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HIV and syphilis testing for heterosexuals aged above 25 years in the Netherlands: possibilities for targeted testing at Sexual Health Centers

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ABSTRACT

Objectives

Targeted testing policy for HIV/syphilis at Dutch sexual health clinics (SHCs) was evaluated for its efficiency in younger heterosexuals but not for heterosexuals ≥25 years. Currently, all older heterosexuals are tested for HIV/syphilis at SHCs. To explore possibilities for increased efficiency of testing in heterosexuals aged >25 years, this study aimed to identify determinants predictive for HIV and syphilis diagnoses that could be used in targeted testing strategies.

Methods

Dutch surveillance data of SHC consultations of women and heterosexual men >25 years between 2015-2021 were included. By univariate and multivariate logistic regression, determinants for HIV and/or syphilis diagnosis were analyzed. Based on these determinants and their applicability in SHC practice, different targeted testing scenarios were evaluated. For each scenario, the percentage of consultations involving HIV and syphilis testing and the total amount of missed HIV and syphilis diagnoses were calculated.

Results

109,122 consultations were included among 75,718 individuals. The strongest determinants for HIV/syphilis diagnosis were HIV/syphilis-specific symptoms and receiving partner notification, followed by low/middle education level, male sex and age ≥30 years. When applying feasible determinants to targeted testing scenarios, HIV/syphilis testing would have been conducted in 54.5% of all consultations, missing 2 HIV and 3 syphilis diagnoses annually (13.4% and 11.4% of all diagnoses, respectively). In the scenario with the lowest number of missed HIV/syphilis diagnoses (0.3 HIV and 2 syphilis diagnoses annually), HIV/syphilis testing would have been conducted in 74.2% of all consultations.

Conclusions

This study is a first step into considering targeted testing for older heterosexuals in SHCs. In any targeted testing scenario studied, HIV and/or syphilis diagnoses would have been missed. This raises the question whether it is acceptable to put any of these scenarios into practice. This study contributes to a discussion about the impact of targeted testing policy.

KEY MESSAGES

What is already known on this topic

- Heterosexuals aged ≥25 years that fulfill high risk triage criteria at sexual health centers in the Netherlands are routinely tested for four STI (chlamydia, gonorrhoea, HIV and syphilis), but possibilities for targeted testing in order to increase effectiveness are unknown.

What this study adds

- HIV/syphilis specific symptoms and partner notification were strongly associated with a positive HIV/syphilis diagnosis, all other associations were less strong.
- In all possible targeted STI testing scenarios in this study, HIV and syphilis diagnoses would still have been missed annually.

How this study might affect research, practice or policy

- This study stresses the importance of continuous evaluation of STI testing policy.
- Further research into ethical considerations and financial costs of targeted STI testing policy is needed.

INTRODUCTION

In many countries, sexually transmitted infections (STI) testing guidelines for women and heterosexual men aged >25 years are different from testing guidelines for those aged <25 years old. This is mainly the case for *Chlamydia trachomatis* (chlamydia) and *Neisseria gonorrhoeae* (gonorrhoea), where testing in women and heterosexual men aged ≥25 years is often recommended at certain indications only.[1-3] However, for syphilis and HIV differentiation in testing guidelines based on age is often not described. According to CDC, HIV screening should be offered to all individuals who seek care at Sexual Health Centers (SHCs) and syphilis screening to individuals at increased risk.[1] According to IUSTI guidelines (contributed by ECDC and the European Office of the WHO), both HIV and syphilis tests should be offered to all SHC attendees.[4 5]

In the Netherlands, all women and heterosexual men aged <25 years are eligible for testing at SHCs. Women and heterosexual men aged ≥25 years are eligible for testing at SHCs if they meet at least one of the following triage criteria: notified by a sexual contact, STI symptoms, having had a STI in the past year, female partner of MSM, commercial sex workers (CSW), originating from or having a partner from a STI-endemic area, or being a victim of sexual violence.[6] This older heterosexual group is routinely tested for four STI (chlamydia, gonorrhoea, HIV and syphilis) while women and heterosexual men aged <25 years are only tested for HIV and syphilis on indication.[6 7] This restrictive testing among young heterosexuals was introduced to decrease costs, as government funding for SHCs changed. Evaluation of this testing policy was conducted,[8] and targeted testing of HIV and syphilis on indication was found to be cost-effective; approximately 3 HIV and 7 syphilis diagnoses were missed annually. Nevertheless, evaluation data of STI testing for older heterosexuals remains limited.

For older women and heterosexual man, more insight is needed in the characteristics of SHC visitors with HIV and syphilis diagnoses, in order to explore possibilities for targeted testing in this group as well. Therefore, the objective of this study was to identify determinants predictive for HIV and syphilis diagnoses among all STI clinic consultations of women and heterosexual men aged above 25 years that could possibly be used in targeted testing strategies.

METHODS

Study population

National surveillance data of Sexual Health Centers (SHCs) in the Netherlands (SOAP) of women and heterosexual men aged above 25 years were used for this study. Consultations were selected from 2015 to 2021, as in 2015 government funding for SHC testing policy changed and consequently the

characteristics of people visiting the SHCs.[9] All women were included and heterosexual men were defined as men with self-reported sexual contact with women only in the past 6 months . Men who had sex with both men and women and men with unknown sexual behavior were excluded. Age was calculated by subtracting birth year (date was not available) from consultation year. To prevent misclassification of 25 year-olds in the study population (who have different testing guidelines), people aged 26 years and older were selected. Consultations were excluded for 1) individuals with specific testing policies (e.g. sex workers, transgender persons, pre-exposure prophylaxis (PrEP)), 2) consultations which did not include routine practice (not tested for chlamydia, gonorrhoea, syphilis and HIV)[6], 3) consultations of people living with HIV and 4) consultations of individuals aged ≥60 years due to small numbers.

Definitions

The outcome of this study was a diagnosis of HIV and/or syphilis (infectious syphilis, being primary/secondary syphilis or syphilis latens recens). Both STI were combined in one dichotomous variable in the main analysis, as HIV and syphilis testing both requires taking a blood sample. Available self-reported demographic and sexual behavioral variables were included in the model as possible determinants for an HIV/syphilis diagnosis. Age was dichotomized into categories 26-29 and ≥30 to create equally distributed groups. Education level was dichotomized to two categories: low/middle education level (no education, primary education only or vocational education) or high level education (all other education levels). Other variables included were; notified for STI (specifically for HIV/syphilis or another/unspecified STI), STI symptoms (overall and if so, HIV/syphilis specific), originating from an STI-endemic area (based on country of birth of both the individual and parents[10]), partner from risk group (STI-endemic area or MSM), STI (gonorrhoea, chlamydia, syphilis) diagnosis in the past year (persons who were not tested, were tested negative or test results were unknown were categorized as no STI history), number of partners in the past six months, being a client of CSW, having a chlamydia and/or gonorrhoea diagnosis at the same consultation, and condom use. Before 2018 condom use was reported at last sexual contact, after 2018 this was reported in the past 6 months at vaginal and/or anal sex; both were combined in one dichotomous variable (always with a condom in the past 6 months/last sex with a condom or not always/never with a condom in the past 6 months/last sex without condom).

Statistical analyses

Determinants predictive for an HIV/syphilis diagnosis were analyzed using logistic regressions. If missing values within one variable were more than 5% they were included in analyses as a separate category, missing values less than 5% were excluded. We first checked whether we had to take into

account that one person could be included in the dataset with multiple consultations. The additional value of adding a random intercept on person level to the model was checked by comparing Akaike Information Criterion (AIC) values between the intercept-only model with and without a random intercept. Then, univariate logistic regression analyses were performed for all determinants separately as independent variable and HIV/syphilis diagnosis as dependent variable. Last, all variables were included in a multivariable model constructed based on backward elimination using AIC. For all significant determinants that remained in the final model, effect modification was examined by adding interaction terms to all univariate regressions separately. For any significant effect modifiers stratified analyses were performed.

Three sensitivity analyses were performed. First, as determinants for an HIV and syphilis diagnosis might be different, separate analyses were performed per STI. Second, the variable anal sex in the past six months was only collected from 2016 onwards, therefore another model was conducted over the years 2016-2021 with anal sex added as a possible determinant.[11-14] Finally, a model was conducted over the years 2015-2019 to restrict the analysis to pre-COVID-19 years. During the COVID-19 pandemic, STI care in the Netherlands was downscaled, resulting in less and more targeted SHC consultations in 2020 and 2021.[9] All analyses were performed in R (version 4.2.0, packages tidyverse, gtsummary, broom, janitor, lme4).

Targeted testing

In order to assess possibilities for targeted testing, different scenarios were built up. The scenarios were based on determinants in the final regression model that were also applicable for use in practice. This was also supplemented with determinants for HIV and syphilis from the separate models. For each scenario the percentage of consultations involving HIV/syphilis testing and the total and average per year of missed HIV and syphilis diagnoses between 2015 and 2021 were calculated.

PATIENT AND PUBLIC INVOLVEMENT

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research. Only data from the national surveillance system were used.

RESULTS

Study population

Between January 2015 and December 2021, 147,003 STI consultations among women and heterosexual men aged >25 years were registered (figure 1). In total, 37,881 (25.8%) consultations were excluded due to various reasons including sex work (n = 28,486), transgender persons (n = 1,154), PrEP consultation (n = 43), non-routine testing (n = 5,708), prevalent HIV infections (n = 10) or age ≥60 years (n = 2,480), leaving 109,122 consultations for analysis among 75,718 individuals. In these consultations, 184 new syphilis diagnoses (0.2%) were reported and 82 HIV diagnoses (0.1%). In one consultation both syphilis and HIV were diagnosed.

In the study population, sex was equally distributed (table 1). Most people had a higher education level and originated from a non-STI/HIV-endemic area. Chlamydia was the most diagnosed STI (12.4% of all consultations). The number of consultations per year decreased over time.

Determinants for HIV and/or syphilis

The strongest determinants for HIV/syphilis diagnosis in univariate analyses were HIV/syphilis specific symptoms and partner notification for HIV/syphilis (table 2). In multivariate analyses these two remained the strongest determinants (adjusted Odds Ratio (aOR) 34.9; 95% Confidence Interval (CI) 24.1-50.2 and OR 18.3; 95% CI 13.2-25.2, resp.). Other significant determinants were male sex, being aged ≥30 years and low/middle education level. Persons who used condoms or had two or more sex partners in the past six months were less likely to have an HIV/syphilis diagnosis. Correcting for multiple consultations within one person was not necessary as the AIC values of the intercept-only model with and without a random intercept were approximately equal.

STI symptoms and partner notification were found to be significant effect modifiers. In stratified analyses for STI symptoms (supplemental table S1) the same determinants were found and the direction of the effects did not change. Additionally, self-reported STI in the past year became an extra predictor for persons with HIV/syphilis-specific symptoms. In stratified analyses for partner notification (supplemental table S2) the direction of the effects also did not change. However, sex and age were no determinants anymore and chlamydia/gonorrhoeae diagnosis in the same consultation became an additional predictor for persons with HIV/syphilis-specific partner notification.

In all sensitivity analyses (HIV/syphilis separately, including anal sex and excluding COVID years) (supplemental table S3) the same determinants and direction of effects were found as the initial model, except for reported HIV/syphilis symptoms which was not a predictor for HIV diagnosis. An additional significant predictor for HIV diagnosis was originating from an STI/HIV-endemic area, while

this was protective for syphilis. For syphilis diagnosis, self-reported STI in the past year was an additional predictive determinant. In analyses including anal sex, anal sex was an additional significant determinant predictive for HIV/syphilis diagnosis. Finally, restricting the analyses to pre-COVID-years made no large differences to the initial model.

Targeted testing

If targeted testing was only applied to SHC consultations who reported HIV/syphilis symptoms (the strongest predictor), in 0.6% of all consultations between 2015 and 2021 HIV/syphilis testing would have been conducted (table 3, scenario 1). Yet 95.1% of HIV diagnoses and 58.2% of syphilis diagnoses would then be missed, which corresponds to 11 and 15 missed diagnoses per year. If notified for HIV/syphilis by a partner would be added as testing criterium (the second most strongest predictor; scenario 2), in approximately 2% of all consultations HIV/syphilis testing would have been conducted, diagnosing 36.6% of all HIV and 64.7% of all syphilis diagnoses. Other significant determinants were education level, sex and age. Only age was assessed as applicable to SHC practice and age > 30 years was added to scenario 3, resulting in 54.5% of all consultations wherein HIV/syphilis testing would have been conducted resulting in missing 2 HIV and 3 syphilis diagnoses annually. Finally, when adding the separate determinants for HIV and syphilis diagnosis (self-reported STI in the past year and originating from STI/HIV-endemic area; scenario 4), in 74.2% of all consultations HIV/syphilis testing would still have been conducted, missing 0.3 HIV and 2 syphilis diagnoses on average per year.

DISCUSSION

The strongest determinants predictive for an HIV/syphilis diagnosis in women and heterosexual men aged over 25 years visiting SHCs were received partner notification for HIV/syphilis and reported HIV/syphilis symptoms. Persons aged ≥30 years were also more likely to have an HIV/syphilis diagnosis. When applying these determinants to targeted testing scenarios, HIV/syphilis testing would still have been conducted in 54.5% of all consultations, missing 2 HIV and 3 syphilis diagnoses annually. The scenario that resulted in the lowest number of missed HIV/syphilis diagnoses was when determinants for HIV or syphilis separately were also included, resulting in 0.3 HIV and 2 syphilis diagnoses missed annually. However, only in 26% of all consultations a HIV/syphilis tests would have been omitted between 2015 and 2021.

This is the first study in the Netherlands to describe determinants predictive for an HIV/syphilis diagnosis among women and heterosexual men aged >25 years. By the use of national surveillance data of Sexual Health Centers a large study sample was guaranteed. However, there were some

limitations. First, SOAP data did not allow to include all variables in the analyses as some questions contained too many missings. Especially victim of sexual violence would have been interesting as it is a HIV/syphilis test criterium for heterosexuals <25 years but could not be included due to too many missings. However, in consultations that did contain information on sexual violence, only one HIV diagnosis was found among victims of sexual violence, so we do not expect that including this variable would have changed our results. Second, HIV and syphilis were included in one combined outcome variable, while one might argue that the main analyses should have been separated in advance. However, as we intended to explore effectiveness of potential STI targeted testing strategies in this study, we think that combined HIV/syphilis testing would be most effective for SHC practice as both HIV and syphilis tests are conducted on a blood sample. Once blood is taken integrated testing for HIV and syphilis is most convenient. Furthermore, since the number of diagnoses were small, combining the two also increased the power. Sensitivity analyses showed different determinants when separating the two. For example, origin from an STI-endemic area was a predictor for HIV only and reported HIV/syphilis symptoms was a strong predictor for syphilis but not for HIV. This could be explained by syphilis symptoms being more often present and more recognizable than HIV symptoms.[15] Finally, in this study we estimated missed HIV/syphilis diagnoses annually based on numbers of HIV/syphilis diagnoses between 2015-2021 and did not take into account an effect of time to diagnosis. Delayed diagnoses could lead to, for example, delayed healthcare and/or further HIV/syphilis transmission, causing different annual numbers of missed HIV/syphilis diagnoses in reality then estimated in this study.

To our knowledge, no other studies have been performed on determinants predictive for both HIV and/or syphilis diagnoses as one outcome, apart from co-infections. For determinants for HIV and syphilis diagnoses separately the targeted populations between studies differ greatly, hampering comparison of our study results.[16-23] However, determinants in our study consistent with existing data were partner notification and lower education level, found to be predictive for both HIV and syphilis[6 9 16-18] and STI symptoms and male sex found to be predictive for syphilis only.[6 19] Yet an unexpected result in our study was that persons with two or more partners would be at decreased risk for HIV/syphilis diagnosis, as multiple partners are usually determinants for STI.[9 17 22] This difference could be explained by the strict triage criteria for heterosexuals ≥25 years at SHC, making this a higher risk group compared to, for example, heterosexuals <25 years who are all eligible for STI testing. Another explanation for these reversed effects in our study might be by unmeasured variables like reasons for testing.

Using the determinants predictive of an HIV/syphilis diagnoses, we constructed potential strategies for targeted testing. The testing scenarios were built up based on significant determinants

in the model, combined with feasibility in SHC practice. Targeted testing based on sex and education level were considered not feasible as this might lead to discrimination and/or stigmatization. Yet these results do stress the importance of reaching out to persons with low/middle-education level and making sure that STI care at SHC is accessible for this group.[24] The regression model showed that the only outstanding determinants predictive for HIV/syphilis diagnosis were HIV/syphilis specific symptoms and partner notification. Partner notification contributed to approximately half of all HIV/syphilis diagnoses found in our study. This underlines the great potential of partner notification in STI case detection, and stresses the importance of partner notification in STI control. All other determinants in the regression model had odds ratios close to one, meaning that specific risk groups were hard to identify within the group of heterosexuals older than 25 years at SHC. This might indicate that the current triage criteria for this group to be eligible for STI testing at SHC are effective in finding the persons at higher risk for STI.

In every targeted scenario evaluated, HIV and/or syphilis diagnoses will be missed. It should be questioned whether it is acceptable in an era of aiming at going towards zero new HIV infections to put any of these targeted testing scenarios into practice. A study on targeted HIV/syphilis testing for heterosexuals <25 years estimated that 3 missed HIV and 7 missed syphilis diagnoses annually were considered to be limited, when 3,3 million euros could be saved.[8] An evaluation of test cost savings for women and heterosexual men aged >25 years is needed to make informed decisions. Additionally, ethical aspects should be considered to decide how many diagnoses are acceptable to be missed. The UNAIDS announced the target to reach zero HIV infections in 2030[25] and STI AIDS Netherlands also set the aim to reach zero new HIV infections as soon as possible.[15] To reach this, any missed diagnosis would be too much and timely diagnosis of HIV is necessary. In the Netherlands, diagnosis of late-stage HIV is more common among women and heterosexual men compared to MSM[26] and also in the UK it is shown that syphilis often remains undiagnosed, especially among heterosexual men.[27] Additionally, there are concerns that syphilis in women of reproductive age could lead to congenital syphilis, a severe disease causing child mortality.[28] Finally, complications of non-detected cases could lead to increased costs, either through treatment of severe disease or additional testing in general practice or hospitals. We recommend all these considerations to be taken into account when assessing targeted testing policy.

Altogether, this study is a first step in considering targeted testing for HIV and syphilis of women and heterosexual men aged >25 years in the Netherlands. It is indicated that no specific group can be identified for targeted testing without missing any HIV/syphilis diagnoses. A discussion with a multidisciplinary team consisting of public health professionals, policy makers, ethicists, economists,

epidemiologists and all others involved about the public health impact of targeted testing policy is needed.

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CONTRIBUTORS

IW, HG and JCMH designed the study. IW and MV cleaned the data. IW analyzed the data and drafted the manuscript. All authors contributed to the interpretation of the results, commented on the manuscript and approved the final version.

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COMPETING INTERESTS

None declared.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval for the study was not necessary following the Dutch Medical Research (involving Human Subjects) Act, as the study uses routinely collected, anonymous surveillance data (Wet medisch-wetenschappelijk onderzoek met mensen 1998 §1 artikel 1).

DATA AVAILABILITY STATEMENT

This study uses data from the Dutch national registration of sexual health centre consultations (SOAP). Data can be requested for scientific use from the SOAP registration committee (contact soap@rivm.nl).

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TABLES

Table 1 Number and percentage of consultations by different characteristics of women and heterosexual men aged >25 years visiting Dutch SHCs between 2015 and 2021

	Consultations	
	n	%
Total number of consultations	109,122	100
Number of individuals	75,718	69.4
Consultation number per individual		
1	75,718	69.4
>1	33,404	30.6
Sex		
Men	54,531	50.0
Women	54,591	50.0
Age		
26-29 years	50,287	46.1
30+ years	58,835	53.9
Education level*		
High	59,453	54.5
Low/middle	41,716	38.2
Unknown/other	7,953	7.3
Originating from STI/HIV-endemic area†		
No	64,782	59.4
Yes	44,234	40.5
Unknown	106	0.1
STI diagnoses‡		
Chlamydia	13,539	12.4
Gonorrhea	2,403	2.2
Syphilis, infectious§	184	0.2
HIV	82	0.1
Year consult		
2015	22,322	20.5
2016	21,306	19.5
2017	19,855	18.2
2018	15,951	14.6
2019	11,395	10.4
2020	8,330	7.6
2021	9,963	9.1

* Low/middle level of education: no education, elementary school, lbo, mavo, vmbo, mbo-1, havo, vwo, gymnasium. High level education: all other education levels.
† STI/HIV-endemic areas include Asia, Africa, the Dutch Caribbean islands, Middle and South America.
‡ Consultations could be counted double when multiple STI were found at the same consultation.
§ Infectious syphilis includes primary syphilis, secondary syphilis and syphilis latens recens.

Table 2 Determinants for an HIV and/or syphilis diagnosis among women and heterosexual men aged >25 years visiting Dutch sexual health services between 2015-2021

	HIV and/or syphilis negative n (%)	HIV and/or syphilis positive n (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
Total number of consultations*	103,580 (99.8)	242 (0.2)		
Sex				
Women	51,905 (99.8)	84 (0.2)	1	1
Men	51,675 (99.7)	158 (0.3)	**1.9 (1.5-2.5)**	**2.2 (1.6-3.0)**
Age				
26-29 years	48,175 (99.9)	58 (0.1)	1	1
30+ years	55,405 (99.7)	184 (0.3)	**2.8 (2.1-3.7)**	**1.8 (1.3-2.5)**
CT and/or GO positivity at same consultation				
No	89,023 (99.8)	211 (0.2)	1	-
Yes	14,557 (99.8)	31 (0.2)	0.90 (0.6-1.3)	-
Self-reported GO/CT/SYPH in past year				
No	94,871 (99.8)	215 (0.2)	1	-
Yes	8,709 (99.7)	27 (0.3)	1.4 (0.9-2.0)	-
Education level†				
High	57,104 (99.9)	54 (0.1)	1	1
Low/middle	39,494 (99.6)	142 (0.4)	**3.8 (2.8-5.2)**	**2.8 (2.0-4.0)**
Unknown/other	6,982 (99.3)	46 (0.7)	**7.0 (4.7-10.3)**	**4.2 (2.7-6.4)**
Number of sex partners in past six months				
0-1	23,673 (99.6)	107 (0.4)	1	1
2-3	42,110 (99.8)	88 (0.2)	**0.5 (0.3-0.6)**	**0.7 (0.5-0.9)**
4+	37,797 (99.9)	47 (0.1)	**0.3 (0.2-0.4)**	**0.4 (0.3-0.6)**
Condom use‡				
No	86,413 (99.8)	214 (0.2)	1	1
Yes	17,167 (99.8)	28 (0.2)	0.7 (0.4-1.0)	**0.6 (0.4-0.9)**
Originating from STI/HIV-endemic area§				

No	61,599 (99.8)	134 (0.2)	1	-
Yes	41,981 (99.7)	108 (0.3)	1.2 (0.9-1.5)	-
Received partner notification				
No	67,817 (99.8)	129 (0.2)	1	1
Yes	34,347 (33.2)	23 (9.5)	**0.4 (0.2-0.5)**	**0.5 (0.3-0.8)**
Yes, notified for HIV/syphilis	1,416 (1.4)	90 (37.2)	**33.4 (25.3-43.9)**	**18.3 (13.2-25.2)**
Reported STI symptoms				
No	58,360 (99.8)	94 (0.2)	1	1
Yes, overall STI symptoms	44,727 (99.8)	78 (0.2)	1.1 (0.8-1.5)	1.3 (1.0-1.8)
Yes, HIV/syphilis symptoms	493 (87.6)	70 (12.4)	**88.2 (63.7-121.4)**	**34.9 (24.1-50.2)**
Partner in risk group**				
No	55,690 (99.8)	134 (0.2)	1	-
Yes	47,890 (99.8)	108 (0.2)	0.9 (0.7-1.2)	-
Client of commercial sex worker				
No	89,374 (99.8)	209 (0.2)	1	-
Yes, in past 6 months	6,356 (99.6)	23 (0.4)	1.5 (1.0-2.3)	-
Unknown	7,850 (99.9)	10 (0.1)	0.5 (0.3-1.0)	-

Bold = <0.05.
OR, Odds Ratio; CT, chlamydia; GO, gonorrhoea; SYPH, syphilis; STI, sexually transmitted infections.
* Consultations with missing values <5% on at least one of the determinants were excluded from the analyses.
† Low/middle level of education: no education, elementary school, lbo, mavo, vmbo, mbo-1, havo, vwo, gymnasium. High level education: all other education levels.
‡ Before 2018, condom use was asked regarding last sexual contact. In 2018 this changed to the past 6 months and during vaginal and/or anal sex.
§ STI/HIV-endemic areas include Asia, Africa, the Dutch Caribbean islands, Middle and South America.
** For heterosexual men: partner originating from a high STI/HIV endemic region. For women: partner originating from a high STI/HIV endemic region or a male partner who had sex with men.

Table 3 Number of missed HIV and/or syphilis diagnoses in targeted test options among women and heterosexual men aged >25 years visiting Dutch sexual health services between 2015-2021

		Consultations tested for HIV and/or syphilis	Diagnosed HIV and/or syphilis in total 2015-2021		Missed HIV and/or syphilis diagnoses in total 2015-2021		Missed HIV and/or syphilis diagnoses on average per year	
			HIV	Syphilis	HIV	Syphilis	HIV	Syphilis
Scenario	Targeted testing	n (%)	n (%)	n (%)	n (%)	n (%)	n	n
Based on significant determinants predictive for HIV/syphilis								
1	Reported HIV/syphilis symptoms (1)	611 (0.6)	4 (4.9)	77 (41.8)	78 (95.1)	107 (58.2)	11	15
2	Reported HIV/syphilis symptoms (1) and/or consultations of persons who received partner notification for HIV/syphilis (2)	2,125 (1.9)	30 (36.6)	119 (64.7)	52 (63.4)	65 (35.3)	7	9
3	Reported HIV/syphilis symptoms (1), consultations of persons who received partner notification for HIV/syphilis (2) and/or aged >30 years (3)	59,451 (54.5)	71 (86.6)	163 (88.6)	11 (13.4)	21 (11.4)	2	3
Based on additional significant determinants predictive for HIV and syphilis in separate models								
4	Reported HIV/syphilis symptoms (1), consultations of persons who received partner notification for HIV/syphilis (2), aged >30 years (3), self-reported STI in past year (4) and/or originating from an STI/HIV-endemic area* (5)	80,964 (74.2)	80 (97.6)	171 (92.9)	2 (2.4)	13 (7.1)	0.3	2
Total number of consultations, 2015-2021		109,122 (100)	82 (100)	184 (100)				

STI, sexually transmitted infections.
* STI/HIV-endemic areas include Asia, Africa, the Dutch Caribbean islands, Middle and South America.

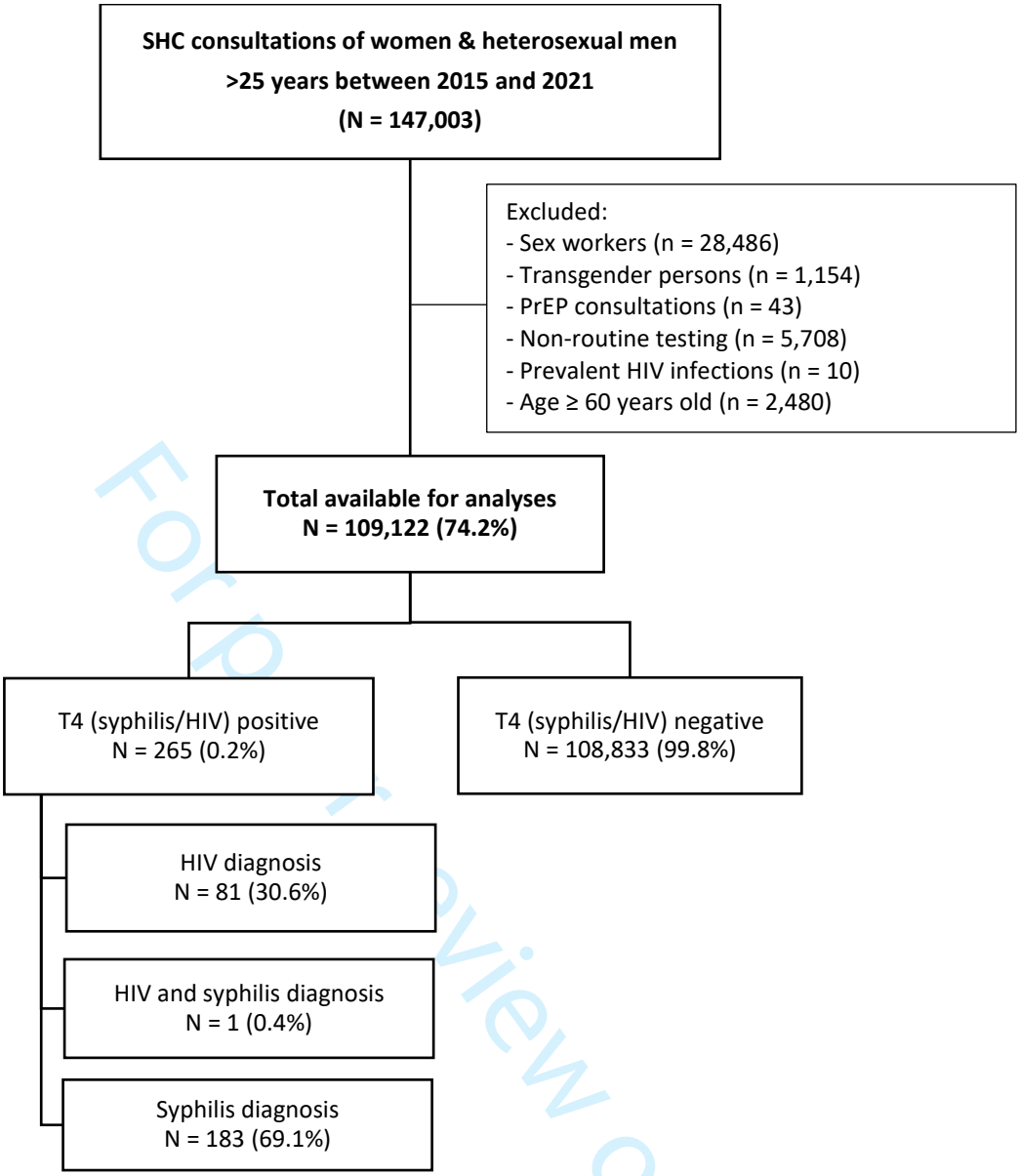

Figure 1 Flowchart of the included consultations in the study population. SHC, Sexual Health Center; T4, tested for chlamydia, gonorrhoea, syphilis and HIV.

Supplemental table S1. Determinants for an HIV and/or syphilis diagnosis among women and heterosexual men aged >25 years visiting Dutch sexual health services between 2015-2021, stratified by STI symptoms

	Overall model	**No reported STI symptoms**	**Reported STI symptoms - overall**	**Reported STI symptoms - HIV/syphilis specific**
	Adjusted OR (95% CI)	**Adjusted OR (95% CI)**	**Adjusted OR (95% CI)**	**Adjusted OR (95% CI)**
Total number of HIV and/or SYPH positive	242	94	78	70
Total number of consultations*	103,822	58,454	44,805	563
Sex				
Women	1	1	1	1
Men	**2.2 (1.6-3.0)**	1.6 (1.0-2.4)	**2.3 (1.4-3.9)**	**2.5 (1.3-5.0)**
Age				
26-29 years	1	1	1	1
30+ years	**1.8 (1.3-2.5)**	1.7 (1.0-2.9)	1.6 (1.0-2.7)	1.9 (1.0-3.7)
CT and/or GO positivity at same consultation				
No	-	-	-	-
Yes	-	-	-	-
Self-reported GO/CT/SYPH in past year				
No	-	-	-	1
Yes	-	-	-	**4.2 (2.0-8.5)**
Education level†				
High	1	1	1	1
Low/middle	**2.8 (2.0-4.0)**	**2.3 (1.4-3.8)**	**3.9 (2.2-7.3)**	**2.5 (1.4-4.8)**
Unknown/other	**4.2 (2.7-6.4)**	**3.9 (2.1-7.1)**	**5.3 (2.4-11.6)**	**2.5 (1.0-6.0)**
Number of sex partners in past six months				
0-1	1	1	1	-
2-3	**0.7 (0.5-0.9)**	**0.4 (0.3-0.7)**	1.0 (0.6-1.7)	-

4+	**0.4 (0.3-0.6)**	**0.3 (0.2-0.6)**	**0.4 (0.2-0.8)**	-
Condom use‡				
No	1	-	-	1
Yes	**0.6 (0.4-0.9)**	-	-	0.4 (0.2-1.0)
Originating from STI/HIV-endemic area§				
No	-	-	-	-
Yes	-	-	-	-
Received partner notification				
No	1	1	1	1
Yes	**0.5 (0.3-0.8)**	0.7 (0.4-1.3)	0.6 (0.3-1.1)	0.2 (0.0-1.0)
Yes, notified for HIV/syphilis	**18.3 (13.2-25.2)**	**30.7 (19.4-49.1)**	**37.7 (20.3-66.6)**	**4.1 (2.2-7.6)**
Partner in risk group**				
No	-	-	-	-
Yes	-	-	-	-
Client of commercial sex worker				
No	-	-	-	-
Yes, in past 6 months	-	-	-	-
Unknown	-	-	-	-

Bold = <0.05.
OR, Odds Ratio; CT, chlamydia; GO, gonorrhoea; SYPH, syphilis; STI, sexually transmitted infections.
* Consultations with missing values <5% on at least one of the determinants were excluded from the analyses.
† Low/middle level of education: no education, elementary school, lbo, mavo, vmbo, mbo-1, havo, vwo, gymnasium. High level education: all other education levels.
‡ Before 2018, condom use was asked regarding last sexual contact. In 2018 this changed to the past 6 months and during vaginal and/or anal sex.
§ STI/HIV-endemic areas include Asia, Africa, the Dutch Caribbean islands, Middle and South America.
** For heterosexual men: partner originating from a high STI/HIV endemic region. For women: partner originating from a high STI/HIV endemic region or a male partner who had sex with men.

Supplemental table S2. Determinants for an HIV and/or syphilis diagnosis among women and heterosexual men aged >25 years visiting Dutch sexual health services between 2015-2021, stratified by partner notification

	Overall model Adjusted OR (95% CI)	**No partner notification Adjusted OR (95% CI)**	**Partner notification - overall Adjusted OR (95% CI)**	**Partner notification - HIV/syphilis specific Adjusted OR (95% CI)**
Total number of HIV and/or SYPH positive	242	129	23	90
Total number of consultations*	103,822	67,946	34,370	1,506
Sex				
Women	1	1	1	-
Men	**2.2 (1.6-3.0)**	**2.8 (1.8-4.5)**	2.3 (0.9-6.4)	-
Age				
26-29 years	1	1	-	-
30+ years	**1.8 (1.3-2.5)**	**1.7 (1.2-2.7)**	-	-
CT and/or GO positivity at same consultation				
No	-	-	-	1
Yes	-	-	-	**2.3 (1.1-4.5)**
Self-reported GO/CT/SYPH in past year				
No	-	1	-	-
Yes	-	1.6 (0.9-2.7)	-	-
Education level†				
High	1	1	1	1
Low/middle	**2.8 (2.0-4.0)**	**2.6 (1.7-4.1)**	**2.8 (1.2-7.2)**	**3.5 (2.0-6.7)**
Unknown/other	**4.2 (2.7-6.4)**	**4.2 (2.5-7.2)**	1.4 (0.1-7.8)	**4.8 (2.3-10.4)**
Number of sex partners in past six months				
0-1	1	1	-	1
2-3	**0.7 (0.5-0.9)**	**0.6 (0.4-0.8)**	-	0.9 (0.5-1.4)
4+	**0.4 (0.3-0.6)**	**0.4 (0.2-0.6)**	-	**0.4 (0.2-0.7)**
Condom use‡				
No	1	-	-	1

Yes	**0.6 (0.4-0.9)**	-	-	**0.4 (0.2-0.9)**
Originating from STI/HIV-endemic area§				
No	-	-	-	-
Yes	-	-	-	-
Reported STI symptoms				
No	1	1	1	1
Yes, overall STI symptoms	1.3 (1.0-1.8)	**1.6 (1.1-2.6)**	1.3 (0.5-3.1)	1.6 (0.8-2.8)
Yes, HIV/syphilis symptoms	**34.9 (24.1-50.2)**	**88.0 (54.5-143.3)**	**28.9 (1.6-150.0)**	**9.9 (5.5-17.5)**
Partner in risk group**				
No	-	-	-	1
Yes	-	-	-	**0.6 (0.3-0.9)**
Client of commercial sex worker				
No	-	1	-	1
Yes, in past 6 months	-	1.4 (0.8-2.4)	-	0.8 (0.2-2.6)
Unknown	-	**2.6 (1.1-5.3)**	**-**	**0.1 (0.0-0.7)**

Bold = <0.05.
OR, Odds Ratio; CT, chlamydia; GO, gonorrhoea; SYPH, syphilis; STI, sexually transmitted infections.
* Consultations with missing values <5% on at least one of the determinants were excluded from the analyses.
† Low/middle level of education: no education, elementary school, lbo, mavo, vmbo, mbo-1, havo, vwo, gymnasium. High level education: all other education levels.
‡ Before 2018, condom use was asked regarding last sexual contact. In 2018 this changed to the past 6 months and during vaginal and/or anal sex.
§ STI/HIV-endemic areas include Asia, Africa, the Dutch Caribbean islands, Middle and South America.
** For heterosexual men: partner originating from a high STI/HIV endemic region. For women: partner originating from a high STI/HIV endemic region or a male partner who had sex with men.

Supplemental table S3. Sensitivity analyses for determinants for an HIV and/or syphilis diagnosis among women and heterosexual men aged >25 years visiting Dutch sexual health services between 2015-2021

	Adjusted OR (95% CI) overall model	Adjusted OR (95% CI) HIV infection	Adjusted OR (95% CI) Syphilis infection	Adjusted OR (95% CI) including anal sex, 2016-2021	Adjusted OR (95% CI) excluding COVID-years, 2015-2019
Total number of HIV and/or SYPH positive	242	74	169	210	165
Total number of consultations*	103,822	103,822	103,822	82,885	86,223
Sex					
Women	1	1	1	1	1
Men	**2.2 (1.6-3.0)**	**2.0 (1.2-3.3)**	**2.4 (1.7-3.4)**	**2.5 (1.8-3.5)**	**1.8 (1.3-2.6)**
Age					
26-29 years	1	1	1	1	1
30+ years	**1.8 (1.3-2.5)**	1.7 (1.0-3.1)	**1.9 (1.3-2.8)**	**1.8 (1.3-2.6)**	1.4 (1.0-2.1)
CT and/or GO positivity at same consultation					
No	-	1	-	-	1
Yes	-	1.7 (0.8-3.0)	-	-	1.4 (0.9-2.3)
Self-reported GO/CT/SYPH in past year					
No	-	1	1	1	-
Yes	-	0.4 (0.1-1.1)	**2.0 (1.2-3.2)**	1.5 (0.9-2.4)	-
Education level†					
High	1	1	1	1	1
Low/middle	**2.8 (2.0-4.0)**	**2.0 (1.1-3.7)**	**3.3 (2.2-4.9)**	**2.4 (1.7-3.5)**	**2.8 (1.9-4.2)**
Unknown/other	**4.2 (2.7-6.4)**	**5.2 (2.7-10.2)**	**3.3 (1.9-5.7)**	**3.9 (2.5-6.1)**	**4.9 (2.9-8.0)**
Number of sex partners in past six months					
0-1	1	1	1	1	1
2-3	**0.7 (0.5-0.9)**	**0.5 (0.3-0.8)**	0.9 (0.6-1.3)	**0.6 (0.4-0.9)**	0.7 (0.5-1.0)
4+	**0.4 (0.3-0.6)**	**0.3 (0.1-0.6)**	**0.5 (0.3-0.8)**	**0.4 (0.3-0.6)**	**0.4 (0.3-0.6)**

Condom use‡					
No	1	-	1	-	-
Yes	**0.6 (0.4-0.9)**	-	0.6 (0.4-1.0)	-	-
Originating from STI/HIV-endemic area§					
No	-	1	1	-	-
Yes	-	**3.1 (1.8-5.4)**	**0.5 (0.3-0.7)**	-	-
Received partner notification					
No	1	1	1	1	1
Yes	**0.5 (0.3-0.8)**	0.7 (0.3-1.3)	**0.4 (0.2-0.7)**	**0.4 (0.2-0.6)**	0.6 (0.3-1.0)
Yes, notified for HIV/syphilis	**18.3 (13.2-25.2)**	**23.4 (13.7-39.3)**	**17.4 (11.6-25.8)**	**15.4 (10.9-21.8)**	**20.4 (13.7-30.1)**
Reported STI symptoms					
No	1	-	1	1	1
Yes, overall STI symptoms	1.3 (1.0-1.8)	-	**1.9 (1.3-2.9)**	1.2 (0.9-1.7)	1.3 (0.9-2.0)
Yes, HIV/syphilis symptoms	**34.9 (24.1-50.2)**	-	**64.4 (41.9-99.6)**	**30.7 (21.0-44.7)**	**36.6 (23.1-57.4)**
Partner in risk group**					
No	-	-	-	-	-
Yes	-	-	-	-	-
Client of commercial sex worker					
No	-	-	-	-	-
Yes, in past 6 months	-	-	-	-	-
Unknown	-	-	-	-	-
Anal sex in past 6 months					
No	NA	NA	NA	1	NA
Yes, either insertive and/or receptive	NA	NA	NA	**1.6 (1.1-2.2)**	NA
Unknown	NA	NA	NA	1.1 (0.6-1.9)	NA

Bold = <0.05.
OR, Odds Ratio; CT, chlamydia; GO, gonorrhoea; SYPH, syphilis; STI, sexually transmitted infections; NA, not available.
* Consultations with missing values <5% on at least one of the determinants were excluded from the analyses.
† Low/middle level of education: no education, elementary school, lbo, mavo, vmbo, mbo-1, havo, vwo, gymnasium. High level education: all other education levels.

‡ Before 2018, condom use was asked regarding last sexual contact. In 2018 this changed to the past 6 months and during vaginal and/or anal sex.
§ STI/HIV-endemic areas include Asia, Africa, the Dutch Caribbean islands, Middle and South America.
** For heterosexual men: partner originating from a high STI/HIV endemic region. For women: partner originating from a high STI/HIV endemic region or a male partner who had sex with men.

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

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

		(*b*) Report category boundaries when continuous variables were categorized	-
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7-8
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
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	8-9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	10
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	11

*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.

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HIV and syphilis testing for women and heterosexual men aged above 25 years in the Netherlands: possibilities for targeted testing at Sexual Health Centers

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HIV and syphilis testing for women and heterosexual men aged above 25 years in the Netherlands: possibilities for targeted testing at Sexual Health Centers

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ABSTRACT

Objectives

Targeted testing policy for HIV/syphilis at Dutch sexual health centers (SHCs) was evaluated for its efficiency in younger heterosexuals but not for heterosexuals ≥25 years. Currently, all older heterosexuals are tested for HIV/syphilis at SHCs. To explore possibilities for increased efficiency of testing in heterosexuals aged >25 years, this study aimed to identify determinants of HIV and syphilis diagnoses that could be used in targeted testing strategies.

Design

An observational study using surveillance data from all Dutch SHC.

Participants

Women and heterosexual men aged >25 years visiting SHC between 2015-2021.

Primary and secondary outcome measures

The primary outcome was HIV/syphilis diagnosis, determinants of a diagnosis were analyzed. Based on these determinants and their applicability in SHC practice, different targeted testing scenarios were evaluated. For each scenario, the percentage of consultations involving HIV and syphilis testing and the total amount of missed HIV and syphilis diagnoses were calculated.

Results

109,122 consultations were included among 75,718 individuals. The strongest determinants of HIV/syphilis diagnosis were HIV/syphilis-specific symptoms (aOR 34.9(24.1-50.2)) and receiving partner notification (aOR 18.3(13.2-25.2)), followed by low/middle education level (aOR 2.8(2.0-4.0)), male sex (aOR 2.2(1.6-3.0)) and age ≥30 years (aOR 1.8(1.3-2.5)). When applying feasible determinants to targeted testing scenarios, HIV/syphilis testing would have been conducted in 54.5% of all consultations, missing 2 HIV and 3 syphilis diagnoses annually (13.4% and 11.4% of all diagnoses, respectively). In the scenario with the lowest number of missed HIV/syphilis diagnoses (0.3 HIV and 2 syphilis diagnoses annually), HIV/syphilis testing would have been conducted in 74.2% of all consultations.

Conclusions

In any targeted testing scenario studied, HIV and/or syphilis diagnoses would have been missed. This raises the question whether it is acceptable to put any of these scenarios into practice. This study contributes to a discussion about the impact of targeted testing policy.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is the first study in the Netherlands describing determinants of HIV/syphilis diagnosis among women and heterosexual men aged >25 years.
- The study used nation-wide surveillance data from Sexual Health Centers.
- This study was limited by the sexual behavioral variables available in the surveillance data.
- Additional cost-effectiveness analyses are needed to facilitate informed decisions regarding HIV/syphilis testing policy.

INTRODUCTION

In many countries, sexually transmitted infections (STI) testing guidelines for women and heterosexual men aged >25 years are different from testing guidelines for those aged <25 years old. This is mainly the case for *Chlamydia trachomatis* (chlamydia) and *Neisseria gonorrhoeae* (gonorrhoea), where testing in women and heterosexual men aged ≥25 years is often recommended at certain indications only.(1, 2, 3) However, for syphilis and HIV differentiation in testing guidelines based on age is often not described. According to CDC, HIV screening should be offered to all individuals who seek care at Sexual Health Centers (SHCs) and syphilis screening to individuals at increased risk.(1) According to IUSTI guidelines (contributed by ECDC and the European Office of the WHO), both HIV and syphilis tests should be offered to all SHC attendees.(4, 5)

In the Netherlands, all women and heterosexual men aged <25 years are eligible for testing at SHCs. Women and heterosexual men aged ≥25 years are eligible for testing at SHCs if they meet at least one of the following triage criteria: notified by a sexual contact, STI symptoms, having had a STI in the past year, female partner of MSM, commercial sex workers (CSW), originating from or having a partner from a STI-endemic area, or being a victim of sexual violence.(6) This older heterosexual group is routinely tested for four STI (chlamydia, gonorrhoea, HIV and syphilis) while women and heterosexual men aged <25 years are only tested for HIV and syphilis on indication.(6, 7) This restrictive testing among young heterosexuals was introduced to decrease costs, as government funding for SHCs changed. Evaluation of this testing policy was conducted,(8) and targeted testing of HIV and syphilis on indication was found to be cost-effective; approximately 3 HIV and 7 syphilis diagnoses were missed annually. Nevertheless, evaluation data of STI testing for older heterosexuals remains limited.

For older women and heterosexual men, more insight is needed in the characteristics of SHC visitors with HIV and syphilis diagnoses, in order to explore possibilities for targeted testing in this group as well. Therefore, the objective of this study was to identify determinants of HIV and syphilis diagnoses among all STI clinic consultations of women and heterosexual men aged above 25 years that could possibly be used in targeted testing strategies.

METHODS

Study population

National surveillance data of Sexual Health Centers (SHCs) in the Netherlands (SOAP) of women and heterosexual men aged above 25 years were used for this study. Consultations were selected from

2015 to 2021, as in 2015 government funding for SHC testing policy changed and consequently the characteristics of people visiting the SHCs.(9) All women were included and heterosexual men were defined as men with self-reported sexual contact with women only in the past 6 months. Men who had sex with both men and women and men with unknown sexual behavior were excluded. Age was calculated by subtracting birth year (date was not available) from consultation year. To prevent misclassification of 25 year-olds in the study population (who have different testing guidelines), people aged 26 years and older were selected. Consultations were excluded for 1) individuals with specific testing policies (e.g. sex workers, transgender persons, pre-exposure prophylaxis (PrEP)), 2) consultations which did not include routine practice (not tested for chlamydia, gonorrhoea, syphilis and HIV)(6), 3) consultations of people living with HIV and 4) consultations of individuals aged ≥60 years due to small numbers.

Definitions

The outcome of this study was a diagnosis of HIV and/or syphilis (infectious syphilis, being primary/secondary syphilis or syphilis latens recens). Both STI were combined in one dichotomous variable in the main analysis, as HIV and syphilis testing both requires taking a blood sample. Available self-reported demographic and sexual behavioral variables were included in the model as possible determinants of an HIV/syphilis diagnosis. Age was dichotomized into categories 26-29 and ≥30 to create equally distributed groups. Education level was dichotomized to two categories: low/middle education level (no education, primary education only or vocational education) or high level education (all other education levels). Other variables included were; notified for STI (specifically for HIV/syphilis or another/unspecified STI), STI symptoms (overall and if so, HIV/syphilis specific (e.g. weight loss, fever, ulcers, swollen lymph nodes), originating from an STI-endemic area (based on country of birth of both the individual and parents(10)), partner from risk group (STI-endemic area or MSM), STI (gonorrhoea, chlamydia, syphilis) diagnosis in the past year (persons who were not tested, were tested negative or test results were unknown were categorized as no STI history), number of partners in the past six months, being a client of CSW, having a chlamydia and/or gonorrhoea diagnosis at the same consultation, and condom use. Before 2018 condom use was reported at last sexual contact, after 2018 this was reported in the past 6 months at vaginal and/or anal sex; both were combined in one dichotomous variable (always with a condom in the past 6 months/last sex with a condom or not always/never with a condom in the past 6 months/last sex without condom).

Statistical analyses

Determinants of an HIV/syphilis diagnosis were analyzed using logistic regressions. If missing values within one variable were more than 5% they were included in analyses as a separate category, missing

values less than 5% were excluded. We first checked whether we had to take into account that one person could be included in the dataset with multiple consultations. The additional value of adding a random intercept on person level to the model was checked by comparing Akaike Information Criterion (AIC) values between the intercept-only model with and without a random intercept. Then, univariate logistic regression analyses were performed for all determinants separately as independent variable and HIV/syphilis diagnosis as dependent variable. Last, all variables were included in a multivariable model constructed based on backward elimination using AIC. For all significant determinants that remained in the final model, effect modification was examined by adding interaction terms to all univariate regressions separately. For any significant effect modifiers stratified analyses were performed.

Three sensitivity analyses were performed. First, as determinants of an HIV and syphilis diagnosis might be different, separate analyses were performed per STI. Second, the variable anal sex in the past six months was only collected from 2016 onwards, therefore another model was conducted over the years 2016-2021 with anal sex added as a possible determinant.(11, 12, 13, 14) Finally, a model was conducted over the years 2015-2019 to restrict the analysis to pre-COVID-19 years. During the COVID-19 pandemic, STI care in the Netherlands was downscaled, resulting in less and more targeted SHC consultations in 2020 and 2021.(9) All analyses were performed in R (version 4.2.0, packages tidyverse, gtsummary, broom, janitor, lme4).

Targeted testing

In order to assess possibilities for targeted testing, different scenarios were built up. The scenarios were based on determinants in the final regression model that were also applicable for use in practice. This was also supplemented with determinants of HIV and syphilis from the separate models. For each scenario the percentage of consultations involving HIV/syphilis testing and the total and average per year of missed HIV and syphilis diagnoses between 2015 and 2021 were calculated.

PATIENT AND PUBLIC INVOLVEMENT

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research. Only data from the national surveillance system were used.

RESULTS

Study population

Between January 2015 and December 2021, 147,003 STI consultations among women and heterosexual men aged >25 years were registered (figure 1). In total, 37,881 (25.8%) consultations were excluded due to various reasons including sex work (n = 28,486), transgender persons (n = 1,154), PrEP consultation (n = 43), non-routine testing (n = 5,708), prevalent HIV infections (n = 10) or age ≥60 years (n = 2,480), leaving 109,122 consultations for analysis among 75,718 individuals. In these consultations, 184 new syphilis diagnoses (0.2%) were reported and 82 HIV diagnoses (0.1%). In one consultation both syphilis and HIV were diagnosed.

In the study population, sex was equally distributed (table 1). Most people had a higher education level and originated from a non-STI/HIV-endemic area. Chlamydia was the most diagnosed STI (12.4% of all consultations). The number of consultations per year decreased over time.

Determinants of HIV and/or syphilis

The strongest determinants of HIV/syphilis diagnosis in univariate analyses were HIV/syphilis specific symptoms and partner notification for HIV/syphilis (table 2). In multivariate analyses these two remained the strongest determinants (adjusted Odds Ratio (aOR) 34.9; 95% Confidence Interval (CI) 24.1-50.2 and aOR 18.3; 95% CI 13.2-25.2, resp.). Other significant determinants were male sex, being aged ≥30 years and low/middle education level. Persons who used condoms or had two or more sex partners in the past six months were less likely to have an HIV/syphilis diagnosis. Correcting for multiple consultations within one person was not necessary as the AIC values of the intercept-only model with and without a random intercept were approximately equal.

STI symptoms and partner notification were found to be significant effect modifiers. In stratified analyses for STI symptoms (supplemental table S1) the same determinants were found and the direction of the effects did not change. Additionally, self-reported STI in the past year became an extra determinant for persons with HIV/syphilis-specific symptoms. In stratified analyses for partner notification (supplemental table S2) the direction of the effects also did not change. However, sex and age were no determinants anymore and chlamydia/gonorrhoeae diagnosis in the same consultation became an additional determinant for persons with HIV/syphilis-specific partner notification.

In all sensitivity analyses (HIV/syphilis separately, including anal sex and excluding COVID years) (supplemental table S3) the same determinants and direction of effects were found as the initial model, except for reported HIV/syphilis symptoms which was not a determinant of HIV diagnosis. An additional significant determinant of HIV diagnosis was originating from an STI/HIV-endemic area,

while this was protective for syphilis. For syphilis diagnosis, self-reported STI in the past year was an additional determinant. In analyses including anal sex, anal sex was an additional significant determinant of HIV/syphilis diagnosis. Finally, restricting the analyses to pre-COVID-years made no large differences to the initial model.

Targeted testing

If targeted testing was only applied to SHC consultations who reported HIV/syphilis symptoms (the strongest determinant), in 0.6% of all consultations between 2015 and 2021 HIV/syphilis testing would have been conducted (table 3, scenario 1). Yet 95.1% of HIV diagnoses and 58.2% of syphilis diagnoses would then be missed, which corresponds to 11 and 15 missed diagnoses per year. If notified for HIV/syphilis by a partner would be added as testing criterium (the second most strongest determinant; scenario 2), in approximately 2% of all consultations HIV/syphilis testing would have been conducted, diagnosing 36.6% of all HIV and 64.7% of all syphilis diagnoses. Other significant determinants were education level, sex and age. Only age was assessed as applicable to SHC practice and age > 30 years was added to scenario 3, resulting in 54.5% of all consultations wherein HIV/syphilis testing would have been conducted resulting in missing 2 HIV and 3 syphilis diagnoses annually. Finally, when adding the separate determinants of HIV and syphilis diagnosis (self-reported STI in the past year and originating from STI/HIV-endemic area; scenario 4), in 74.2% of all consultations HIV/syphilis testing would still have been conducted, missing 0.3 HIV and 2 syphilis diagnoses on average per year.

DISCUSSION

The strongest determinants of an HIV/syphilis diagnosis in women and heterosexual men aged over 25 years visiting SHCs were received partner notification for HIV/syphilis and reported HIV/syphilis symptoms. Persons aged ≥30 years were also more likely to have an HIV/syphilis diagnosis. When applying these determinants to targeted testing scenarios, HIV/syphilis testing would still have been conducted in 54.5% of all consultations, missing 2 HIV and 3 syphilis diagnoses annually. The scenario that resulted in the lowest number of missed HIV/syphilis diagnoses was when determinants of HIV or syphilis separately were also included, resulting in 0.3 HIV and 2 syphilis diagnoses missed annually. However, only in 26% of all consultations a HIV/syphilis tests would have been omitted between 2015 and 2021.

This is the first study in the Netherlands to describe determinants of an HIV/syphilis diagnosis among women and heterosexual men aged >25 years. By the use of national surveillance data of Sexual Health Centers a large study sample was guaranteed. However, there were some

limitations. First, we were limited to variables as available in SOAP data. For example, HIV/syphilis-specific symptoms is one combined variable. We do note that clinical symptoms of recent HIV infection and early syphilis infection do overlap, so a clinical distinction would not be possible. More detailed clinical data may have improved the results of the regression model and the application of possible targeted testing scenarios in clinical practice. In addition, SOAP data did not allow to include all variables in the analyses as some questions contained too many missings. Especially victim of sexual violence would have been interesting as it is a HIV/syphilis test criterium for heterosexuals <25 years but could not be included due to too many missings. However, in consultations that did contain information on sexual violence, only one HIV diagnosis was found among victims of sexual violence, so we do not expect that including this variable would have changed our results. Second, HIV and syphilis were included in one combined outcome variable, while one might argue that the main analyses should have been separated in advance. However, as we intended to explore effectiveness of potential STI targeted testing strategies in this study, we think that combined HIV/syphilis testing would be most effective for SHC practice as both HIV and syphilis tests are conducted on a blood sample. Once blood is taken integrated testing for HIV and syphilis is most convenient. Furthermore, since the number of diagnoses were small, combining the two also increased the power. Sensitivity analyses showed different determinants when separating the two. For example, origin from an STI-endemic area was a determinant of HIV only and reported HIV/syphilis symptoms was a strong determinant of syphilis but not for HIV. This could be explained by syphilis symptoms being more often present and more recognizable than HIV symptoms.(15) Third, in this study we estimated missed HIV/syphilis diagnoses annually based on numbers of HIV/syphilis diagnoses between 2015-2021 and did not take into account an effect of time to diagnosis. Delayed diagnoses could lead to, for example, delayed healthcare and/or further HIV/syphilis transmission, causing different annual numbers of missed HIV/syphilis diagnoses in reality then estimated in this study. Finally, it should be noted that the results of our study might be different when evaluating future years, based on possible differences in population and/or STI testing policy. Therefore continuous evaluation remains needed. To our knowledge, no other studies have been performed on determinants of both HIV and/or syphilis diagnoses as one outcome, apart from co-infections. For determinants of HIV and syphilis diagnoses separately the targeted populations between studies differ greatly, hampering comparison of our study results.(16, 17, 18, 19, 20, 21, 22, 23) However, determinants in our study consistent with existing data were partner notification and lower education level, found to be determinants of both HIV and syphilis(6, 9, 16, 17, 18) and STI symptoms and male sex found to be determinants of syphilis only.(6, 19) Yet an unexpected result in our study was that persons with two or more partners would be at decreased risk for HIV/syphilis diagnosis, as multiple partners are usually determinants of STI.(9,

17, 22) This difference could be explained by the strict triage criteria for heterosexuals ≥25 years at SHC, making this a higher risk group compared to, for example, heterosexuals <25 years who are all eligible for STI testing. Another explanation for these reversed effects in our study might be by unmeasured variables like reasons for testing.

Using the determinants of an HIV/syphilis diagnoses, we constructed potential strategies for targeted testing. The testing scenarios were built up based on significant determinants in the model, combined with feasibility in SHC practice. Targeted testing based on sex and education level were considered not feasible as this might lead to discrimination and/or stigmatization. Yet these results do stress the importance of reaching out to persons with low/middle-education level and making sure that STI care at SHC is accessible for this group.(24) The regression model showed that the only outstanding determinants of HIV/syphilis diagnosis were HIV/syphilis specific symptoms and partner notification. Partner notification contributed to approximately half of all HIV/syphilis diagnoses found in our study. This underlines the great potential of partner notification in STI case detection, and stresses the importance of partner notification in STI control. All other determinants in the regression model had odds ratios close to one, meaning that specific risk groups were hard to identify within the group of heterosexuals older than 25 years at SHC. Also, when adding all of these significant determinants to targeted testing, most participants would still have been tested (74%). This raises the question whether you would be able to calling this targeted testing. This might indicate that the current triage criteria for this group to be eligible for STI testing at SHC are effective in finding the persons at higher risk for STI and might need to remain as they are for surveillance purposes.In every targeted scenario evaluated, HIV and/or syphilis diagnoses will be missed. It should be questioned whether it is acceptable in an era of aiming at going towards zero new HIV infections to put any of these targeted testing scenarios into practice. A study on targeted HIV/syphilis testing for heterosexuals <25 years estimated that 3 missed HIV and 7 missed syphilis diagnoses annually were considered to be limited, when 3,3 million euros could be saved.(8) An evaluation of test cost savings for women and heterosexual men aged >25 years is needed to make informed decisions. To find the optimal strategy, HIV and syphilis treatment costs should also be included in these evaluations. Additionally, ethical aspects should be considered to decide how many diagnoses are acceptable to be missed. The UNAIDS announced the target to reach zero HIV infections in 2030(25) and STI AIDS Netherlands also set the aim to reach zero new HIV infections as soon as possible.(15) To reach this, any missed diagnosis would be too much and timely diagnosis of HIV is necessary. In the Netherlands, diagnosis of late-stage HIV is more common among women and heterosexual men compared to MSM(26) and also in the UK it is shown that syphilis often remains undiagnosed, especially among heterosexual men.(27) Untreated syphilis could lead to latent syphilis with severe neurological and

cardiovascular damage.(28) Finally, complications of non-detected cases could lead to increased costs, either through treatment of severe disease or additional testing in general practice or hospitals. We recommend all these considerations to be taken into account when assessing targeted testing policy.

Altogether, this study is a first step in considering targeted testing for HIV and syphilis of women and heterosexual men aged >25 years in the Netherlands. It is indicated that no specific group can be identified for targeted testing without missing any HIV/syphilis diagnoses. A discussion with a multidisciplinary team consisting of public health professionals, policy makers, ethicists, economists, epidemiologists and all others involved about the public health impact of targeted testing policy is needed.

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CONTRIBUTORS

IW, HG and JCMH designed the study. IW and MV cleaned the data. IW analyzed the data and drafted the manuscript. All authors contributed to the interpretation of the results, commented on the manuscript and approved the final version.

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COMPETING INTERESTS

None declared.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval for the study was not necessary following the Dutch Medical Research (involving Human Subjects) Act, as the study uses routinely collected, anonymous surveillance data (Wet medisch-wetenschappelijk onderzoek met mensen 1998 §1 artikel 1).

DATA AVAILABILITY STATEMENT

This study uses data from the Dutch national registration of sexual health centre consultations (SOAP). Data can be requested for scientific use from the SOAP registration committee (contact soap@rivm.nl).

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TABLES

Table 1 Number and percentage of consultations by different characteristics of women and heterosexual men aged >25 years visiting Dutch sexual health centers between 2015 and 2021

	Consultations	
	n	%
Total number of consultations	109,122	100
Number of individuals	75,718	69.4
Consultation number per individual		
1	75,718	69.4
>1	33,404	30.6
Sex		
Men	54,531	50.0
Women	54,591	50.0
Age		
26-29 years	50,287	46.1
30+ years	58,835	53.9
Education level*		
High	59,453	54.5
Low/middle	41,716	38.2
Unknown/other	7,953	7.3
Originating from STI/HIV-endemic area†		
No	64,782	59.4
Yes	44,234	40.5
Unknown	106	0.1
STI diagnoses‡		
Chlamydia	13,539	12.4
Gonorrhea	2,403	2.2
Syphilis, infectious§	184	0.2
HIV	82	0.1
Year consult		
2015	22,322	20.5
2016	21,306	19.5
2017	19,855	18.2
2018	15,951	14.6
2019	11,395	10.4
2020	8,330	7.6
2021	9,963	9.1

* Low/middle level of education: no education, elementary school, lbo, mavo, vmbo, mbo-1, havo, vwo, gymnasium. High level education: all other education levels.
† STI/HIV-endemic areas include Asia, Africa, the Dutch Caribbean islands, Middle and South America.
‡ Consultations could be counted double when multiple STI were found at the same consultation.
§ Infectious syphilis includes primary syphilis, secondary syphilis and syphilis latens recens.

Table 2 Determinants of an HIV and/or syphilis diagnosis among women and heterosexual men aged >25 years visiting Dutch sexual health centers between 2015-2021

	HIV and/or syphilis negative n (%)	HIV and/or syphilis positive n (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
Total number of consultations*	103,580 (99.8)	242 (0.2)		
Sex				
Women	51,905 (99.8)	84 (0.2)	1	1
Men	51,675 (99.7)	158 (0.3)	**1.9 (1.5-2.5)**	**2.2 (1.6-3.0)**
Age				
26-29 years	48,175 (99.9)	58 (0.1)	1	1
30+ years	55,405 (99.7)	184 (0.3)	**2.8 (2.1-3.7)**	**1.8 (1.3-2.5)**
CT and/or GO positivity at same consultation				
No	89,023 (99.8)	211 (0.2)	1	-
Yes	14,557 (99.8)	31 (0.2)	0.90 (0.6-1.3)	-
Self-reported GO/CT/SYPH in past year				
No	94,871 (99.8)	215 (0.2)	1	-
Yes	8,709 (99.7)	27 (0.3)	1.4 (0.9-2.0)	-
Education level†				
High	57,104 (99.9)	54 (0.1)	1	1
Low/middle	39,494 (99.6)	142 (0.4)	**3.8 (2.8-5.2)**	**2.8 (2.0-4.0)**
Unknown/other	6,982 (99.3)	46 (0.7)	**7.0 (4.7-10.3)**	**4.2 (2.7-6.4)**
Number of sex partners in past six months				
0-1	23,673 (99.6)	107 (0.4)	1	1
2-3	42,110 (99.8)	88 (0.2)	**0.5 (0.3-0.6)**	**0.7 (0.5-0.9)**
4+	37,797 (99.9)	47 (0.1)	**0.3 (0.2-0.4)**	**0.4 (0.3-0.6)**
Condom use‡				
No	86,413 (99.8)	214 (0.2)	1	1
Yes	17,167 (99.8)	28 (0.2)	0.7 (0.4-1.0)	**0.6 (0.4-0.9)**
Originating from STI/HIV-endemic area§				

No	61,599 (99.8)	134 (0.2)	1	-
Yes	41,981 (99.7)	108 (0.3)	1.2 (0.9-1.5)	-
Received partner notification				
No	67,817 (99.8)	129 (0.2)	1	1
Yes	34,347 (33.2)	23 (9.5)	**0.4 (0.2-0.5)**	**0.5 (0.3-0.8)**
Yes, notified for HIV/syphilis	1,416 (1.4)	90 (37.2)	**33.4 (25.3-43.9)**	**18.3 (13.2-25.2)**
Reported STI symptoms				
No	58,360 (99.8)	94 (0.2)	1	1
Yes, overall STI symptoms	44,727 (99.8)	78 (0.2)	1.1 (0.8-1.5)	1.3 (1.0-1.8)
Yes, HIV/syphilis symptoms	493 (87.6)	70 (12.4)	**88.2 (63.7-121.4)**	**34.9 (24.1-50.2)**
Partner in risk group**				
No	55,690 (99.8)	134 (0.2)	1	-
Yes	47,890 (99.8)	108 (0.2)	0.9 (0.7-1.2)	-
Client of commercial sex worker				
No	89,374 (99.8)	209 (0.2)	1	-
Yes, in past 6 months	6,356 (99.6)	23 (0.4)	1.5 (1.0-2.3)	-
Unknown	7,850 (99.9)	10 (0.1)	0.5 (0.3-1.0)	-

Bold = <0.05.

OR, Odds Ratio; CT, chlamydia; GO, gonorrhoea; SYPH, syphilis; STI, sexually transmitted infections.

* Consultations with missing values <5% on at least one of the determinants were excluded from the analyses.

† Low/middle level of education: no education, elementary school, lbo, mavo, vmbo, mbo-1, havo, vwo, gymnasium. High level education: all other education levels.

‡ Before 2018, condom use was asked regarding last sexual contact. In 2018 this changed to the past 6 months and during vaginal and/or anal sex.

§ STI/HIV-endemic areas include Asia, Africa, the Dutch Caribbean islands, Middle and South America.

** For heterosexual men: partner originating from a high STI/HIV endemic region. For women: partner originating from a high STI/HIV endemic region or a male partner who had sex with men.

Table 3 Number of missed HIV and/or syphilis diagnoses in targeted test options among women and heterosexual men aged >25 years visiting Dutch sexual health centers between 2015-2021

		Consultations tested for HIV and/or syphilis	Diagnosed HIV and/or syphilis in total 2015-2021		Missed HIV and/or syphilis diagnoses in total 2015-2021		Missed HIV and/or syphilis diagnoses on average per year	
			HIV	Syphilis	HIV	Syphilis	HIV	Syphilis
Scenario	Targeted testing	n (%)	n (%)	n (%)	n (%)	n (%)	n	n
Based on significant determinants of HIV/syphilis								
1	Reported HIV/syphilis symptoms (1)	611 (0.6)	4 (4.9)	77 (41.8)	78 (95.1)	107 (58.2)	11	15
2	Reported HIV/syphilis symptoms (1) and/or consultations of persons who received partner notification for HIV/syphilis (2)	2,125 (1.9)	30 (36.6)	119 (64.7)	52 (63.4)	65 (35.3)	7	9
3	Reported HIV/syphilis symptoms (1), consultations of persons who received partner notification for HIV/syphilis (2) and/or aged >30 years (3)	59,451 (54.5)	71 (86.6)	163 (88.6)	11 (13.4)	21 (11.4)	2	3
Based on additional significant determinants of HIV and syphilis in separate models								
4	Reported HIV/syphilis symptoms (1), consultations of persons who received partner notification for HIV/syphilis (2), aged >30 years (3), self-reported STI in past year (4) and/or originating from an STI/HIV-endemic area* (5)	80,964 (74.2)	80 (97.6)	171 (92.9)	2 (2.4)	13 (7.1)	0.3	2
Total number of consultations, 2015-2021		109,122 (100)	82 (100)	184 (100)				

STI, sexually transmitted infections.
* STI/HIV-endemic areas include Asia, Africa, the Dutch Caribbean islands, Middle and South America.

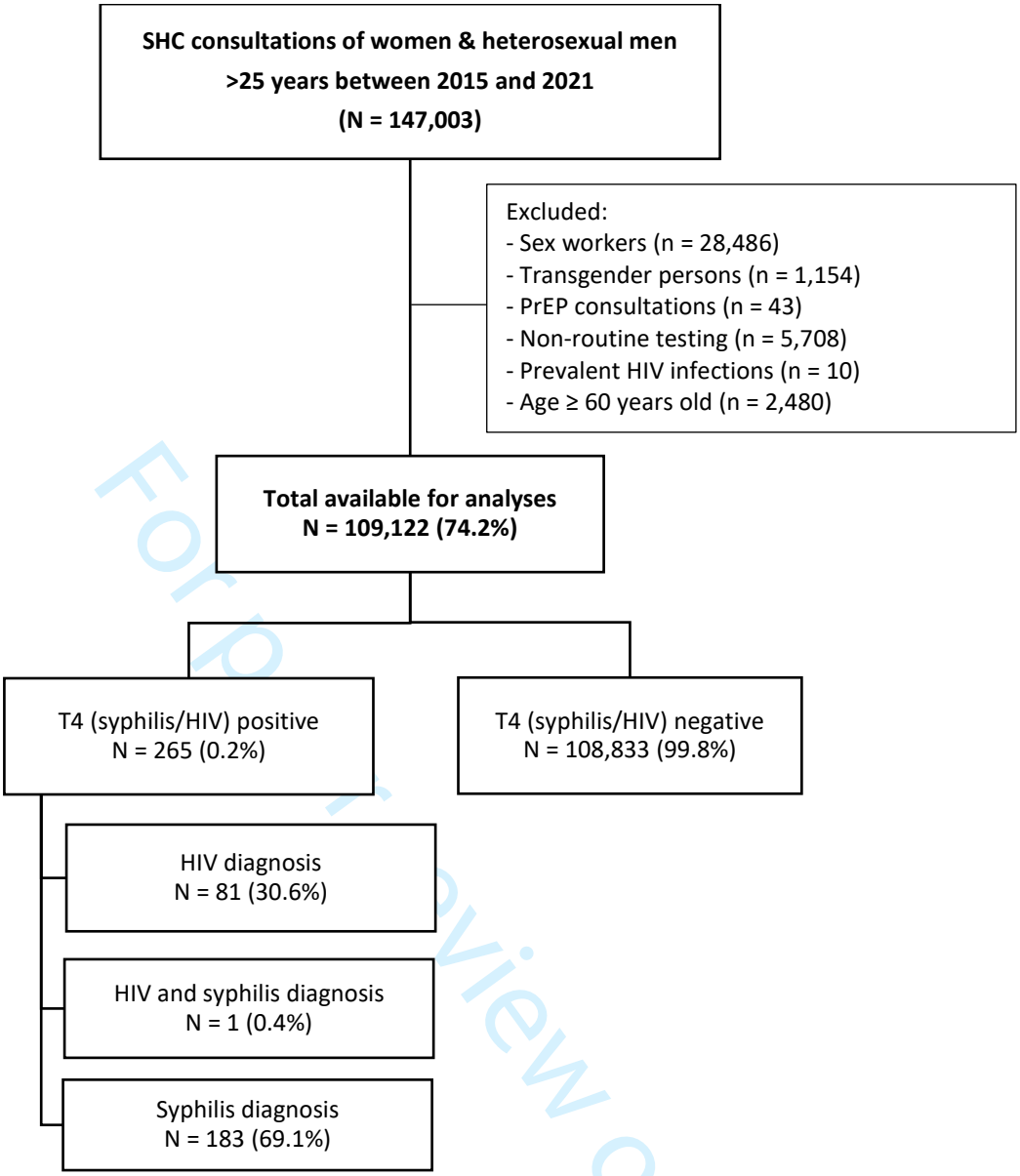

Figure 1 Flowchart of the included consultations in the study population. SHC, Sexual Health Center; T4, tested for chlamydia, gonorrhoea, syphilis and HIV.

Supplemental table S1. Determinants of an HIV and/or syphilis diagnosis among women and heterosexual men aged >25 years visiting Dutch sexual health centers between 2015-2021, stratified by STI symptoms

	Overall model	**No reported STI symptoms**	**Reported STI symptoms - overall**	**Reported STI symptoms - HIV/syphilis specific**
	Adjusted OR (95% CI)	**Adjusted OR (95% CI)**	**Adjusted OR (95% CI)**	**Adjusted OR (95% CI)**
Total number of HIV and/or SYPH positive	242	94	78	70
Total number of consultations*	103,822	58,454	44,805	563
Sex				
Women	1	1	1	1
Men	**2.2 (1.6-3.0)**	1.6 (1.0-2.4)	**2.3 (1.4-3.9)**	**2.5 (1.3-5.0)**
Age				
26-29 years	1	1	1	1
30+ years	**1.8 (1.3-2.5)**	1.7 (1.0-2.9)	1.6 (1.0-2.7)	1.9 (1.0-3.7)
CT and/or GO positivity at same consultation				
No	-	-	-	-
Yes	-	-	-	-
Self-reported GO/CT/SYPH in past year				
No	-	-	-	1
Yes	-	-	-	**4.2 (2.0-8.5)**
Education level†				
High	1	1	1	1
Low/middle	**2.8 (2.0-4.0)**	**2.3 (1.4-3.8)**	**3.9 (2.2-7.3)**	**2.5 (1.4-4.8)**
Unknown/other	**4.2 (2.7-6.4)**	**3.9 (2.1-7.1)**	**5.3 (2.4-11.6)**	**2.5 (1.0-6.0)**
Number of sex partners in past six months				
0-1	1	1	1	-
2-3	**0.7 (0.5-0.9)**	**0.4 (0.3-0.7)**	1.0 (0.6-1.7)	-

4+	**0.4 (0.3-0.6)**	**0.3 (0.2-0.6)**	**0.4 (0.2-0.8)**	-
Condom use‡				
No	1	-	-	1
Yes	**0.6 (0.4-0.9)**	-	-	0.4 (0.2-1.0)
Originating from STI/HIV-endemic area§				
No	-	-	-	-
Yes	-	-	-	-
Received partner notification				
No	1	1	1	1
Yes	**0.5 (0.3-0.8)**	0.7 (0.4-1.3)	0.6 (0.3-1.1)	0.2 (0.0-1.0)
Yes, notified for HIV/syphilis	**18.3 (13.2-25.2)**	**30.7 (19.4-49.1)**	**37.7 (20.3-66.6)**	**4.1 (2.2-7.6)**
Partner in risk group**				
No	-	-	-	-
Yes	-	-	-	-
Client of commercial sex worker				
No	-	-	-	-
Yes, in past 6 months	-	-	-	-
Unknown	-	-	-	-

Bold = <0.05.
OR, Odds Ratio; CT, chlamydia; GO, gonorrhoea; SYPH, syphilis; STI, sexually transmitted infections.
* Consultations with missing values <5% on at least one of the determinants were excluded from the analyses.
† Low/middle level of education: no education, elementary school, lbo, mavo, vmbo, mbo-1, havo, vwo, gymnasium. High level education: all other education levels.
‡ Before 2018, condom use was asked regarding last sexual contact. In 2018 this changed to the past 6 months and during vaginal and/or anal sex.
§ STI/HIV-endemic areas include Asia, Africa, the Dutch Caribbean islands, Middle and South America.
** For heterosexual men: partner originating from a high STI/HIV endemic region. For women: partner originating from a high STI/HIV endemic region or a male partner who had sex with men.

Supplemental table S2. Determinants of HIV and/or syphilis diagnosis among women and heterosexual men aged >25 years visiting Dutch sexual health centers between 2015-2021, stratified by partner notification

	Overall model Adjusted OR (95% CI)	**No partner notification Adjusted OR (95% CI)**	**Partner notification - overall Adjusted OR (95% CI)**	**Partner notification - HIV/syphilis specific Adjusted OR (95% CI)**
Total number of HIV and/or SYPH positive	242	129	23	90
Total number of consultations*	103,822	67,946	34,370	1,506
Sex				
Women	1	1	1	-
Men	**2.2 (1.6-3.0)**	**2.8 (1.8-4.5)**	2.3 (0.9-6.4)	-
Age				
26-29 years	1	1	-	-
30+ years	**1.8 (1.3-2.5)**	**1.7 (1.2-2.7)**	-	-
CT and/or GO positivity at same consultation				
No	-	-	-	1
Yes	-	-	-	**2.3 (1.1-4.5)**
Self-reported GO/CT/SYPH in past year				
No	-	1	-	-
Yes	-	1.6 (0.9-2.7)	-	-
Education level†				
High	1	1	1	1
Low/middle	**2.8 (2.0-4.0)**	**2.6 (1.7-4.1)**	**2.8 (1.2-7.2)**	**3.5 (2.0-6.7)**
Unknown/other	**4.2 (2.7-6.4)**	**4.2 (2.5-7.2)**	1.4 (0.1-7.8)	**4.8 (2.3-10.4)**
Number of sex partners in past six months				
0-1	1	1	-	1
2-3	**0.7 (0.5-0.9)**	**0.6 (0.4-0.8)**	-	0.9 (0.5-1.4)
4+	**0.4 (0.3-0.6)**	**0.4 (0.2-0.6)**	-	**0.4 (0.2-0.7)**
Condom use‡				
No	1	-	-	1

Yes	**0.6 (0.4-0.9)**	-	-	**0.4 (0.2-0.9)**
Originating from STI/HIV-endemic area§				
No	-	-	-	-
Yes	-	-	-	-
Reported STI symptoms				
No	1	1	1	1
Yes, overall STI symptoms	1.3 (1.0-1.8)	**1.6 (1.1-2.6)**	1.3 (0.5-3.1)	1.6 (0.8-2.8)
Yes, HIV/syphilis symptoms	**34.9 (24.1-50.2)**	**88.0 (54.5-143.3)**	**28.9 (1.6-150.0)**	**9.9 (5.5-17.5)**
Partner in risk group**				
No	-	-	-	1
Yes	-	-	-	**0.6 (0.3-0.9)**
Client of commercial sex worker				
No	-	1	-	1
Yes, in past 6 months	-	1.4 (0.8-2.4)	-	0.8 (0.2-2.6)
Unknown	-	**2.6 (1.1-5.3)**	**-**	**0.1 (0.0-0.7)**

Bold = <0.05.
OR, Odds Ratio; CT, chlamydia; GO, gonorrhoea; SYPH, syphilis; STI, sexually transmitted infections.
* Consultations with missing values <5% on at least one of the determinants were excluded from the analyses.
† Low/middle level of education: no education, elementary school, lbo, mavo, vmbo, mbo-1, havo, vwo, gymnasium. High level education: all other education levels.
‡ Before 2018, condom use was asked regarding last sexual contact. In 2018 this changed to the past 6 months and during vaginal and/or anal sex.
§ STI/HIV-endemic areas include Asia, Africa, the Dutch Caribbean islands, Middle and South America.
** For heterosexual men: partner originating from a high STI/HIV endemic region. For women: partner originating from a high STI/HIV endemic region or a male partner who had sex with men.

Supplemental table S3. Sensitivity analyses for determinants of HIV and/or syphilis diagnosis among women and heterosexual men aged >25 years visiting Dutch sexual health centers between 2015-2021

	Adjusted OR (95% CI) overall model	Adjusted OR (95% CI) HIV infection	Adjusted OR (95% CI) Syphilis infection	Adjusted OR (95% CI) including anal sex, 2016-2021	Adjusted OR (95% CI) excluding COVID-years, 2015-2019
Total number of HIV and/or SYPH positive	242	74	169	210	165
Total number of consultations*	103,822	103,822	103,822	82,885	86,223
Sex					
Women	1	1	1	1	1
Men	**2.2 (1.6-3.0)**	**2.0 (1.2-3.3)**	**2.4 (1.7-3.4)**	**2.5 (1.8-3.5)**	**1.8 (1.3-2.6)**
Age					
26-29 years	1	1	1	1	1
30+ years	**1.8 (1.3-2.5)**	1.7 (1.0-3.1)	**1.9 (1.3-2.8)**	**1.8 (1.3-2.6)**	1.4 (1.0-2.1)
CT and/or GO positivity at same consultation					
No	-	1	-	-	1
Yes	-	1.7 (0.8-3.0)	-	-	1.4 (0.9-2.3)
Self-reported GO/CT/SYPH in past year					
No	-	1	1	1	-
Yes	-	0.4 (0.1-1.1)	**2.0 (1.2-3.2)**	1.5 (0.9-2.4)	-
Education level†					
High	1	1	1	1	1
Low/middle	**2.8 (2.0-4.0)**	**2.0 (1.1-3.7)**	**3.3 (2.2-4.9)**	**2.4 (1.7-3.5)**	**2.8 (1.9-4.2)**
Unknown/other	**4.2 (2.7-6.4)**	**5.2 (2.7-10.2)**	**3.3 (1.9-5.7)**	**3.9 (2.5-6.1)**	**4.9 (2.9-8.0)**
Number of sex partners in past six months					
0-1	1	1	1	1	1
2-3	**0.7 (0.5-0.9)**	**0.5 (0.3-0.8)**	0.9 (0.6-1.3)	**0.6 (0.4-0.9)**	0.7 (0.5-1.0)
4+	**0.4 (0.3-0.6)**	**0.3 (0.1-0.6)**	**0.5 (0.3-0.8)**	**0.4 (0.3-0.6)**	**0.4 (0.3-0.6)**

Condom use‡					
No	1	-	1	-	-
Yes	**0.6 (0.4-0.9)**	-	0.6 (0.4-1.0)	-	-
Originating from STI/HIV-endemic area§					
No	-	1	1	-	-
Yes	-	**3.1 (1.8-5.4)**	**0.5 (0.3-0.7)**	-	-
Received partner notification					
No	1	1	1	1	1
Yes	**0.5 (0.3-0.8)**	0.7 (0.3-1.3)	**0.4 (0.2-0.7)**	**0.4 (0.2-0.6)**	0.6 (0.3-1.0)
Yes, notified for HIV/syphilis	**18.3 (13.2-25.2)**	**23.4 (13.7-39.3)**	**17.4 (11.6-25.8)**	**15.4 (10.9-21.8)**	**20.4 (13.7-30.1)**
Reported STI symptoms					
No	1	-	1	1	1
Yes, overall STI symptoms	1.3 (1.0-1.8)	-	**1.9 (1.3-2.9)**	1.2 (0.9-1.7)	1.3 (0.9-2.0)
Yes, HIV/syphilis symptoms	**34.9 (24.1-50.2)**	-	**64.4 (41.9-99.6)**	**30.7 (21.0-44.7)**	**36.6 (23.1-57.4)**
Partner in risk group**					
No	-	-	-	-	-
Yes	-	-	-	-	-
Client of commercial sex worker					
No	-	-	-	-	-
Yes, in past 6 months	-	-	-	-	-
Unknown	-	-	-	-	-
Anal sex in past 6 months					
No	NA	NA	NA	1	NA
Yes, either insertive and/or receptive	NA	NA	NA	**1.6 (1.1-2.2)**	NA
Unknown	NA	NA	NA	1.1 (0.6-1.9)	NA

Bold = <0.05.
OR, Odds Ratio; CT, chlamydia; GO, gonorrhoea; SYPH, syphilis; STI, sexually transmitted infections; NA, not available.
* Consultations with missing values <5% on at least one of the determinants were excluded from the analyses.
† Low/middle level of education: no education, elementary school, lbo, mavo, vmbo, mbo-1, havo, vwo, gymnasium. High level education: all other education levels.

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** For heterosexual men: partner originating from a high STI/HIV endemic region. For women: partner originating from a high STI/HIV endemic region or a male partner who had sex with men.

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

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	4-5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	-
		(*e*) Describe any sensitivity analyses	6
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	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7 & 15-17
		(b) Indicate number of participants with missing data for each variable of interest	15-17
Outcome data	15*	Report numbers of outcome events or summary measures	15-17
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	7 & 16-17

		(*b*) Report category boundaries when continuous variables were categorized	-
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7-8
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
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	8-9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	10
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	11

*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.