional characteristics and Ct positivity and measures of variation in Ct positivity between regions in the Netherlands, 2015, obtained from two-level logistic regression

		N (% of total)	Model 0*	Model 1**	Model 2#	Model 3†
MEASURES OF ASSOCIATION – AOR (95% CI)						
Triage criteria						
Age	<20	10,208 (10.1)		**1.00**	**1.00**	**1.00**
	20-24	55,508 (54.2)		0.73 (0.70;0.78)	0.78 (0.73;0.82)	0.78 (0.73;0.82)
	25-29	19,482 (19.2)		0.47 (0.44;0.51)	0.51 (0.47;0.54)	0.51 (0.47;0.54)
	30-34	6,852 (6.8)		0.38 (0.34;0.41)	0.40 (0.36;0.44)	0.40 (0.36;0.44)
	≥35	9,945 (9.8)		0.29 (0.26;0.32)	0.28 (0.25;0.31)	0.28 (0.25;0.31)
Notified for chlamydia	No	80,862 (79.7)		**1.00**	**1.00**	**1.00**
	Yes	15,507 (14.8)		4.52 (4.33;4.71)	4.52 (4.33;4.72)	4.51 (4.32;4.71)
	Yes, other/unknown STI	5,159 (5.1)		1.52 (1.39;1.65)	1.37 (1.26;1.49)	1.37 (1.26;1.49)
	Unknown	417 (0.4)		0.86 (0.61;1.21)	0.85 (0.60;1.21)	0.86 (0.60;1.21)
STI-related symptoms	No	65,555 (64.6)		**1.00**	**1.00**	**1.00**
	Yes	35,940 (35.4)		1.72 (1.66;1.79)	1.65 (1.59;1.72)	1.65 (1.59;1.72)
CSW	No or unknown	95,484 (94.1)		**1.00**	**1.00**	**1.00**
	Yes	6,011 (5.9)		0.88 (0.79;0.98)	0.66 (0.58;0.76)	0.66 (0.58;0.76)
Originating from an STI-endemic country	No	74,990 (73.9)		**1.00**	**1.00**	**1.00**
	Yes, first generation	11,376 (11.2)		1.25 (1.17;1.33)	1.13 (1.06;1.21)	1.13 (1.06;1.21)
	Yes, second generation	14,978 (14.8)		1.27 (1.21;1.34)	1.13 (1.07;1.19)	1.14 (1.08;1.20)
	Unknown	151 (0.1)		0.68 (0.37;1.24)	0.68 (0.37;1.24)	0.67 (0.37;1.23)
Partner in risk group	No	74,816 (73.7)		**1.00**	**1.00**	**1.00**
	Yes	25,408 (25.0)		0.96 (0.91;1.00)	0.90 (0.86;0.95)	0.90 (0.86;0.95)
	Unknown	1,271 (1.3)		0.84 (0.69;1.03)	0.81 (0.66;0.99)	0.80 (0.65;0.98)
Chlamydia, gonorrhoea or syphilis in past year	No	90,009 (88.7)		**1.00**	**1.00**	**1.00**
	Yes	11,486 (11.3)		1.25 (1.19;1.32)	1.14 (1.08;1.21)	1.14 (1.08;1.21)
Other client characteristics						
Gender	Men	35,628 (35.1)			**1.00**	**1.00**
	Women	65,867 (64.9)			0.97 (0.93;1.01)	0.96 (0.93;1.00)
Level of education^	Low or intermediate	33,387 (32.9)			**1.00**	**1.00**
	High	61,591 (60.7)			0.75 (0.72;0.78)	0.75 (0.72;0.78)
	Unknown	6,517 (6.4)			0.90 (0.82;0.99)	0.90 (0.82;0.99)
Number of partners in past 6 months	0-1	25,718 (25.3)			**1.00**	**1.00**
	2-3	41,843 (41.2)			1.20 (1.14;1.26)	1.20 (1.14;1.25)

		N (% of total)	Model 0*	Model 1**	Model 2#	Model 3†
	4-9	23,908 (23.6)			1.32 (1.25;1.39)	1.32 (1.25;1.39)
	≥10	9,332 (9.2)			1.48 (1.35;1.62)	1.47 (1.34;1.62)
	Unknown	694 (0.7)			1.08 (0.86;1.36)	1.09 (0.87;1.38)
Condom use in last sexual contact	No	74,028 (72.9)			**1.00**	**1.00**
	Yes	23,695 (23.3)			0.77 (0.73;0.81)	0.77 (0.73;0.81)
	Unknown	3,772 (3.7)			0.95 (0.86;1.05)	0.96 (0.86;1.06)
Gonorrhoea co-infection	No	99,796 (98.3)			**1.00**	**1.00**
	Yes	1,699 (1.7)			3.75 (3.37;4.17)	3.74 (3.36;4.17)
HIV/HBV/Syphilis infection	No	101,358 (99.9)			**1.00**	**1.00**
	Yes	137 (0.1)			1.15 (0.69;1.90)	1.13 (0.68;1.88)
Repeated consultation	No	89,948 (88.6)			**1.00**	**1.00**
	Yes	11,547 (11.4)			1.87 (1.78;1.97)	1.87 (1.77;1.97)
SES on neighbourhood level	Low	43,012 (42.4)			**1.00**	**1.00**
	Medium	21,453 (21.1)			0.97 (0.92;1.02)	0.97 (0.92;1.02)
	High	30,274 (29.8)			0.91 (0.86;0.95)	0.91 (0.87;0.95)
	Unknown	6,756 (6.7)			0.93 (0.60;1.45)	0.94 (0.61;1.47)
Degree of urbanisation$	Very high	52,094 (51.3)			**1.00**	**1.00**
	High or intermediate	30,877 (30.4)			1.09 (1.04;1.14)	1.08 (1.04;1.14)
	Low or very low	11,948 (11.8)			1.07 (1.00;1.15)	1.06 (0.99;1.14)
	Unknown	6,567 (6.5)			1.24 (0.77;1.99)	1.22 (0.76;1.96)
STI consultation in region of living	No	10,947 (10.8)			**1.00**	**1.00**
	Yes	85,306 (84.0)			0.95 (0.89;1.01)	0.95 (0.89;1.01)
	Unknown	5,242 (5.2)			0.79 (0.65;0.97)	0.79 (0.65;0.97)
Regional characteristics						
Percentage men	<median	69,367 (68.3)				**1.00**
	≥median	32,128 (31.7)				0.99 (0.88;1.11)
Percentage 15-45 years	<median	24,320 (24.0)				**1.00**
	≥median	77,175 (76.0)				1.04 (0.94;1.14)
Percentage non-Western migrants	<median	33,950 (33.4)				**1.00**
	≥median	67,545 (66.6)				1.11 (0.94;1.31)
Percentage with high degree of urbanisation	<median	31,407 (30.9)				**1.00**
	≥median	70,088 (69.1)				0.79 (0.66;0.94)
Percentage with low SES	<median	38,057 (37.5)				**1.00**
	≥median	63,438 (62.5)				1.01 (0.92;1.11)
MEASURES OF VARIATION – RANDOM INTERCEPT ONLY						
Area level variance			0.01919	0.01695	0.01301	0.007810

		N (% of total)	Model 0*	Model 1**	Model 2#	Model 3†
(95% CI)			(0.0111;0.04094)	(0.00968;0.03704)	(0.007313;0.02933)	(0.004275;0.01859)
P-value			0.0010	0.0013	0.0018	0.0029
PCV			-	-11.7%	-32.2%	-59.3%
MOR			1.14	1.13	1.11	1.09
AIC			85118	78623	77018	77018
MEASURES OF VARIATION – RANDOM INTERCEPT AND SIGNIFICANT RANDOM SLOPES‡						
Area level variance (95% CI)						0
P-value						-
PCV						-100%
MOR (95% CI)						1
AIC						76842

**Empty model*

***Model with all triage criteria*

#Model with all triage criteria and other patient characteristics

†Model with all triage criteria, individual level characteristics and regional characteristics

‡Significant random slopes included: age, gender, notified, STI-related symptoms, partner in risk group and repeated consultation.

^Low/intermediate level of education: everyone who did not have education at all or who enrolled in or completed elementary school, preparatory secondary vocational education or lower general secondary education; high level of education: everyone enrolled in or who completed the school of higher general secondary education, the pre-university education, university of applied sciences or university.

$Very high degree of urbanisation: those living in neighbourhoods with more than 2,500 addresses per km^2; high or intermediate level of education: those living in neighbourhoods with 1,000 to 2,500 addresses per km^2; low or very low degree of urbanisation: those living in neighbourhoods with less than 1,000 addresses per km^2.

Table 4 Contribution of triage criteria, other client characteristics and regional characteristics to the regional variation in Ct and Ng positivity in the Netherlands, 2015, obtained from two-level logistic regression

	% contribution of variable to variance*	
	Ct	Ng
TRIAGE CRITERIA		
Age	-38.2%	-4.3%
Notified for chlamydia/gonorrhoea	-15.0%	+3.1%
STI-related symptoms	+44.8%	+30.7%
CSW	+1.4%	+4.2%
STI-endemic migrant	+2.6%	-17.2%
Partner in risk group	+8.2%	-11.3%
Chlamydia, gonorrhoea or syphilis in past year	+0.8%	-3.0%
OTHER CLIENT CHARACTERISTICS		
Gender	-0.4%	-2.0%
Level of education	-15.4%	-16.1%
Number of partners in past 6 months	+15.0%	+2.6%
Condom use in last sexual contact	+2.2%	-1.0%
Gonorrhoea/chlamydia infection	-5.0%	-0.1%
HIV/HBV/Syphilis infection	+1.1%	-0.1%
Repeated consultation	+18.0%	+2.1%
SES on neighbourhood level	-2.9%	-9.4%
Degree of urbanisation	+1.4%	1.1%
STI consultation in region of living	-1.1%	-1.4%
REGIONAL CHARACTERISTICS		
Percentage men	0.0%	-0.2%
Percentage between 15-45 years	-1.1%	+0.2%
Percentage non-Western migrants	-5.8%	-0.5%
Percentage with high degree of urbanisation	-24.0%	-1.5%
Percentage with low SES	+1.2%	-18.6%

**Percentage contribution of variable to regional variance. Separate variables are deleted from full model and variance is compared to variance in full model. Percentage contribution=-((variance full model without 1 variable – variance full model)/variance full model without 1 variable)*100%. This is a different measure than the PCV; therefore, these percentages do not add up to the total PCV of the full model.*

Table 5 Measures of association between triage criteria, other client characteristics and regional characteristics and Ng positivity and measures of variation in Ng positivity between regions in the Netherlands, 2015, obtained from two-level logistic regression

		N (% of total)	Model 0*	Model 1**	Model 2#	Model 3†
MEASURES OF ASSOCIATION – AOR (95% CI)						
Triage criteria						
Age	<20	10,093 (10.0)		**1.00**	**1.00**	**1.00**
	20-24	54,734 (54.1)		0.47 (0.41;0.54)	0.59 (0.50;0.69)	0.59 (0.50;0.69)
	25-39	29,538 (29.2)		0.46 (0.39;0.54)	0.65 (0.55;0.77)	0.65 (0.55;0.77)
	≥40	6,716 (6.6)		0.74 (0.61;0.91)	1.07 (0.87;1.32)	1.07 (0.87;1.32)
Notified for gonorrhoea	No	80,547 (79.7)		**1.00**	**1.00**	**1.00**
	Yes	1,452 (1.4)		18.51 (15.95;21.48)	15.36 (13.15;17.94)	15.35 (13.14;17.93)
	Yes, other/unknown STI	18,755 (18.6)		1.09 (0.94;1.26)	0.78 (0.67;0.91)	0.78 (0.67;0.91)
	Unknown	327 (0.3)		0.61 (0.19;1.97)	0.63 (0.19;2.06)	0.61 (0.19;2.01)
STI-related symptoms	No	65,195 (64.5)		**1.00**	**1.00**	**1.00**
	Yes	35,886 (35.5)		2.24 (2.02;2.48)	1.91 (1.72;2.13)	1.91 (1.72;2.13)
CSW	No or unknown	95,069 (94.1)		**1.00**	**1.00**	**1.00**
	Yes	6.012 (5.9)		1.95 (1.62;2.34)	1.44 (1.11;1.86)	1.44 (1.12;1.87)
STI-endemic migrant	No	74,584 (73.8)		**1.00**	**1.00**	**1.00**
	Yes, first generation	11,374 (11.3)		2.47 (2.15;2.84)	1.88 (1.62;2.18)	1.88 (1.62;2.18)
	Yes, second generation	14,972 (14.8)		2.47 (2.18;2.79)	1.86 (1.63;2.13)	1.86 (1.63;2.12)
	Unknown	151 (0.1)		0.70 (0.09;5.73)	0.72 (0.09;5.50)	0.73 (0.10;5.53)
Partner in risk group	No	74,528 (73.7)		**1.00**	**1.00**	**1.00**
	Yes	25,383 (25.1)		1.31 (1.16;1.46)	1.24 (1.10;1.39)	1.23 (1.10;1.39)
	Unknown	1,170 (1.2)		1.64 (1.10;2.44)	1.63 (1.09;2.43)	1.63 (1.09;2.44)
Chlamydia, gonorrhoea or syphilis in past year	No	89,611 (88.7)		**1.00**	**1.00**	**1.00**
	Yes	11,470 (11.3)		1.71 (1.51;1.94)	1.49 (1.32;1.70)	1.49 (1.31;1.69)
Other individual level characteristics						
Gender	Men	35,516 (35.1)			**1.00**	**1.00**

		N (% of total)	Model 0*	Model 1**	Model 2#	Model 3†
	Women	65,565 (64.9)			0.90 (0.80;1.01)	0.90 (0.80;1.01)
Level of education^	Low or intermediate	33,184 (32.8)			**1.00**	**1.00**
	High	61,406 (60.7)			0.44 (0.39;0.49)	0.44 (0.39;0.49)
	Unknown	6,491 (6.4)			0.73 (0.59;0.89)	0.73 (0.59;0.89)
Number of partners in past 6 months	0-1	25,535 (25.3)			**1.00**	**1.00**
	2-3	41,669 (41.2)			1.09 (0.96;1.25)	1.09 (0.96;1.25)
	4-9	23,873 (23.6)			1.03 (0.88;1.21)	1.03 (0.88;1.21)
	≥10	9,331 (9.2)			1.38 (1.11;1.71)	1.38 (1.11;1.71)
	Unknown	673 (0.7)			1.27 (0.75;2.15)	1.27 (0.75;2.16)
Condom use in last sexual contact	No	73,755 (73.0)			**1.00**	**1.00**
	Yes	23,645 (23.4)			0.92 (0.81;1.04)	0.92 (0.81;1.04)
	Unknown	3,681 (3.6)			0.98 (0.75;1.27)	1.00 (0.77;1.29)
Chlamydia co-infection	No	86,009 (85.1)			**1.00**	**1.00**
	Yes	15,072 (14.9)			3.88 (3.48;4.33)	3.88 (3.48;4.33)
HIV/HBV/Syphilis infection	No	100,944 (99.9)			**1.00**	**1.00**
	Yes	137 (0.1)			1.28 (0.49;3.35)	1.30 (0.50;3.38)
Repeated consultation	No	89,578 (88.6)			**1.00**	**1.00**
	Yes	11,503 (11.4)			1.51 (1.33;1.72)	1.51 (1.33;1.72)
SES on neighbourhood level	Low	42,802 (52.3)			**1.00**	**1.00**
	Medium	21,340 (21.1)			0.77 (0.67;0.90)	0.78 (0.67;0.91)
	High	30,215 (29.9)			0.74 (0.64;0.85)	0.74 (0.64;0.86)
	Unknown	6,724 (6.7)			1.02 (0.31;3.41)	1.01 (0.30;3.39)
Degree of urbanisation$	Very high	51,942 (51.4)			**1.00**	**1.00**
	High or intermediate	30,756 (30.4)			1.01 (0.89;1.15)	1.02 (0.89;1.16)
	Low or very low	11,839 (11.7)			0.89 (0.73;1.10)	0.90 (0.73;1.11)
	Unknown	6,544 (6.5)			0.83 (0.23;2.96)	0.83 (0.23;3.00)
STI consultation in region of living	No	10,886 (10.8)			**1.00**	**1.00**
	Yes	84,973 (84.1)			0.79 (0.67;0.92)	0.79 (0.67;0.93)
	Unknown	5,222 (5.2)			0.92 (0.58;1.45)	0.94 (0.59;1.48)
Regional characteristics						
Percentage men	<median	69,194 (68.5)				**1.00**

		N (% of total)	Model 0*	Model 1**	Model 2#	Model 3†
	≥median	31,887 (31.5)				1.02 (0.75;1.38)
Percentage 15-45 years	<median	24,153 (23.9)				**1.00**
	≥median	76,928 (76.1)				1.02 (0.79;1.32)
Percentage non-Western migrants	<median	33,581 (33.2)				**1.00**
	≥median	67,500 (66.8)				1.04 (0.69;1.58)
Percentage with high degree of urbanisation	<median	31,038 (30.7)				**1.00**
	≥median	70,043 (69.3)				1.10 (0.70;1.73)
Percentage with low SES	<median	38,008 (37.6)				**1.00**
	≥median	63,073 (62.4)				1.26 (0.99;1.59)
MEASURES OF VARIATION – RANDOM INTERCEPT						
Area level variance (95% CI)			0.1497 (0.08470;0.3335)	0.09182 (0.04878;0.2328)	0.05812 (0.02917;0.1674)	0.04624 (0.02257;0.1426)
P-value			0.0016	0.0046	0.0095	0.0127
PCV			-	-38.7%	-61.2%	-69.1%
MOR			1.44	1.33	1.26	1.23
AIC			17021	15032	14157	14164
MEASURES OF VARIATION – RANDOM INTERCEPT PLUS SIGNIFICANT RANSOM SLOPE‡						
Area level variance (95% CI)						0.01914 (0.005044;0.9379)
P-value						0.1666
PCV						-87.2%
MOR						1.14
AIC						14146

**Empty model*

***Model with all triage criteria*

#Model with all triage criteria and other client characteristics

†Model with all triage criteria, other clients' characteristics and regional characteristics

‡Significant random slope for age included

^Low/intermediate level of education: everyone who did not have education at all or who enrolled in or completed elementary school, preparatory secondary vocational education or lower general secondary education; high level of education: everyone enrolled in or who completed the school of higher general secondary education, the pre-university education, university of applied sciences or university.

$Very high degree of urbanisation: those living in neighbourhoods with more than 2,500 addresses per km^2; high or intermediate level of education: those living in neighbourhoods with 1,000 to 2,500 addresses per km^2; low or very low degree of urbanisation: those living in neighbourhoods with less than 1,000 addresses per km^2.

Figure legends

Figure 1 STI clinics in Public Health Service Regions.

Legend: Blue dot is location clinic.

Figure 2 Ct positivity rate by STI clinic region in the Netherlands, 2015

Figure 3 Ng positivity by STI clinic region in the Netherlands, 2015

Figure 1 STI clinics in Public Health Service Regions. Legend: Blue dot is location clinic.

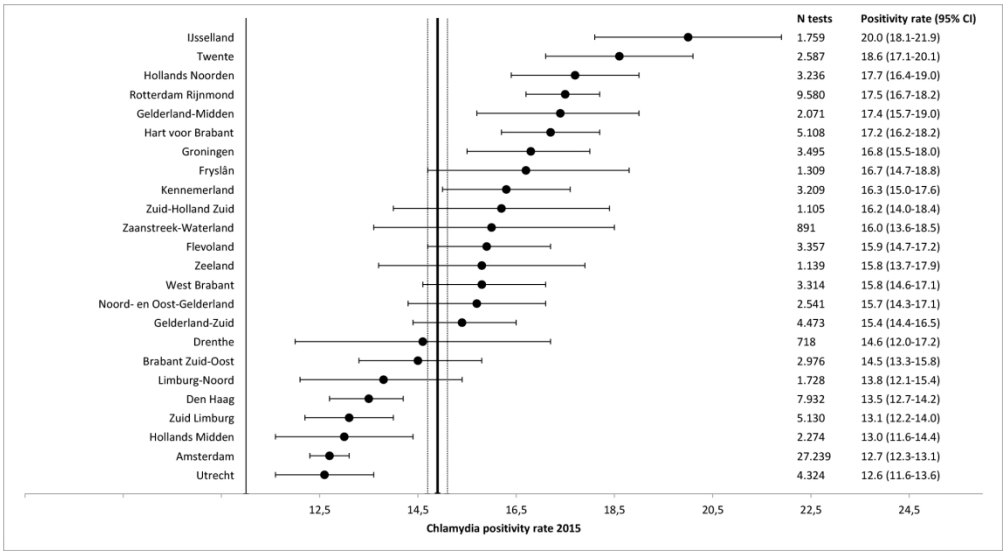

Figure 2

174x95mm (300 x 300 DPI)

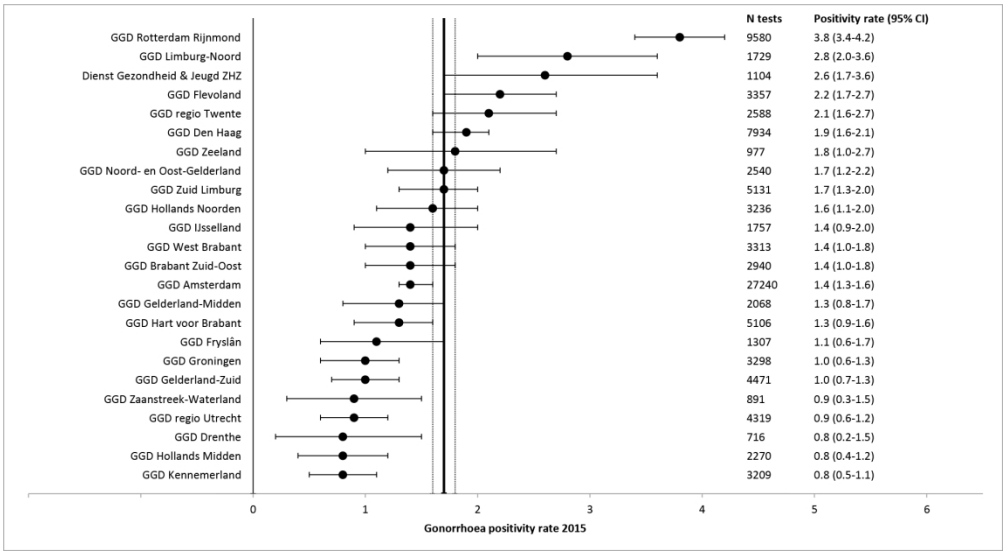

Figure 3

174x95mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1/2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-9, 32
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	7-9
Bias	9	Describe any efforts to address potential sources of bias	9
Study size	10	Explain how the study size was arrived at	7-8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10-12
		(*b*) Describe any methods used to examine subgroups and interactions	10-12
		(*c*) Explain how missing data were addressed	9, 12
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	n.a.
		(*e*) Describe any sensitivity analyses	n.a.
Results			
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	10
		(b) Give reasons for non-participation at each stage	n.a.
		(c) Consider use of a flow diagram	n.a.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	34
Outcome data	15*	Report numbers of outcome events or summary measures	12-14; 25-31
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear	12-14; 25-31

		which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	12-14; 25-31
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n.a.
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
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	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15-18
Generalisability	21	Discuss the generalisability (external validity) of the study results	18
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	20

*Give information separately for exposed and unexposed groups.

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.

BMJ Open

Regional differences in chlamydia and gonorrhoea positivity rate among heterosexual STI clinic visitors in the Netherlands: contribution of client and regional characteristics as assessed by cross-sectional surveillance data

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Regional differences in chlamydia and gonorrhoea positivity rate among heterosexual STI clinic visitors in the Netherlands: contribution of client and regional characteristics as assessed by cross-sectional surveillance data

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Chlamydia trachomatis, Neisseria gonorrhoeae, heterosexual behaviour, diagnosis, genitourinary medicine.

Word count : main text 3313

Abstract 300

ABSTRACT

Objectives

To assess to what extent triage criteria, client and regional characteristics explain regional differences in *Chlamydia trachomatis* (Ct) and *Neisseria gonorrhoeae* (Ng) positivity in STI clinics

Design

Retrospective cross-sectional study on the Dutch STI surveillance database of all 24 STI clinics

Participants

STI clinic visits of heterosexual persons in 2015 with a Ct (N=101,495) and/or Ng test (N=101,081)

Primary outcome measure

Ct and Ng positivity and 95% CI was assessed for each STI clinic. Two-level logistic regression analyses were performed to calculate the percentage change in regional variance (PCV) after adding triage criteria (model 1), other client characteristics (model 2) and regional characteristics (model 3) to the empty model. The contribution of single characteristics was determined after removing them from model 3.

Results

Ct positivity was 14.9% and ranged from 12.6% to 20.0% regionally. Ng positivity was 1.7% and ranged from 0.8% to 3.8% regionally. For Ct, the PCV was 11.7% in model 1, 32.2 % in model 2 and 59.3% in model 3. Age, notified for Ct (triage), level of education (other

characteristics) and regional degree of urbanisation (region) explained variance most. For Ng, the PCV was 38.7% in model 1, 61.2% in model 2 and 69.1% in model 3. Ethnicity (triage), partner in risk group, level of education and neighbourhood (other characteristics), and regional socioeconomic status (SES) explained variance most. A significant part of regional variance remained unexplained.

Conclusions

Regional variance was explained by differences in client characteristics, indicating that triage and self-selection influence positivity rates in the surveillance data.

Clustering of Ng in low SES regions additionally explained regional variance in Ng; targeted interventions in low SES regions may assist Ng control. Including educational level as triage criterion is recommended. Studies incorporating prevalence data are needed to assess whether regional clustering underlies unexplained regional variance.

Strengths and limitations

- The large nationwide database covering all STI clinic consultations of heterosexuals with a large set of demographic and behavioural characteristics enabled us to study a range of explanatory variables for regional Ct and Ng positivity differences.
- By using a multilevel approach, it was possible to quantify the contribution of characteristics of STI clinic visitors to the regional variance in positivity.
- Some consultation data was incomplete for some variables of interest (15%) which limited the generalisability of our results although a separate analysis did not show distortion of our results.
- As we studied only STI clinic visitors and did not include patients from GP practices our results are not generalizable to all STI patients.

INTRODUCTION

Chlamydia trachomatis (Ct) and *Neisseria gonorrhoeae* (Ng) are the most common bacterial sexually transmitted infections (STI) among heterosexual men and women in Europe.(1) In the Netherlands, Ct and Ng diagnostic tests are mainly performed by general practitioners (GP) and STI clinics at Public Health Services, resulting in an estimated total number of 400,000 STI consultations nationwide. In 2016, it was estimated that approximately 20,000 Ct infections were diagnosed at the STI clinics and 35,000 at the GP. For Ng infections these number are 6,000 and 8,000 respectively.(2) The GP is accessible to everyone in society and offers Ct and Ng testing on request. Laboratory tests at the GP are reimbursed by the insurance. However, a drawback is that the first few hundred Euros of health care costs are not deductible, and consequently STI tests are not always reimbursed. Public health oriented STI clinics have been introduced nationwide in 2006 to provide confidential and free of charge STI testing and treatment for high-risk groups. Men who have sex with men (MSM) are eligible for regular testing at STI clinics and MSM consultations are disproportionally high at STI clinics. Heterosexuals are eligible to the STI clinic testing and treatment when they fulfil at least one of the high-risk triage criteria: notified by a partner for STI, STI-related symptoms, aged below 25 years of age, having a high risk for STI (e.g. originating from or having a partner from an STI-endemic country or working as a commercial sex worker (CSW)) and/or victims of sexual violence. All STI clinic visitors are routinely tested for chlamydia and gonorrhoeae, syphilis, HIV (with the possibility to opt-out) and hepatitis B/C (on indication). Previously all visitors to the STI clinics got fully tested for Ct and Ng and for HIV and syphilis, but since 2015, those younger than 25 years are all tested for Ct and Ng and on indication for HIV and syphilis.(3) Despite national triage criteria and test policy, there are regional differences in the number of consultations and in Ct and Ng positivity among heterosexual STI clinic visitors. Explanations might be found in variations in the proportion

of certain high-risk characteristics of STI clinic visitors and in variations in regional characteristics related to positivity. Knowledge about these underlying factors might improve our understanding of the surveillance data and may possibly inform priority setting for STI clinics. In this study, we assess regional differences in Ct and Ng positivity among heterosexual STI clinic visitors between the 24 Dutch public health STI clinic regions. Our main objective is to identify explanatory factors of regional variance in Ct and Ng positivity, especially client and regional characteristics.

METHODS

Data collection

Data on STI clinic consultations and diagnoses in 2015 were obtained from the Dutch national STI surveillance database (SOAP), in which a predefined set of characteristics (including STI risk factors, diagnostic tests performed and outcomes measured) of all consultations at the 24 Dutch Public Health STI clinics is mandatory and routinely collected on a pseudonymous basis (unique numerical identifier per person which is not traceable to a person).(4) The 24 STI clinics are scattered throughout the country (See Figure 1). In the SOAP database all consultations of heterosexual STI clinic visitors in 2015 were selected (N=101,710). This database was merged with demographic data for each clients' four-digit zip code (degree of urbanisation, socioeconomic status (SES)on neighbourhood level) and for each of the 24 STI clinic regions (distribution of age, gender, non-Western origin, degree of urbanisation, SES). Demographic data on age, gender, origin and degree of urbanisation in 2015 were obtained from 'Statline' (statline.cbs.nl), an open-access platform providing freely downloadable data of Statistics Netherlands (CBS). Demographic data on SES in 2014 was requested at the Netherlands Institute for Social Research (SCP). In this merged dataset, only consultations

with a Ct test were selected for Ct analyses (101,495) and only consultations with an Ng test were selected for Ng analyses (N=101,081). For an overview of all variables see Table 1.

The data was routinely and pseudonymously collected for surveillance purposes and therefore the study was exempt from formal medical ethical approval under prevailing laws in the Netherlands.

Explanatory variables

Triage criteria

All triage criteria were included in the analyses: age, being notified by a sex partner for chlamydia (in Ct analyses), notified for gonorrhoea (in Ng analyses), STI-related symptoms, commercial sex worker (CSW), originating from an STI-endemic country, partner from risk group and Ct/Ng/syphilis infection in the previous year.(3)

The continuous variable age was categorised in age groups because of the non-linear relation between age and the log odds of the outcomes chlamydia and gonorrhoea. The categories were based on the relation between age and the outcomes on a log odds scale. We chose <20, 20-24, 25-29, 30-34, ≥35 for Ct analyses and <20, 20-24, 25-39, ≥40 years for Ng analyses. The presence of STI-related symptoms was unknown in 0.6% of consultations. We assumed that these persons did not have symptoms and were therefore included in the category 'no symptoms'. Migratory background was based on the definition of Statistics Netherlands, which is based on country of birth of the person, mother and father. STI-endemic countries include Turkey and all countries in Africa, Asia, Eastern Europe and Latin-America.(5) Categories include persons with a first generation migratory background (person born in an STI endemic country), and second generation migratory background (mother or father born in an STI endemic country) and persons originating from a non STI-endemic country.(6)

A partner from risk group was defined as having a partner originating from an STI-endemic country or in women as having a partner with MSM contacts. Missing data were incorporated in a separate category.

Other individual level client characteristics

The following other client characteristics were also included in the analyses: gender, level of education, number of sex partners in past six months, condom use in last sexual contact, infections diagnosed in the current consultation (Ng infection (for Ct analyses), Ct infection (for Ng analyses), infection with HIV/hepatitis B/syphilis), repeated consultation at the same STI clinic during 2015, living in the region of the STI clinic consulted, neighbourhood SES and degree of urbanisation. The continuous variable number of sex partners was categorised in the groups 0-1, 2-3, 4-9, and ≥10 based on the relation between number of sex partners and the outcomes on a log odds scale. CSW who had an unknown number of partners were allocated to the group ≥10. A consultation was assigned 'repeated' when the person had a previous STI clinic consultation in 2015.

Client characteristics on neighbourhood level

Degree of urbanisation of the clients residence address was obtained from CBS per four-digit zip code and categorised in three groups (1,000 to 2,500 addresses per km^2 and less or more than this range). Neighbourhood SES was obtained from SCP providing a continuous 'status score' per four-digit zip code in 2014, based on level of education, employment and income of inhabitants.(7) The status scores were transformed into tertiles, with tertile one representing the lowest SES. Missing data were incorporated in a separate category.

Regional characteristics of STI clinic regions

Regional characteristics included the percentage of men, 15-44 year olds (the age group to whom the majority of heterosexual STI clinic visitors belong), persons originating from an STI-endemic country (first and second generation), persons with a high degree of urbanisation and persons with a low SES within each of the 24 STI clinic regions. The median of these 24 percentages was used to construct dichotomized variables (percentage in region <median, percentage in region ≥median).

Outcome variables

Outcome variables were binary (positive/negative) for either Ct or Ng infection as indicated by a positive NAAT test at one or more anatomic locations. All analyses were performed at the level of visit for Ct and Ng separately.

Statistical analyses

Main analyses

For each region, the Ct and Ng positivity was calculated by dividing the number of positives by the number of tests performed. The corresponding 95% confidence interval (95%CI) was calculated with the following formula: $\hat{p} \pm z \sqrt{\frac{\hat{p}(1-\hat{p})}{n}}$,

where p=proportion with positive test, z=1.96, z-value for a 95% confidence interval, n=number of tests performed. 95% CI were depicted with forest plots.

Two-level logistic regression at client level was used to analyse explanatory factors of regional differences in positivity, with consultations (level 1) nested within regions (level 2). First, a random intercept model (model 0) without any explanatory variables was conducted to obtain baseline regional variance (V).

Besides model 0, three extended models were conducted with random intercepts and fixed slopes: model 1 included triage criteria, model 2 triage criteria and other individual level characteristics and model 3 triage criteria, other individual level characteristics and regional characteristics. For every model, the association between characteristics and outcomes were computed as adjusted odds ratio's (aOR) with 95%CI. Furthermore, the regional variance was noted and the MOR calculated. The proportional change in variance (*PCV*) was calculated to assess the extent to which the characteristics in the model explained regional variance.(8)

$$PCV_i = \frac{V_0 - V_i}{V_0},$$

where V_0 is the regional variance of model 0, V_i is regional variance of model i, and $i = 2, 3$.

To investigate which characteristics contributed most to regional variance, the percentage of contribution was computed for each variable separately.

$$\%\ contribution = \frac{V_4 - V_{3,(.)}}{V_{3,(-k)}},$$

where $V_{3,(-k)}$ is the regional variance of model 3 without characteristic k, $V_{3,(.)}$ to the variance of model 3 with all characteristics.

Cleaning and merging of datasets and calculation of positivity rates were performed with SPSS 24.0. Two-level logistic regression analyses were performed with SAS 9.4. Forest plots were produced with Microsoft Excel 2010.

Additional analyses

To examine whether the associations between client characteristics and the outcomes differ between regions, model 3 was extended with random slopes for all client characteristics. With a backward selection procedure, only statistically significant ($p<0.05$) random slopes were

included in the model. Subsequently, the PCV was calculated to investigate into what extent random slopes additionally explained regional variance. Furthermore, all analyses were repeated after missing values were imputed using multiple imputation (data not shown).

'Patient and Public Involvement'.

Patients and or public were not involved in this retrospective study based on STI surveillance data.

RESULTS

The characteristics of the study population are shown in Table 2.

Ct positivity

Ct positivity was 14.9% (95% CI 14.7% -15.1%) and ranged from 12.6% (95%CI 11.6%-13.6%) to 20.0% (95%CI 18.1%-21.9%) regionally (Figure 2). After including triage criteria, 11.7% of regional variance was explained (Table 3). In this model, almost all triage criteria were statistically significantly associated with Ct, except for CSW and partner in risk group. After including other client characteristics, 32.2% of regional variance was explained. The triage criteria CSW and partner in risk group also became independently associated with Ct: CSW and those with a partner in risk group had lower Ct positivity. Other patient characteristics associated with Ct were level of education, number of partners in past six months, condom use in last sexual contact, Ng co-infection, repeated consultation, neighbourhood SES and degree of urbanisation. After including regional characteristics, 59.3% of regional variance was explained. The only regional characteristic independently associated with Ct was degree of urbanisation: those living in highly urbanised regions had lower Ct positivity when visiting the STI clinic.

The variables age, being notified for Ct, level of education and regional degree of urbanisation contributed most to regional variance, respectively -38.2%, -15.0%, -15.4% and -24.0% (Table 4). On the other hand, STI-related symptoms, number of partners in past six months and repeated consultation increased regional variance after including them in the model, respectively +44.8%, +15.0% and +18.0%.

There were significant random slopes for age, notified, STI-related symptoms, partner in risk group, gender and repeated consultation. After adding these random slopes to model 3, the PCV increased to 100% (Table 3).

Ng positivity

Ng positivity was 1.7% (95% CI 1.6 %-1.8%) and ranged from 0.8% (95% CI 0.5%-1.1%) to 3.8% (95% CI 3.4%-4.2%) regionally (Figure 3). After including triage criteria, 38.7% of regional variance was explained. All triage criteria were statistically significantly associated with Ng (Table 5). After adding other client characteristics, 61.2% of regional variance was explained. Level of education, number of partners in past six months, Ct infection, repeated consultation, neighbourhood SES and living in region of STI clinic consultation were associated with Ng. After adding regional characteristics, 69.1% of regional variance was explained. One regional characteristic independently associated with Ng was SES: those living in "low SES regions" (defined as SES < median) had a borderline statistically significant higher Ng positivity when visiting the STI clinic.

The variables STI-endemic migrant, partner in risk group, level of education and SES on neighbourhood and regional level contributed most to regional variance, respectively -17.2%, -11.3%, -16.1%, -9.4% and -18.6% (Table 4). On the other hand, STI-related symptoms increased regional variance after including it in the model (+30.7%).

There was a significant random slope for age. After adding this random slope to model 3, the PCV increased from 69.1% to 87.2%, with no statistically significant regional variance left (Table 5).

DISCUSSION

Main findings

Our study showed moderate statistically significant regional variance in Ct and Ng positivity among Dutch heterosexual STI clinic visitors. For Ct, about one-third of regional variance was explained by differences in client characteristics (mainly age, being notified for Ct and level of education), and 69% when adding regional characteristics (mainly low degree of urbanisation). For Ng, about two-thirds of regional variance was explained by differences in client characteristics (mainly STI-endemic migrant, partner from risk group, level of education and neighbourhood SES), and 59% when adding regional characteristics (mainly low SES).

Regional variance explained by client level characteristics

In order to contribute to regional variance, a client characteristic has to fulfil the following conditions: 1) the characteristic has to be related to the outcome, 2) the proportion of the characteristic has to vary between regions and 3) the prevalence of the characteristic has to be sufficiently high. The client characteristics reducing variance most are strongly associated with Ct and Ng positivity, as reported previously.(9-16) Furthermore, the proportion of visitors with these characteristics is higher in regions with higher positivity. Consequently, correcting for these variables decreased regional variance. Some client characteristics however increased regional variance when included in the model, mainly STI-related symptoms. This indicates that the proportion of visitors with STI-related symptoms in regions

with higher positivity is lower. The reasons behind different proportions of client characteristics between regions might be related to STI clinic location by familiarity with and accessibility of STI clinics, balance between availability of consultations and requests and subsequent stringent triage application, and differences in demography of STI clinics adherence area like urbanisation and ethnicity.

The characteristics contributing most to regional variance differed between Ct and Ng, mainly because of varying associations between these characteristics and the two outcomes. For example, STI-endemic migrant, partner in risk group and neighbourhood SES were more strongly related to Ng positivity than to Ct positivity. Furthermore, although being notified for Ng was strongly associated with Ng positivity, the prevalence of Ng notifications was too low to influence regional variance.

Low/intermediate level of education was independently associated with Ct and/or Ng positivity and contributed strongly to regional variance, which confirms previous studies.(15, 17) We advise to include education as a triage criterion into the STI clinic access policy, as persons with low/intermediate education are underrepresented at STI clinics (33%) compared to 70% in the general Dutch population.(4)

Regional variance explained by regional characteristics

Regional SES explained part of regional variance in Ng positivity. Living in a low SES region increased Ng positivity independent of neighbourhood SES and level of education. This suggests that there is clustering of Ng among heterosexuals within low SES neighbourhoods and regions. Previous studies also found clustering of Ng within low SES regions and among migrant populations.(9-11, 16, 18) Neighbourhood and regional SES had no influence on regional variance in Ct positivity, as is also described previously.(19) However, regional degree of urbanisation was an important contributor to regional variance in Ct. Living in

urbanised regions decreased Ct positivity at STI clinics. This is apparently in contrast to previous Dutch studies in which a high degree of urbanisation was related to higher Ct prevalence.(17, 20) A large proportion of visitors is from urbanised areas where most STI clinics are located. Visitors from low urbanised areas visit STI clinics less frequently but those that do visit the STI clinic have a higher Ct positivity rate possibly due to effective self-selection. Additional analyses showed that high urbanised regions had lower Ct positivity rates among those notified for Ct and among those with STI-related symptoms than low urbanised regions (not shown). Possibly, inhabitants of urbanised regions are more familiar with and have easier access to STI clinics.

Unexplained regional variance

Part of regional variance remained unexplained. After including significant random slopes in model 3, all regional variance was explained. The differential association between these characteristics and infection between regions explained all remaining regional variance. This implies that Ct/Ng risk of an STI clinic visitor differs between regions, even when client characteristics are similar. This may be caused by differences in the self-selection of persons visiting the STI clinic and in prioritising practices at STI clinics between regions, but it may also reflect real regional differences. Previous studies reported strong evidence for spatial Ng clustering in the UK and the USA, independent of sociodemographic regional factors.(10, 18, 21-24) Also regional Ct clusters have been reported, although they were less strong and more diffuse compared to Ng clusters.(25) Studies incorporating prevalence data are needed to assess whether regional clustering of Ct and Ng is present in the Netherlands.

Strengths and limitations

Analysing a nationwide database with a large set of demographic and behavioural characteristics enabled us to study a range of explanatory variables. By using a multilevel

approach, it was possible to quantify the contribution of characteristics of STI clinic visitors to the regional variance in positivity. To the best of our knowledge, this has not been done before. There are also some limitations to address. First, in 15% of consultations data was incomplete for some variables of interest, varying between 0.1% and 6.7%. Missing data were incorporated as a separate group, which could have distorted results. However, missing data were imputed using multiple imputation, and results remained robust (not shown).(26) Secondly our study is limited to STI clinic visitors, and did not account for STI related consultations at GP practices. STI visitors are at high risk, partially due to self-selection and due to triage, and therefore do not reflect the Dutch population.(27, 28) As our aim was to explain regional variance within the STI clinic data and not to investigate the real positivity, this is in fact not limiting the results of our study. Third, although a large set of characteristics was available, residual confounding remains possible.

CONCLUSION AND RECOMMENDATIONS

We found statistically significant regional variance in Ct and Ng positivity among Dutch heterosexual STI clinic visitors. Regional variance was explained by differences in client characteristics, indicating that triage and self-selection influence positivity rates in the surveillance data. Client characteristics explained a larger part of regional variance in Ng than in Ct suggesting that Ng is more concentrated in high-risk persons.(29) Furthermore, our results indicate Ng clustering among heterosexuals within low SES neighbourhoods and regions; targeted interventions in low SES regions may therefore be valuable for Ng control. STI clinics might strengthen their efforts to include young lower educated heterosexuals to improve Ct control, and also increase their efforts in reaching more low educated persons from low SES and/or migrant origin in case of Ng control. Although prevalence studies are known to have methodological and practical challenges and are scarce, they are needed to assess whether real regional differences appear. Furthermore, each STI clinic should

investigate the characteristics of their clients at highest risk to develop targeted prioritising policy and ideally combine this information with data from GP patients to get a complete regional perspective.

COMPETING INTERESTS

The authors declare that they have no competing interests.

CONTRIBUTORSHIP

HG initiated the study, helped interpreting the data and drafted and revised the manuscript. LvO initiated the study, analysed and interpreted the data and drafted the manuscript. BvB and CH helped interpreting the data and revised the manuscript draft. All authors read and approved the final manuscript.

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DATA SHARING STATEMENT STI

Results of analyses on the imputed datasets are available upon request from the corresponding author after permission of the registration committee for the Dutch STI clinic database. "The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non-exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd to permit this article (if accepted) to be published in BMJ open and any other BMJPGL products and sub-licences such use and

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Competing interests statement.

The authors declare no competing interests.

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TABLES

Table 1: Overview source of data collection & level of analysis

	SOAP	Statistics Netherlands	Institute for Social Research	categories
Triage criteria				
Age Chlamydia	x	x		<20, 20-24, 25-29, 30-34, ≥35
Age Gonorrhoea				<20, 20-24, 25-39, ≥40
Notified for chlamydia / Ng	x			Yes, other/unknown STI, unknown
STI-related symptoms	x			No, yes
CSW	x			No or unknown, yes
Originating from an STI-endemic country	x	x		No, first generation, second generation, unknown
Partner in risk group	x			No, yes, unknown
Chlamydia, gonorrhoea or syphilis in past year	x			No, yes
Other client characteristics				
Gender	x	x		Men, women
Level of education ^	x			Low or intermediate, high, unknown
Number of partners in past 6 months	x			0-1, 2-3, 4-9, ≥10, unknown
Condom use in last sexual contact	x			No, yes, unknown
Ct/Ng infection	x			No, yes
HIV/HBV/Syphilis infection	x			No, yes
Repeated consultation	x			No, yes
SES on neighbourhood level (4zip code) #			x	Low, medium, high, unknown
Degree of urbanization $ (4zip code)		x		Very high, high or intermediate, low or very low, unknown
STI consultation in region of living	x			No, yes, unknown

(4zip code)				
Regional characteristics				
Percentage men		x		< median, ≥ median
Percentage 15-45 years		x		< median, ≥ median
Percentage non-Western migrants		x		< median, ≥ median
Percentage with high degree of urbanisation		x		< median, ≥ median
Percentage with low SES		x	x	< median, ≥ median

Legend : light grey: Individual level, medium grey: Neighbourhood level; dark grey Regional level ^Low/intermediate level of education: everyone who did not have education at all or who enrolled in or completed elementary school, preparatory secondary vocational education or lower general secondary education; high level of education: everyone enrolled in or who completed the school of higher general secondary education, the pre-university education, university of applied sciences or university.

 # SES was obtained from the SCP providing a continuous 'status score' per four-digit zip code of the entire Netherlands in 2014. This status score was based on level of education, employment and income of the inhabitants of the four-digit zip codes. The status scores were transformed into tertiles, with tertile one representing the lowest SES and tertile three representing the highest SES.

$Very high degree of urbanisation: those living in neighbourhoods with more than 2,500 addresses per km2; high or intermediate level of education: those living in neighbourhoods with 1,000 to 2,500 addresses per km2; low or very low degree of urbanisation: those living in neighbourhoods with less than 1,000 addresses per km2.

Table 2: Descriptive analyses of the Study population

		Male	%	Female	%	Total	%
Agegroup							
	<20	2175	6%	8054	12%	10229	10%
	20-24	17748	50%	37339	57%	55087	54%
	25-29	8245	23%	11276	17%	19521	19%
	30-34	3231	9%	3639	6%	6870	7%
	>34	4320	12%	5683	9%	10003	10%
Total		35719	100%	65991	100%	101710	100%
Notified STI		9501	27%	10749	16%	20250	20%
Notified chlamydia		*7147*	20%	*7924*	12%	*15071*	15%
Notified gonorrhoea		*630*	2%	*824*	1%	*1454*	1%
Not notified		26075	73%	54962	83%	81037	80%
Missing		143	0%	280	0%	423	0%
STI-related symptoms	Yes	12972	36%	23052	35%	36024	35%
	No	22747	64%	42939	65%	65686	65%
Originating from an STI-endemic country							
	No	24337	68%	50799	77%	75136	74%
	Yes 1st generation	4630	13%	6788	10%	11418	11%
	Yes 2nd generation	6695	19%	8307	13%	15002	15%
	missing	57	0%	97	0%	154	0%
Partner in risk group		8888	25%	16592	25%	25480	25%
Commercial sex worker		198	1%	5829	9%	6027	6%

Chlamydia, gonorrhea or syphilis in past year		3550	10%	7960	12%	11510	11%
Level of education	Low/intermediate	12583	35%	20885	32%	33468	33%
	High	21175	59%	40504	61%	61679	61%
	Unkwown	1961	5%	4602	7%	6563	6%
SES on neighbourhood level	Low	16252	45%	26862	41%	43114	42%
	Medium	7282	20%	14223	22%	21505	21%
	High	10344	29%	19968	30%	30312	30%
	Unknown	1841	5%	4938	7%	6779	7%
Degree of urbanisation	Very high	18400	52%	33781	51%	52181	51%
	High or intermediate	11335	32%	19606	30%	30941	30%
	Low or very low	4211	12%	7780	12%	11991	12%
	Unknown	1773	5%	4824	7%	6597	6%

Table 3 Measures of association between triage criteria, other client characteristics and regional characteristics and Ct positivity and measures of variation in Ct positivity between regions in the Netherlands, 2015, obtained from two-level logistic regression

		N (% of total)	Model 0*	Model 1**	Model 2#	Model 3†
MEASURES OF ASSOCIATION – AOR (95% CI)						
Triage criteria						
Age	<20	10,208 (10.1)		**1.00**	**1.00**	**1.00**
	20-24	55,508 (54.2)		0.73 (0.70;0.78)	0.78 (0.73;0.82)	0.78 (0.73;0.82)
	25-29	19,482 (19.2)		0.47 (0.44;0.51)	0.51 (0.47;0.54)	0.51 (0.47;0.54)
	30-34	6,852 (6.8)		0.38 (0.34;0.41)	0.40 (0.36;0.44)	0.40 (0.36;0.44)
	≥35	9,945 (9.8)		0.29 (0.26;0.32)	0.28 (0.25;0.31)	0.28 (0.25;0.31)
Notified for chlamydia	No	80,862 (79.7)		**1.00**	**1.00**	**1.00**
	Yes	15,507 (14.8)		4.52 (4.33;4.71)	4.52 (4.33;4.72)	4.51 (4.32;4.71)
	Yes, other/unknown STI	5,159 (5.1)		1.52 (1.39;1.65)	1.37 (1.26;1.49)	1.37 (1.26;1.49)
	Unknown	417 (0.4)		0.86 (0.61;1.21)	0.85 (0.60;1.21)	0.86 (0.60;1.21)
STI-related symptoms	No	65,555 (64.6)		**1.00**	**1.00**	**1.00**
	Yes	35,940 (35.4)		1.72 (1.66;1.79)	1.65 (1.59;1.72)	1.65 (1.59;1.72)
CSW	No or unknown	95,484 (94.1)		**1.00**	**1.00**	**1.00**
	Yes	6,011 (5.9)		0.88 (0.79;0.98)	0.66 (0.58;0.76)	0.66 (0.58;0.76)
Originating from an STI-endemic country	No	74,990 (73.9)		**1.00**	**1.00**	**1.00**
	Yes, first generation	11,376 (11.2)		1.25 (1.17;1.33)	1.13 (1.06;1.21)	1.13 (1.06;1.21)
	Yes, second generation	14,978 (14.8)		1.27 (1.21;1.34)	1.13 (1.07;1.19)	1.14 (1.08;1.20)
	Unknown	151 (0.1)		0.68 (0.37;1.24)	0.68 (0.37;1.24)	0.67 (0.37;1.23)
Partner in risk group	No	74,816 (73.7)		**1.00**	**1.00**	**1.00**
	Yes	25,408 (25.0)		0.96 (0.91;1.00)	0.90 (0.86;0.95)	0.90 (0.86;0.95)
	Unknown	1,271 (1.3)		0.84 (0.69;1.03)	0.81 (0.66;0.99)	0.80 (0.65;0.98)
Chlamydia, gonorrhoea or syphilis in past year	No	90,009 (88.7)		**1.00**	**1.00**	**1.00**
	Yes	11,486 (11.3)		1.25 (1.19;1.32)	1.14 (1.08;1.21)	1.14 (1.08;1.21)
Other client characteristics						
Gender	Men	35,628 (35.1)			**1.00**	**1.00**

		N (% of total)	Model 0*	Model 1**	Model 2#	Model 3†
	Women	65,867 (64.9)			0.97 (0.93;1.01)	0.96 (0.93;1.00)
Level of education^	Low or intermediate	33,387 (32.9)			**1.00**	**1.00**
	High	61,591 (60.7)			0.75 (0.72;0.78)	0.75 (0.72;0.78)
	Unknown	6,517 (6.4)			0.90 (0.82;0.99)	0.90 (0.82;0.99)
Number of partners in past 6 months	0-1	25,718 (25.3)			**1.00**	**1.00**
	2-3	41,843 (41.2)			1.20 (1.14;1.26)	1.20 (1.14;1.25)
	4-9	23,908 (23.6)			1.32 (1.25;1.39)	1.32 (1.25;1.39)
	≥10	9,332 (9.2)			1.48 (1.35;1.62)	1.47 (1.34;1.62)
	Unknown	694 (0.7)			1.08 (0.86;1.36)	1.09 (0.87;1.38)
Condom use in last sexual contact	No	74,028 (72.9)			**1.00**	**1.00**
	Yes	23,695 (23.3)			0.77 (0.73;0.81)	0.77 (0.73;0.81)
	Unknown	3,772 (3.7)			0.95 (0.86;1.05)	0.96 (0.86;1.06)
Gonorrhoea co-infection	No	99,796 (98.3)			**1.00**	**1.00**
	Yes	1,699 (1.7)			3.75 (3.37;4.17)	3.74 (3.36;4.17)
HIV/HBV/Syphilis infection	No	101,358 (99.9)			**1.00**	**1.00**
	Yes	137 (0.1)			1.15 (0.69;1.90)	1.13 (0.68;1.88)
Repeated consultation	No	89,948 (88.6)			**1.00**	**1.00**
	Yes	11,547 (11.4)			1.87 (1.78;1.97)	1.87 (1.77;1.97)
SES on neighbourhood level	Low	43,012 (42.4)			**1.00**	**1.00**
	Medium	21,453 (21.1)			0.97 (0.92;1.02)	0.97 (0.92;1.02)
	High	30,274 (29.8)			0.91 (0.86;0.95)	0.91 (0.87;0.95)
	Unknown	6,756 (6.7)			0.93 (0.60;1.45)	0.94 (0.61;1.47)
Degree of urbanisation$	Very high	52,094 (51.3)			**1.00**	**1.00**
	High or intermediate	30,877 (30.4)			1.09 (1.04;1.14)	1.08 (1.04;1.14)
	Low or very low	11,948 (11.8)			1.07 (1.00;1.15)	1.06 (0.99;1.14)
	Unknown	6,567 (6.5)			1.24 (0.77;1.99)	1.22 (0.76;1.96)
STI consultation in region of living	No	10,947 (10.8)			**1.00**	**1.00**
	Yes	85,306 (84.0)			0.95 (0.89;1.01)	0.95 (0.89;1.01)
	Unknown	5,242 (5.2)			0.79 (0.65;0.97)	0.79 (0.65;0.97)
Regional characteristics						
Percentage men	<median	69,367 (68.3)				**1.00**

		N (% of total)	Model 0*	Model 1**	Model 2#	Model 3†
	≥median	32,128 (31.7)				0.99 (0.88;1.11)
Percentage 15-45 years	<median	24,320 (24.0)				**1.00**
	≥median	77,175 (76.0)				1.04 (0.94;1.14)
Percentage non-Western migrants	<median	33,950 (33.4)				**1.00**
	≥median	67,545 (66.6)				1.11 (0.94;1.31)
Percentage with high degree of urbanisation	<median	31,407 (30.9)				**1.00**
	≥median	70,088 (69.1)				0.79 (0.66;0.94)
Percentage with low SES	<median	38,057 (37.5)				**1.00**
	≥median	63,438 (62.5)				1.01 (0.92;1.11)
MEASURES OF VARIATION – RANDOM INTERCEPT ONLY						
Area level variance (95% CI)			0.01919 (0.0111;0.04094)	0.01695 (0.00968;0.03704)	0.01301 (0.007313;0.02933)	0.007810 (0.004275;0.01859)
P-value			0.0010	0.0013	0.0018	0.0029
PCV			-	-11.7%	-32.2%	-59.3%
AIC			85118	78623	77018	77018
MEASURES OF VARIATION – RANDOM INTERCEPT AND SIGNIFICANT RANDOM SLOPES‡						
Area level variance (95% CI)						0
P-value						-
PCV						-100%
AIC						76842

**Empty model*

***Model with all triage criteria*

#Model with all triage criteria and other patient characteristics

†Model with all triage criteria, individual level characteristics and regional characteristics

‡Significant random slopes included: age, gender, notified, STI-related symptoms, partner in risk group and repeated consultation.

^Low/intermediate level of education: everyone who did not have education at all or who enrolled in or completed elementary school, preparatory secondary vocational education or lower general secondary education; high level of education: everyone enrolled in or who completed the school of higher general secondary education, the pre-university education, university of applied sciences or university.

$Very high degree of urbanisation: those living in neighbourhoods with more than 2,500 addresses per km^2; high or intermediate level of education: those living in neighbourhoods with 1,000 to 2,500 addresses per km^2; low or very low degree of urbanisation: those living in neighbourhoods with less than 1,000 addresses per km^2.

Table 4 Contribution of triage criteria, other client characteristics and regional characteristics to the regional variation in Ct and Ng positivity in the Netherlands, 2015, obtained from two-level logistic regression

	% contribution of variable to variance*	
	Ct	**Ng**
TRIAGE CRITERIA		
Age	-38.2%	-4.3%
Notified for chlamydia/gonorrhoea	-15.0%	+3.1%
STI-related symptoms	+44.8%	+30.7%
CSW	+1.4%	+4.2%
STI-endemic migrant	+2.6%	-17.2%
Partner in risk group	+8.2%	-11.3%
Chlamydia, gonorrhoea or syphilis in past year	+0.8%	-3.0%
OTHER CLIENT CHARACTERISTICS		
Gender	-0.4%	-2.0%
Level of education	-15.4%	-16.1%
Number of partners in past 6 months	+15.0%	+2.6%
Condom use in last sexual contact	+2.2%	-1.0%
Gonorrhoea/chlamydia infection	-5.0%	-0.1%
HIV/HBV/Syphilis infection	+1.1%	-0.1%
Repeated consultation	+18.0%	+2.1%
SES on neighbourhood level	-2.9%	-9.4%
Degree of urbanisation	+1.4%	1.1%

STI consultation in region of living	-1.1%	-1.4%
REGIONAL CHARACTERISTICS		
Percentage men	0.0%	-0.2%
Percentage between 15-45 years	-1.1%	+0.2%
Percentage non-Western migrants	-5.8%	-0.5%
Percentage with high degree of urbanisation	-24.0%	-1.5%
Percentage with low SES	+1.2%	-18.6%

**Percentage contribution of variable to regional variance. Separate variables are deleted from full model and variance is compared to variance in full model. Percentage contribution=-((variance full model without 1 variable – variance full model)/variance full model without 1 variable)*100%. This is a different measure than the PCV; therefore, these percentages do not add up to the total PCV of the full model.*

Table 5 Measures of association between triage criteria, other client characteristics and regional characteristics and Ng positivity and measures of variation in Ng positivity between regions in the Netherlands, 2015, obtained from two-level logistic regression

		N (% of total)	Model 0*	Model 1**	Model 2#	Model 3†
MEASURES OF ASSOCIATION – AOR (95% CI)						
Triage criteria						
Age	<20	10,093 (10.0)		**1.00**	**1.00**	**1.00**
	20-24	54,734 (54.1)		0.47 (0.41;0.54)	0.59 (0.50;0.69)	0.59 (0.50;0.69)
	25-39	29,538 (29.2)		0.46 (0.39;0.54)	0.65 (0.55;0.77)	0.65 (0.55;0.77)
	≥40	6,716 (6.6)		0.74 (0.61;0.91)	1.07 (0.87;1.32)	1.07 (0.87;1.32)
Notified for gonorrhoea	No	80,547 (79.7)		**1.00**	**1.00**	**1.00**
	Yes	1,452 (1.4)		18.51 (15.95;21.48)	15.36 (13.15;17.94)	15.35 (13.14;17.93)
	Yes, other/unknown STI	18,755 (18.6)		1.09 (0.94;1.26)	0.78 (0.67;0.91)	0.78 (0.67;0.91)

		N (% of total)	Model 0*	Model 1**	Model 2#	Model 3†
	Unknown	327 (0.3)		0.61 (0.19;1.97)	0.63 (0.19;2.06)	0.61 (0.19;2.01)
STI-related symptoms	No	65,195 (64.5)		**1.00**	**1.00**	**1.00**
	Yes	35,886 (35.5)		2.24 (2.02;2.48)	1.91 (1.72;2.13)	1.91 (1.72;2.13)
CSW	No or unknown	95,069 (94.1)		**1.00**	**1.00**	**1.00**
	Yes	6.012 (5.9)		1.95 (1.62;2.34)	1.44 (1.11;1.86)	1.44 (1.12;1.87)
STI-endemic migrant	No	74,584 (73.8)		**1.00**	**1.00**	**1.00**
	Yes, first generation	11,374 (11.3)		2.47 (2.15;2.84)	1.88 (1.62;2.18)	1.88 (1.62;2.18)
	Yes, second generation	14,972 (14.8)		2.47 (2.18;2.79)	1.86 (1.63;2.13)	1.86 (1.63;2.12)
	Unknown	151 (0.1)		0.70 (0.09;5.73)	0.72 (0.09;5.50)	0.73 (0.10;5.53)
Partner in risk group	No	74,528 (73.7)		**1.00**	**1.00**	**1.00**
	Yes	25,383 (25.1)		1.31 (1.16;1.46)	1.24 (1.10;1.39)	1.23 (1.10;1.39)
	Unknown	1,170 (1.2)		1.64 (1.10;2.44)	1.63 (1.09;2.43)	1.63 (1.09;2.44)
Chlamydia, gonorrhoea or syphilis in past year	No	89,611 (88.7)		**1.00**	**1.00**	**1.00**
	Yes	11,470 (11.3)		1.71 (1.51;1.94)	1.49 (1.32;1.70)	1.49 (1.31;1.69)
Other individual level characteristics						
Gender	Men	35,516 (35.1)			**1.00**	**1.00**
	Women	65,565 (64.9)			0.90 (0.80;1.01)	0.90 (0.80;1.01)
Level of education^	Low or intermediate	33,184 (32.8)			**1.00**	**1.00**
	High	61,406 (60.7)			0.44 (0.39;0.49)	0.44 (0.39;0.49)
	Unknown	6,491 (6.4)			0.73 (0.59;0.89)	0.73 (0.59;0.89)
Number of partners in past 6 months	0-1	25,535 (25.3)			**1.00**	**1.00**
	2-3	41,669 (41.2)			1.09 (0.96;1.25)	1.09 (0.96;1.25)
	4-9	23,873 (23.6)			1.03 (0.88;1.21)	1.03 (0.88;1.21)
	≥10	9,331 (9.2)			1.38 (1.11;1.71)	1.38 (1.11;1.71)
	Unknown	673 (0.7)			1.27 (0.75;2.15)	1.27 (0.75;2.16)
Condom use in last sexual contact	No	73,755 (73.0)			**1.00**	**1.00**
	Yes	23,645 (23.4)			0.92 (0.81;1.04)	0.92 (0.81;1.04)

		N (% of total)	Model 0*	Model 1**	Model 2#	Model 3†
	Unknown	3,681 (3.6)			0.98 (0.75;1.27)	1.00 (0.77;1.29)
Chlamydia co-infection	No	86,009 (85.1)			**1.00**	**1.00**
	Yes	15,072 (14.9)			3.88 (3.48;4.33)	3.88 (3.48;4.33)
HIV/HBV/Syphilis infection	No	100,944 (99.9)			**1.00**	**1.00**
	Yes	137 (0.1)			1.28 (0.49;3.35)	1.30 (0.50;3.38)
Repeated consultation	No	89,578 (88.6)			**1.00**	**1.00**
	Yes	11,503 (11.4)			1.51 (1.33;1.72)	1.51 (1.33;1.72)
SES on neighbourhood level	Low	42,802 (52.3)			**1.00**	**1.00**
	Medium	21,340 (21.1)			0.77 (0.67;0.90)	0.78 (0.67;0.91)
	High	30,215 (29.9)			0.74 (0.64;0.85)	0.74 (0.64;0.86)
	Unknown	6,724 (6.7)			1.02 (0.31;3.41)	1.01 (0.30;3.39)
Degree of urbanisation$	Very high	51,942 (51.4)			**1.00**	**1.00**
	High or intermediate	30,756 (30.4)			1.01 (0.89;1.15)	1.02 (0.89;1.16)
	Low or very low	11,839 (11.7)			0.89 (0.73;1.10)	0.90 (0.73;1.11)
	Unknown	6,544 (6.5)			0.83 (0.23;2.96)	0.83 (0.23;3.00)
STI consultation in region of living	No	10,886 (10.8)			**1.00**	**1.00**
	Yes	84,973 (84.1)			0.79 (0.67;0.92)	0.79 (0.67;0.93)
	Unknown	5,222 (5.2)			0.92 (0.58;1.45)	0.94 (0.59;1.48)
Regional characteristics						
Percentage men	<median	69,194 (68.5)				**1.00**
	≥median	31,887 (31.5)				1.02 (0.75;1.38)
Percentage 15-45 years	<median	24,153 (23.9)				**1.00**
	≥median	76,928 (76.1)				1.02 (0.79;1.32)
Percentage non-Western migrants	<median	33,581 (33.2)				**1.00**
	≥median	67,500 (66.8)				1.04 (0.69;1.58)
Percentage with high degree of urbanisation	<median	31,038 (30.7)				**1.00**
	≥median	70,043 (69.3)				1.10 (0.70;1.73)

		N (% of total)	Model 0*	Model 1**	Model 2#	Model 3†
Percentage with low SES	<median	38,008 (37.6)				**1.00**
	≥median	63,073 (62.4)				1.26 (0.99;1.59)
MEASURES OF VARIATION – RANDOM INTERCEPT						
Area level variance (95% CI)			0.1497 (0.08470;0.3335)	0.09182 (0.04878;0.2328)	0.05812 (0.02917;0.1674)	0.04624 (0.02257;0.1426)
P-value			0.0016	0.0046	0.0095	0.0127
PCV			-	-38.7%	-61.2%	-69.1%
AIC			17021	15032	14157	14164
MEASURES OF VARIATION – RANDOM INTERCEPT PLUS SIGNIFICANT RANSOM SLOPE‡						
Area level variance (95% CI)						0.01914 (0.005044;0.9379)
P-value						0.1666
PCV						-87.2%
AIC						14146

**Empty model*

***Model with all triage criteria*

#Model with all triage criteria and other client characteristics

†Model with all triage criteria, other clients' characteristics and regional characteristics

‡Significant random slope for age included

^Low/intermediate level of education: everyone who did not have education at all or who enrolled in or completed elementary school, preparatory secondary vocational education or lower general secondary education; high level of education: everyone enrolled in or who completed the school of higher general secondary education, the pre-university education, university of applied sciences or university.

$Very high degree of urbanisation: those living in neighbourhoods with more than 2,500 addresses per km^2; high or intermediate level of education: those living in neighbourhoods with 1,000 to 2,500 addresses per km^2; low or very low degree of urbanisation: those living in neighbourhoods with less than 1,000 addresses per km^2.

Figure legends

Figure 1 STI clinics in Public Health Service Regions.

Legend: Blue dot is location clinic.

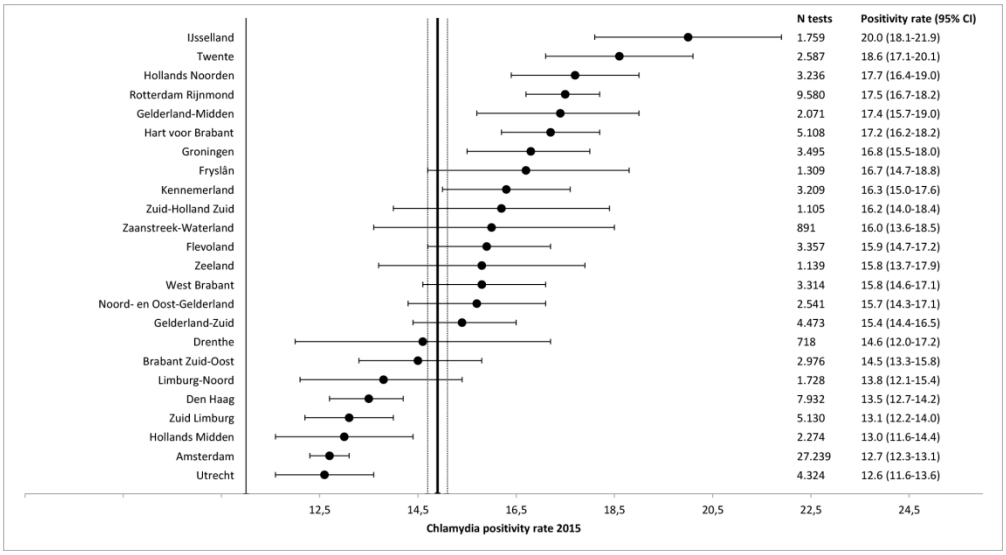
Figure 2 Ct positivity rate by STI clinic region in the Netherlands, 2015

Legend: Black dot Ct positivity rate, line depicts lower and upper limit of 95% CI. Total Ct positivity rate is depicted as vertical line, and 95% CI lines on the left and right.

Figure 3 Ng positivity by STI clinic region in the Netherlands, 2015

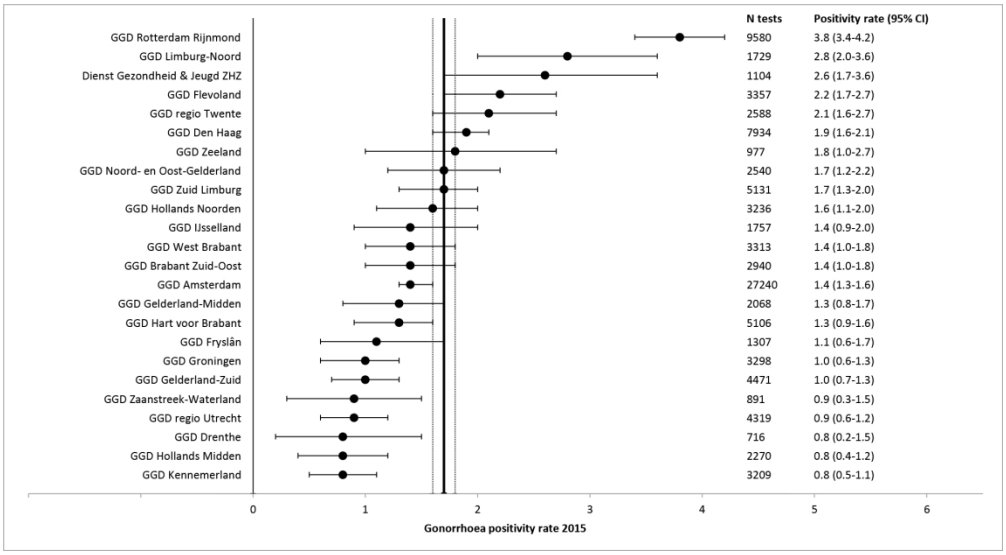
Legend: Black dot Ng positivity rate, line depicts lower and upper limit of 95% CI. Total Ng positivity rate is depicted as vertical line, and 95% CI lines on the left and right.

Figure 1 STI clinics in Public Health Service Regions. Legend: Blue dot is location clinic.



Black dot Ct positivity rate, line depicts lower and upper limit of 95% CI. Total Ct positivity rate is depicted as vertical line, and 95% CI lines on the left and right.

174x95mm (300 x 300 DPI)



Black dot Ng positivity rate, line depicts lower and upper limit of 95% CI. Total Ng positivity rate is depicted as vertical line, and 95% CI lines on the left and right.

174x95mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1/2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-9, 27
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	7-9
Bias	9	Describe any efforts to address potential sources of bias	9
Study size	10	Explain how the study size was arrived at	7-8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10-12
		(*b*) Describe any methods used to examine subgroups and interactions	10-12
		(*c*) Explain how missing data were addressed	9, 12
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	n.a.
		(*e*) Describe any sensitivity analyses	n.a.
Results			
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	10
		(b) Give reasons for non-participation at each stage	n.a.
		(c) Consider use of a flow diagram	n.a.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	27,28
Outcome data	15*	Report numbers of outcome events or summary measures	12-14; 29-36
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear	12-14; 29-36

		which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	12-14; 29-36
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n.a.
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
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	16-17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	17
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	20

*Give information separately for exposed and unexposed groups.

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.