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Regional differences in chlamydia and gonorrhoeae 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 in sexually transmitted infection (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 of this study

- The large nationwide database covering all sexually transmitted infection (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 *Chlamydia trachomatis* and *Neisseria gonorrhoeae* 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 were 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 general practitioners, our results are not generalisable to all patients with STI.

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 6000 and 8000, 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 healthcare 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, having a high risk for STI (eg, 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 (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

Figure 1 Sexually transmitted infection clinics in public health service regions. Blue dot is location clinic.

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 (n=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 were 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, 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.

Table 1 Overview source of data collection and 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 CT/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 (four-digit zip code)†			x	Low, medium, high, unknown
Degree of urbanisation‡ (four-digit zip code)		x		Very high, high or intermediate, low or very low, unknown
STI consultation in region of living (four-digit zip 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

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 >2500 addresses per km^2; high or intermediate level of education: those living in neighbourhoods with 1000–2500 addresses per km^2; low or very low degree of urbanisation: those living in neighbourhoods with <1000 addresses per km^2.
Ct, *Chlamydia trachomatis*; Ng, *Neisseria gonorrhoeae*.

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

Table 2 Descriptive analyses of the study population

	Male	%	Female	%	Total	%
Age group (years)						
<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 first generation	4630	13	6788	10	11418	11
Yes second 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, gonorrhoea 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

SES, socioeconomic status; STI, sexually transmitted infection.

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 6 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/

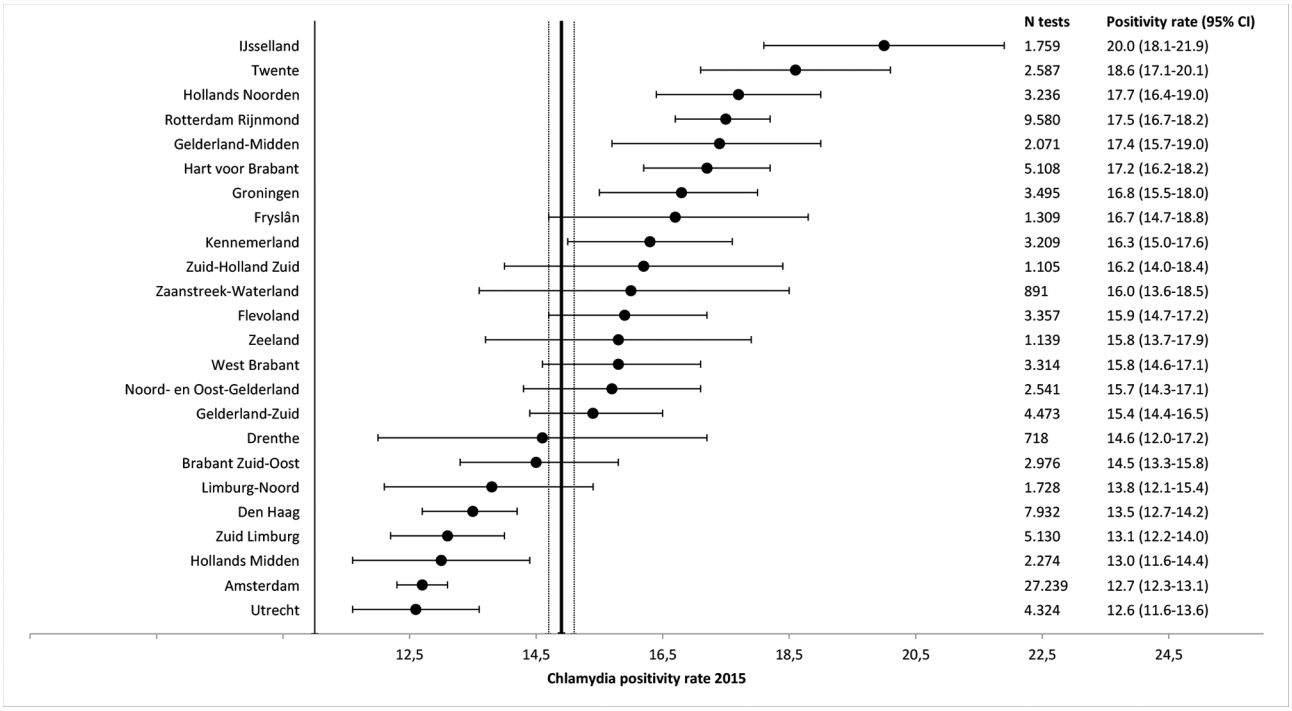

Figure 2 *Chlamydia trachomatis* (Ct) positivity rate by sexually transmitted infection clinic region in the Netherlands, 2015. Black dot Ct positivity rate, line depicts lower and upper limit of 95% CI. Total Ct positivity rate is depicted as vertical line, and 95% CI lines on the left and right.

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 (1000–2500 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, aged 15–44 years (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 dichotomised 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 Nucleic Acid Amplification Test (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% CI was calculated with the following formula: $\hat{p} \pm z\sqrt{\frac{\hat{p}(1-p)}{n}}$, where p=proportion with positive test, z=1.96, z-value for a 95% CI, 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

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—adjusted OR (95% CI)						
Triage criteria						
Age (years)	<20	10208 (10.1)		**1.00**	**1.00**	**1.00**
	20–24	55508 (54.2)		0.73 (0.70 to 0.78)	0.78 (0.73 to 0.82)	0.78 (0.73 to 0.82)
	25–29	19482 (19.2)		0.47 (0.44 to 0.51)	0.51 (0.47 to 0.54)	0.51 (0.47 to 0.54)
	30–34	6852 (6.8)		0.38 (0.34 to 0.41)	0.40 (0.36 to 0.44)	0.40 (0.36 to 0.44)
	≥35	9945 (9.8)		0.29 (0.26 to 0.32)	0.28 (0.25 to 0.31)	0.28 (0.25 to 0.31)
Notified for chlamydia	No	80862 (79.7)		**1.00**	**1.00**	**1.00**
	Yes	15507 (14.8)		4.52 (4.33 to 4.71)	4.52 (4.33 to 4.72)	4.51 (4.32 to 4.71)
	Yes, other/unknown STI	5159 (5.1)		1.52 (1.39 to 1.65)	1.37 (1.26 to 1.49)	1.37 (1.26 to 1.49)
	Unknown	417 (0.4)		0.86 (0.61 to 1.21)	0.85 (0.60 to 1.21)	0.86 (0.60 to 1.21)
STI-related symptoms	No	65555 (64.6)		**1.00**	**1.00**	**1.00**
	Yes	35940 (35.4)		1.72 (1.66 to 1.79)	1.65 (1.59 to 1.72)	1.65 (1.59 to 1.72)
CSW	No or unknown	95484 (94.1)		**1.00**	**1.00**	**1.00**
	Yes	6011 (5.9)		0.88 (0.79 to 0.98)	0.66 (0.58 to 0.76)	0.66 (0.58 to 0.76)
Originating from an STI-endemic country	No	74990 (73.9)		**1.00**	**1.00**	**1.00**
	Yes, first generation	11376 (11.2)		1.25 (1.17 to 1.33)	1.13 (1.06 to 1.21)	1.13 (1.06 to 1.21)
	Yes, second generation	14978 (14.8)		1.27 (1.21 to 1.34)	1.13 (1.07 to 1.19)	1.14 (1.08 to 1.20)
	Unknown	151 (0.1)		0.68 (0.37 to 1.24)	0.68 (0.37 to 1.24)	0.67 (0.37 to 1.23)
Partner in risk group	No	74816 (73.7)		**1.00**	**1.00**	**1.00**
	Yes	25408 (25.0)		0.96 (0.91 to 1.00)	0.90 (0.86 to 0.95)	0.90 (0.86 to 0.95)
	Unknown	1271 (1.3)		0.84 (0.69 to 1.03)	0.81 (0.66 to 0.99)	0.80 (0.65 to 0.98)
Chlamydia, gonorrhoea or syphilis in past year	No	90009 (88.7)		**1.00**	**1.00**	**1.00**
	Yes	11486 (11.3)		1.25 (1.19 to 1.32)	1.14 (1.08 to 1.21)	1.14 (1.08 to 1.21)
Other client characteristics						
Gender	Men	35628 (35.1)			**1.00**	**1.00**
	Women	65867 (64.9)			0.97 (0.93 to 1.01)	0.96 (0.93 to 1.00)
Level of education¶	Low or intermediate	33387 (32.9)			**1.00**	**1.00**
	High	61591 (60.7)			0.75 (0.72 to 0.78)	0.75 (0.72 to 0.78)
	Unknown	6517 (6.4)			0.90 (0.82 to 0.99)	0.90 (0.82 to 0.99)

Continued

Table 3 Continued

		N (% of total)	Model 0*	Model 1†	Model 2‡	Model 3§
Number of partners in past 6 months	0–1	25718 (25.3)			**1.00**	**1.00**
	2–3	41843 (41.2)			1.20 (1.14 to 1.26)	1.20 (1.14 to 1.25)
	4–9	23908 (23.6)			1.32 (1.25 to 1.39)	1.32 (1.25 to 1.39)
	≥10	9332 (9.2)			1.48 (1.35 to 1.62)	1.47 (1.34 to 1.62)
	Unknown	694 (0.7)			1.08 (0.86 to 1.36)	1.09 (0.87 to 1.38)
Condom use in last sexual contact	No	74028 (72.9)			**1.00**	**1.00**
	Yes	23695 (23.3)			0.77 (0.73 to 0.81)	0.77 (0.73 to 0.81)
	Unknown	3772 (3.7)			0.95 (0.86 to 1.05)	0.96 (0.86 to 1.06)
Gonorrhoea co-infection	No	99796 (98.3)			**1.00**	**1.00**
	Yes	1699 (1.7)			3.75 (3.37 to 4.17)	3.74 (3.36 to 4.17)
HIV/HBV/syphilis infection	No	101358 (99.9)			**1.00**	**1.00**
	Yes	137 (0.1)			1.15 (0.69 to 1.90)	1.13 (0.68 to 1.88)
Repeated consultation	No	89948 (88.6)			**1.00**	**1.00**
	Yes	11547 (11.4)			1.87 (1.78 to 1.97)	1.87 (1.77 to 1.97)
SES on neighbourhood level	Low	43012 (42.4)			**1.00**	**1.00**
	Medium	21453 (21.1)			0.97 (0.92 to 1.02)	0.97 (0.92 to 1.02)
	High	30274 (29.8)			0.91 (0.86 to 0.95)	0.91 (0.87 to 0.95)
	Unknown	6756 (6.7)			0.93 (0.60 to 1.45)	0.94 (0.61 to 1.47)
Degree of urbanisation**	Very high	52094 (51.3)			**1.00**	**1.00**
	High or intermediate	30877 (30.4)			1.09 (1.04 to 1.14)	1.08 (1.04 to 1.14)
	Low or very low	11948 (11.8)			1.07 (1.00 to 1.15)	1.06 (0.99 to 1.14)
	Unknown	6567 (6.5)			1.24 (0.77 to 1.99)	1.22 (0.76 to 1.96)
STI consultation in region of living	No	10947 (10.8)			**1.00**	**1.00**
	Yes	85306 (84.0)			0.95 (0.89 to 1.01)	0.95 (0.89 to 1.01)
	Unknown	5242 (5.2)			0.79 (0.65 to 0.97)	0.79 (0.65 to 0.97)
Regional characteristics						
Percentage men	<median	69367 (68.3)				**1.00**
	≥median	32128 (31.7)				0.99 (0.88 to 1.11)
Percentage 15–45 years	<median	24320 (24.0)				**1.00**
	≥median	77175 (76.0)				1.04 (0.94 to 1.14)
Percentage non-Western migrants	<median	33950 (33.4)				**1.00**
	≥median	67545 (66.6)				1.11 (0.94 to 1.31)
Percentage with high degree of urbanisation	<median	31407 (30.9)				**1.00**
	≥median	70088 (69.1)				0.79 (0.66 to 0.94)

Continued

Table 3 Continued

		N (% of total)	Model 0*	Model 1†	Model 2‡	Model 3§
Percentage with low SES	<median	38057 (37.5)				**1.00**
	≥median	63438 (62.5)				1.01 (0.92 to 1.11)
Measures of variation—random intercept only						
Area level variance (95% CI)			0.01919 (0.0111 to 0.04094)	0.01695 (0.00968 to 0.03704)	0.01301 (0.007313 to 0.02933)	0.007810 (0.004275 to 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.
¶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 preuniversity education, university of applied sciences or university.
**Very high degree of urbanisation: those living in neighbourhoods with >2500 addresses per km^2; high or intermediate level of education: those living in neighbourhoods with 1000–2500 addresses per km^2; low or very low degree of urbanisation: those living in neighbourhoods with <1000 addresses per km^2.
††Significant random slopes included: age, gender, notified, STI-related symptoms, partner in risk group and repeated consultation.
AIC, Akaike Information Criterion; Ct, *Chlamydia trachomatis*; CSW, commercial sex worker; PCV, proportional change in variance; SES, socioeconomic status; STI, sexually transmitted infection.
Reference values for the analysis are shown in bold.

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 and 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 with variance in full model. Percentage contribution=−((variance full model without one variable−variance full model)/variance full model without one 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.
Ct, *Chlamydia trachomatis*; CSW, commercial sex worker; Ng, *Neisseria gonorrhoeae*; PCV, proportional change in variance; SES, socioeconomic status; STI, sexually transmitted infection.

regional characteristics. For every model, the association between characteristics and outcomes were computed as adjusted ORs with 95% CI. Furthermore, the regional variance was noted. 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 V.24.0. Two-level logistic regression analyses were performed with SAS V.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% to 15.1%) and ranged from 12.6% (95% CI 11.6% to 13.6%) to 20.0% (95% CI 18.1% to 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 6 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.

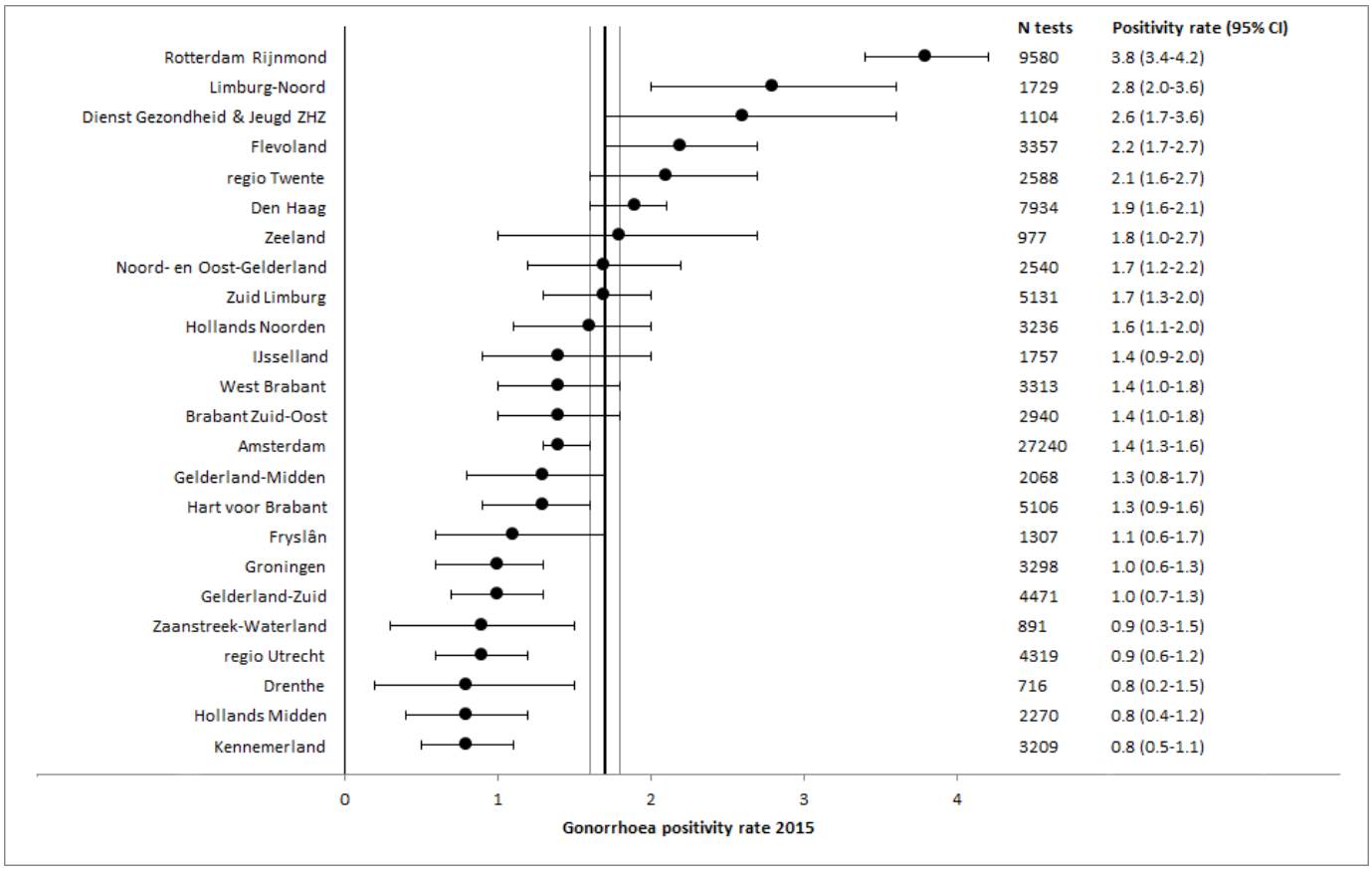

Figure 3 *Neisseria gonorrhoeae* (Ng) positivity by sexually transmitted infection clinic region in the Netherlands, 2015. Black dot Ng positivity rate, line depicts lower and upper limit of 95% CI. Total Ng positivity rate is depicted as vertical line, and 95% CI lines on the left and right.

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 6 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% to 1.8%) and ranged from 0.8% (95% CI 0.5% to 1.1%) to 3.8% (95% CI 3.4% to 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 6 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

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—adjusted OR (95% CI)						
Triage criteria						
Age (years)	<20	10 093 (10.0)		**1.00**	**1.00**	**1.00**
	20–24	54 734 (54.1)		0.47 (0.41 to 0.54)	0.59 (0.50 to 0.69)	0.59 (0.50 to 0.69)
	25–39	29 538 (29.2)		0.46 (0.39 to 0.54)	0.65 (0.55 to 0.77)	0.65 (0.55 to 0.77)
	≥40	6716 (6.6)		0.74 (0.61 to 0.91)	1.07 (0.87 to 1.32)	1.07 (0.87 to 1.32)
Notified for gonorrhoea	No	80 547 (79.7)		**1.00**	**1.00**	**1.00**
	Yes	1452 (1.4)		18.51 (15.95 to 21.48)	15.36 (13.15 to 17.94)	15.35 (13.14 to 17.93)
	Yes, other/unknown STI	18 755 (18.6)		1.09 (0.94 to 1.26)	0.78 (0.67 to 0.91)	0.78 (0.67 to 0.91)
	Unknown	327 (0.3)		0.61 (0.19 to 1.97)	0.63 (0.19 to 2.06)	0.61 (0.19 to 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 to 2.48)	1.91 (1.72 to 2.13)	1.91 (1.72 to 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 to 2.34)	1.44 (1.11 to 1.86)	1.44 (1.12 to 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 to 2.84)	1.88 (1.62 to 2.18)	1.88 (1.62 to 2.18)
	Yes, second generation	14 972 (14.8)		2.47 (2.18 to 2.79)	1.86 (1.63 to 2.13)	1.86 (1.63 to 2.12)
	Unknown	151 (0.1)		0.70 (0.09 to 5.73)	0.72 (0.09 to 5.50)	0.73 (0.10 to 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 to 1.46)	1.24 (1.10 to 1.39)	1.23 (1.10 to 1.39)
	Unknown	1170 (1.2)		1.64 (1.10 to 2.44)	1.63 (1.09 to 2.43)	1.63 (1.09 to 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 to 1.94)	1.49 (1.32 to 1.70)	1.49 (1.31 to 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 to 1.01)	0.90 (0.80 to 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 to 0.49)	0.44 (0.39 to 0.49)
	Unknown	6491 (6.4)			0.73 (0.59 to 0.89)	0.73 (0.59 to 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 to 1.25)	1.09 (0.96 to 1.25)
	4–9	23 873 (23.6)			1.03 (0.88 to 1.21)	1.03 (0.88 to 1.21)
	≥10	9331 (9.2)			1.38 (1.11 to 1.71)	1.38 (1.11 to 1.71)
	Unknown	673 (0.7)			1.27 (0.75 to 2.15)	1.27 (0.75 to 2.16)

Continued

Table 5 Continued

		N (% of total)	Model 0*	Model 1†	Model 2‡	Model 3§
Condom use in last sexual contact	No	73 755 (73.0)			**1.00**	**1.00**
	Yes	23 645 (23.4)			0.92 (0.81 to 1.04)	0.92 (0.81 to 1.04)
	Unknown	3681 (3.6)			0.98 (0.75 to 1.27)	1.00 (0.77 to 1.29)
Chlamydia co-infection	No	86 009 (85.1)			**1.00**	**1.00**
	Yes	15 072 (14.9)			3.88 (3.48 to 4.33)	3.88 (3.48 to 4.33)
HIV/HBV/syphilis infection	No	100 944 (99.9)			**1.00**	**1.00**
	Yes	137 (0.1)			1.28 (0.49 to 3.35)	1.30 (0.50 to 3.38)
Repeated consultation	No	89 578 (88.6)			**1.00**	**1.00**
	Yes	11 503 (11.4)			1.51 (1.33 to 1.72)	1.51 (1.33 to 1.72)
SES on neighbourhood level	Low	42 802 (52.3)			**1.00**	**1.00**
	Medium	21 340 (21.1)			0.77 (0.67 to 0.90)	0.78 (0.67 to 0.91)
	High	30 215 (29.9)			0.74 (0.64 to 0.85)	0.74 (0.64 to 0.86)
	Unknown	6724 (6.7)			1.02 (0.31 to 3.41)	1.01 (0.30 to 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 to 1.15)	1.02 (0.89 to 1.16)
	Low or very low	11 839 (11.7)			0.89 (0.73 to 1.10)	0.90 (0.73 to 1.11)
	Unknown	6544 (6.5)			0.83 (0.23 to 2.96)	0.83 (0.23 to 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 to 0.92)	0.79 (0.67 to 0.93)
	Unknown	5222 (5.2)			0.92 (0.58 to 1.45)	0.94 (0.59 to 1.48)
Regional characteristics						
Percentage men	<median	69 194 (68.5)				**1.00**
	≥median	31 887 (31.5)				1.02 (0.75 to 1.38)
Percentage 15–45 years	<median	24 153 (23.9)				**1.00**
	≥median	76 928 (76.1)				1.02 (0.79 to 1.32)
Percentage non-Western migrants	<median	33 581 (33.2)				**1.00**
	≥median	67 500 (66.8)				1.04 (0.69 to 1.58)
Percentage with high degree of urbanisation	<median	31 038 (30.7)				**1.00**
	≥median	70 043 (69.3)				1.10 (0.70 to 1.73)
Percentage with low SES	<median	38 008 (37.6)				**1.00**
	≥median	63 073 (62.4)				1.26 (0.99 to 1.59)
Measures of variation—random intercept						
Area level variance (95% CI)			0.1497 (0.08470 to 0.3335)	0.09182 (0.04878 to 0.2328)	0.05812 (0.02917 to 0.1674)	0.04624 (0.02257 to 0.1426)
P value			0.0016	0.0046	0.0095	0.0127
PCV			–	–38.7%	–61.2%	–69.1%

Continued

Table 5 Continued

	N (% of total)	Model 0*	Model 1†	Model 2‡	Model 3§
AIC		17 021	15 032	14 157	14 164
Measures of variation—random intercept plus significant ransom slope††					
Area level variance (95% CI)					0.01914 (0.005044 to 0.9379)
P value					0.1666
PCV					−87.2%
AIC					14 146

*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.
¶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 preuniversity education, university of applied sciences or university.
**Very high degree of urbanisation: those living in neighbourhoods with >2500 addresses per km^2; high or intermediate level of education: those living in neighbourhoods with 1000–2500 addresses per km^2; low or very low degree of urbanisation: those living in neighbourhoods with <1000 addresses per km^2.
††Significant random slope for age included.
CSW, commercial sex worker; Ng, *Neisseria gonorrhoeae*; PCV, proportional change in variance; SES, socioeconomic status; STI, sexually transmitted infection.

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 under-represented at STI clinics (33%) compared with 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 with 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 were 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] Second 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.

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