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Oropharyngeal gonorrhoea among heterosexual men and women at a sexual health centre in Rotterdam, the Netherlands, 2023: reservoir for transmission?

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ABSTRACT

Background Sexual health centres (SHCs) in the Netherlands report a surge in gonorrhoea, especially among young women (notably oropharyngeal) and men who have sex with women (MSW) since the second half of 2022. MSW are not routinely oropharyngeal tested, and women only when reporting oral sex. This cross-sectional study aimed to assess oropharyngeal gonorrhoea in MSW and women, and potential underdiagnosis.

Methods From 10 August to 10 November 2023, the SHC in Rotterdam, the Netherlands, extended its gonorrhoea testing protocol, requiring oropharyngeal tests for all MSW and women. Positive cobas nucleic acid amplification test (NAAT) results were followed by culture sampling. Oropharyngeal infections were confirmed with a second NAAT (opa gene-based PCR), and for discrepancies a third NAAT (GeneXpert CT/NG test) was employed. The impact of extended testing on detection rates, along with the corresponding 95% CIs, was analysed.

Results The overall gonorrhoea detection rate was 6.4% (95% CI 4.7% to 8.8%) among MSW and 6.0% (95% CI 4.8% to 7.6%) among women, compared with 3.6% (95% CI 2.3% to 5.4%) and 6.0% (95% CI 4.8% to 7.6%) without expanded testing. Oropharyngeal rates were 6.4% (95% CI 4.4% to 9.2%) for MSW and 4.3% (95% CI 3.2% to 5.7%) for women. Highest positivity was among individuals notified, <25 years, without migratory background, with lower educational levels and more sex partners. Oropharyngeal cultures confirmed viable gonorrhoea in 39.1% of MSW and 35.5% of women. False positives were 7.4% among MSW and 10.8% among women. Confirmed oropharyngeal gonorrhoea positivity rate was 5.9% (95% CI 4.0% to 8.6%) among MSW and 3.9% (95% CI 2.8% to 5.2%) among women.

Conclusion Oropharyngeal gonorrhoea is common and currently underdiagnosed among MSW. The impact of this underdiagnosis on transmission dynamics under the current testing policy remains unclear. Further research is needed to inform prevention and control strategies, especially given the recent surge in gonorrhoea.

INTRODUCTION

In the Netherlands, sexual health centres (SHCs) play a crucial role testing for sexually transmitted infections (STIs). SHCs provide free and anonymous testing for populations at increased risk of STIs, supplementing the regular healthcare provided

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Research suggests that oropharyngeal gonorrhoea may be transmitted through tongue kissing and saliva exchange. Since mid-2022, there is an increase in gonorrhoea diagnoses in the Netherlands and other countries, particularly among women and men who have sex with women (MSW). The most significant rise has been observed in oropharyngeal infections among women. Current guidelines do not recommend routine oropharyngeal testing for MSW and suggest it for women only if they report oral sex, which potentially leads to underdiagnosis. In response to the surge in gonorrhoea cases, the sexual health centre in Rotterdam, the Netherlands, expanded testing to include oropharyngeal swabs for all MSW and women to estimate gonorrhoea prevalence and investigate potential underdiagnosis.

WHAT THIS STUDY ADDS

⇒ Our findings reveal that the current testing policy leads to underdiagnosis of gonorrhoea among MSW. The overall detection rate increased from 3.6% with regular testing to 6.4% with extended oropharyngeal testing. For women, the detection rate remained unchanged at 6.0%. A notable proportion of infections were isolated in the oropharynx, with a majority confirmed and over one-third proven viable. This suggests that oropharyngeal gonorrhoea may be an under-recognised source of ongoing transmission.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our findings highlight the inadequacy of current testing policies in detecting oropharyngeal gonorrhoea. The substantial increase in detection rates with extended oropharyngeal testing in MSW, along with a significant proportion of viable infections, suggests a hidden reservoir that may contribute to ongoing transmission. The results can enhance mathematical models of gonorrhoea transmission and underscore the need for further research to improve prevention and control strategies. This is especially important considering the current surge in gonorrhoea cases.

by general practitioners. SHC surveillance data, gathered from all SHCs in the Netherlands, revealed a noteworthy trend in gonorrhoea. In contrast to relatively stable rates of chlamydia, the number of gonorrhoea diagnoses and the gonorrhoea detection rate have been on the rise since the second half of 2022. This surge is especially prominent among women (from 2.3% in 2022 to 4.1% in 2023) and cisgender men who exclusively have sex with women (MSW; from 2.4% to 3.5%) under the age of 25 with a high educational level and Dutch nationality, but is not observed among men who have sex with men (MSM).¹ An increase in gonorrhoea cases among young heterosexual people is also observed in other European countries.^{2–5}

In addition to this gonorrhoea surge, there is a shift in anatomical site of gonorrhoea infection. Among women at Dutch SHCs, the increase was especially seen at the oropharyngeal site (1.7% in 2021 vs 4.5% in 2023).¹ The increase in gonorrhoea cases, shifting population characteristics and the change in anatomical location are not yet fully understood. Test strategies have not been altered. Both global and local guidelines recommend gonorrhoea testing for women through vaginal testing, with additional anorectal and oropharyngeal testing based on reported sexual behaviour and exposure.^{6–9} It is recommended to test MSM both genital, oropharyngeal and rectal irrespective of reported exposure. Meanwhile, Dutch guidelines do not consider oral sex in MSW as a risk for gonorrhoea transmission, and, therefore, only urogenital testing is recommended for MSW. Consequently, the prevalence of oropharyngeal gonorrhoea is unknown among MSW.

In recent years, the potential role of oropharyngeal gonorrhoea in transmission is debated, with a particular focus on the role of kissing.^{10–16} Increasing evidence suggests that infections can be transmitted between two oropharynges via tongue kissing and saliva exchange.¹⁰ Oropharyngeal testing among individuals notified for gonorrhoea has shown positive results in 35–46% of women and 18–20% of MSW.^{17,18} A study examining individuals with urogenital gonorrhoea and subsequent oropharyngeal testing found oropharyngeal infections in 29.1% of MSW and 45.6% of women.¹⁹ These findings emphasise that infections are missed when oropharyngeal testing is not performed for MSW and women.

Recognising the rising trend in gonorrhoea diagnoses, particularly among heterosexual women and MSW, we extended our regular testing protocol at the SHC of the Public Health Service of the Greater Rotterdam Area, the Netherlands. This included oropharyngeal testing for all MSW and women over a specific period. We aimed to provide a prevalence estimate for oropharyngeal gonorrhoea in MSW and investigate potential underdiagnosis in both MSW and women. Underdiagnosis of oropharyngeal gonorrhoea may contribute to the overall increase in gonorrhoea cases.

METHODS

Data source

For this cross-sectional observational study, we used surveillance data of all STI consultations from the SHC in Rotterdam, the Netherlands. At each STI consultation, information on demographics, sexual behaviour, symptoms, being a contact of a person with gonorrhoea, STI history and laboratory test results for STI are systematically recorded.

Procedure

Between 10 August and 10 November 2023 (pilot period), the gonorrhoea testing protocol was extended. SHC staff was

instructed to perform oropharyngeal tests for all MSW and women in response to the national increase in gonorrhoea cases (further referred as pilot). Clients were not obligated to undergo additional testing. Clients self-sampled urine, rectal and vaginal specimens. Oropharyngeal swabbing was mainly self-collected and occasionally performed by the healthcare professional.

The cobas CT/NG test, a nucleic acid amplification test (NAAT), was performed on the cobas 6800 platform (Roche Diagnostics) for detecting and diagnosing *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (NG). If NAAT positive, ceftriaxone treatment is intramuscularly administered at a dosage of 500 mg, which is the first-choice policy. However, due to shortages of 500 mg vials during the study period, the alternative guideline was to administer 1000 mg when 500 mg vials were unavailable. For pharyngeal infections, the ceftriaxone dosage is standard 1000 mg. Clients with clinical gonorrhoea and severe complaints, or those who have been informed (notified) that they were in contact with someone diagnosed with gonorrhoea within the last 14 days, are promptly treated without waiting for NAAT diagnosis. Before treatment administration for clients diagnosed by the initial NAAT, gonorrhoea culture sampling is conducted at positive anatomical sites to determine antibiotic susceptibility for surveillance purposes. In case of direct treatment, culture sampling is performed concurrently with NAAT sampling. Culture specimens were directly inoculated onto Chocolate agar PolyviteX VCAT3 (BioMérieux) agar plates and placed inside a candle jar in an incubator at the SHC. After incubation, cultures were transferred to the laboratory within 24–50 hours.

To rule out false positive NAAT outcomes in the oropharyngeal site, we retrospectively introduced confirmation tests based on cobas cycle threshold (Ct) values. Ct values serve as a surrogate marker for bacterial load, with lower Ct values indicating higher load. Gonorrhoea NAAT cobas positive samples with a Ct value >35, and those with a Ct value ≤35 but without a positive culture result, underwent second laboratory-developed NAAT test known as the ‘opa’ gene-based PCR.²⁰ If the two NAAT results were discordant, a third NAAT was performed (Xpert CT/NG test (Cepheid GeneXpert)). Samples were considered to be true positive if two out of three test results were positive.

Data analysis

Descriptive analyses were used to describe the characteristics of the study population within the pilot. Detection rates of gonorrhoea were calculated along with their corresponding 95% CIs. X² tests are used to compare the detection rate with and without oropharyngeal gonorrhoea testing. The Ct values obtained by the cobas NAAT were compared with the culture result. The analyses were focused on MSW and women, considering the extended testing protocol. All analyses were performed using RStudio (V.4.3.1). Statistical significance was defined as p<0.05.

RESULTS

Population characteristics

During the pilot period, the SHC Rotterdam conducted 3317 STI test consultations with a gonorrhoea test (49.7% with MSM or gender diverse individuals, 33.5% with women, 16.9% with MSW). MSM and gender diverse individuals were excluded from the pilot as they are standard oropharyngeal tested. Three-quarters of the MSW (75.4%; n=442/560) underwent oropharyngeal testing. The reasons for not testing the remaining MSW were not reported. Among women, this was 97.3% (n=1070/1110), with the majority already being standardly oropharyngeal tested because of their history of engaging in oral

Table 1 Characteristics of MSW clients undergoing regular testing (regular) and extended oral testing (pilot)

Characteristics	Overall n (%)	Regular n (%)	Pilot n (%)	P value regular versus pilot
Total	560 (100.0)	138 (100.0)	422 (100.0)	
Age				0.278
Mean (SD)	26.6 (7.8)	27.3 (9.3)	26.4 (7.3)	
Median (min, max)	24.0 (17.0, 70.0)	24.0 (17.0, 70.0)	24.0 (17.0, 66.0)	
Age category				0.820
<25 years	307 (54.8)	74 (53.6)	233 (55.2)	
25 years and older	253 (45.2)	64 (46.4)	189 (44.8)	
Non-western migratory background				0.142
Yes, first generation	108 (19.3)	34 (24.6)	74 (17.5)	
Yes, second generation	143 (25.5)	36 (26.1)	107 (25.4)	
No	309 (55.2)	68 (49.3)	241 (57.1)	
Educational level*				0.241
Low	56 (10.0)	18 (13.0)	38 (9.0)	
Middle	179 (32.0)	48 (34.8)	131 (31.0)	
High	306 (54.6)	66 (47.8)	240 (56.9)	
Other/unknown	19 (3.4)	6 (4.3)	13 (3.1)	
Notified for any STI	189 (33.8)	43 (31.2)	146 (34.6)	0.524
Notified for chlamydia	144 (25.7)	36 (26.1)	108 (25.6)	0.997
Notified for gonorrhoea	19 (3.4)	4 (2.9)	15 (3.6)	0.921
Any STI-related complaints	195 (34.8)	47 (34.1)	148 (35.1)	0.909
Number of sex partners in the last 6 months				0.898
0	6 (1.1)	1 (0.7)	5 (1.2)	
1	122 (21.8)	28 (20.3)	94 (22.3)	
2	102 (18.2)	22 (15.9)	80 (19.0)	
3–5	219 (39.1)	60 (43.5)	159 (37.7)	
6–10	96 (17.1)	24 (17.4)	72 (17.1)	
≥10	14 (2.5)	3 (2.2)	11 (2.6)	
Unknown	1 (0.2)	0 (0.0)	1 (0.2)	
Sex worker	3 (0.5)	0 (0.0)	3 (0.7)	0.748
Urogenital gonorrhoea test	560 (100)	138 (100)	422 (100)	1.000
Anorectal gonorrhoea test	5 (0.9)	0 (0.0)	5 (1.2)	0.445
Oropharyngeal gonorrhoea test	422 (75.4)	0 (0.0)	422 (100)	<0.001

*Educational level: Low—no education, elementary school, (pre-)vocational education. Middle—senior secondary education, pre-university education. High—university of applied sciences, university.
max, maximum; min, minimum; MSW, men who have sex with women; SD, standard deviation; STI, sexually transmitted infection.

sex. **Table 1** describes and compares MSW undergoing extended testing (pilot) versus those tested according to the standard protocol. Pilot MSW clients had a median age of 24 years (min 17 years and max 66 years); the majority had a western migratory background (57.1%) and were highly educated (56.9%). Pilot MSW clients did not differ from regular MSW clients (**table 1**). In online supplemental table 1, women within the pilot period are described.

Gonorrhoea positivity by first NAAT

The overall gonorrhoea detection rate based on the initial NAAT test was 6.4% (95% CI 4.7% to 8.8%) among MSW and 6.0% (95% CI 4.8% to 7.6%) among women (**table 2**). At the oropharyngeal location, the detection rates were 6.4% (95% CI 4.4% to 9.2%) for MSW and 4.3% (95% CI 3.2% to 5.7%) for women. An overview of the number of gonorrhoea diagnoses per anatomical location is presented in **figure 1**, and the characteristics of positive gonorrhoea cases are shown in online supplemental table 2. Among MSW, 44.4% (n=16/36) of all gonorrhoea infections were isolated in the pharynx. Specifically, for MSW with an oropharyngeal diagnosis, 59.3% (n=16/27)

were solely diagnosed at the oropharyngeal site. This means that the overall gonorrhoea detection rate during the pilot period excluding oropharyngeal testing was 3.6% (95% CI 2.3% to 5.4%) for MSW. The overall gonorrhoea detection rate of 6.0% (95% CI 4.8% to 7.6%) among women clients remained consistent with and without additional oropharyngeal testing. Two women who would typically only receive a vaginal test and diagnosis have now also been diagnosed with an oral infection as part of the pilot.

The highest overall and oropharyngeal positivity rates were observed among individuals notified for gonorrhoea, <25 years, without migratory background, with lower educational levels and those with a higher number of sex partners (**table 2**). For MSW, a gonorrhoea diagnosis overall was most common among those with lower educational levels, whereas oropharyngeal gonorrhoea is more frequently diagnosed among those with higher educational levels. For women, the detection rates, both overall and specifically for oropharyngeal gonorrhoea, are highest among those with lowest educational levels.

Table 2 Gonorrhoea positivity rate per characteristic among MSW and women

Characteristics	Overall Any location n/N (%; 95% CI)	Overall Oropharyngeal n/N (%; 95% CI)	MSW Any location n/N (%; 95% CI)	MSW Oropharyngeal n/N (%; 95% CI)	Women Any location n/N (%; 95% CI)	Women Oropharyngeal n/N (%; 95% CI)
Total	103/1670 (6.2; 5.1 to 7.4)	73/1492 (4.9; 3.9 to 6.1)	36/560 (6.4; 4.7 to 8.8)	27/422 (6.4; 4.4 to 9.2)	67/1110 (6.0; 4.8 to 7.6)	46/1070 (4.3; 3.2 to 5.7)
Age category						
<25 years	77/1045 (7.4; 5.9 to 9.1)	56/942 (5.9; 4.6 to 7.6)	25/307 (8.1; 5.6 to 11.7)	21/233 (9.0; 6.0 to 13.4)	52/738 (7.0; 5.4 to 9.1)	35/709 (4.9; 3.6 to 6.8)
25 years and older	26/625 (4.2; 2.9 to 6.0)	17/550 (3.1; 1.9 to 4.9)	11/253 (4.3; 2.4 to 7.6)	6/189 (3.2; 1.5 to 6.8)	15/372 (4.0; 2.5 to 6.5)	11/361 (3.0; 1.7 to 5.4)
Non-western migratory background						
Yes, first generation	14/281 (5.0; 3.0 to 8.2)	6/242 (2.5; 1.1 to 5.3)	6/108 (5.6; 2.6 to 11.6)	2/74 (2.7; 0.7 to 9.3)	8/173 (4.6; 2.4 to 8.9)	4/168 (2.4; 0.9 to 5.9)
Yes, second generation	15/366 (4.1; 2.5 to 6.6)	9/325 (2.8; 1.5 to 5.2)	9/143 (6.3; 3.3 to 11.5)	6/107 (5.6; 2.6 to 11.7)	6/223 (2.7; 1.2 to 5.7)	3/218 (1.4; 0.4 to 3.9)
No	73/1021 (7.1; 5.7 to 8.9)	57/923 (6.2; 4.8 to 7.9)	21/309 (6.8; 4.5 to 10.2)	19/241 (7.9; 5.1 to 12.0)	52/712 (7.3; 5.6 to 9.4)	38/682 (5.6; 4.1 to 7.6)
Unknown	1/2 (50.0; 9.5 to 90.5)	1/2 (50.0; 9.4 to 90.5)	–	–	1/2 (50.0; 9.4 to 90.5)	1/2 (50.0; 9.4 to 90.5)
Educational level*						
Low	11/120 (9.2; 5.2 to 15.6)	5/97 (5.2; 2.2 to 11.5)	5/56 (8.9; 3.9 to 19.3)	2/38 (5.3; 1.5 to 17.3)	6/64 (9.4; 4.4 to 18.9)	3/59 (5.1; 1.7 to 13.9)
Middle	34/460 (7.4; 5.3 to 10.2)	20/400 (5.0; 3.3 to 7.6)	15/179 (8.4; 5.1 to 13.3)	9/131 (6.9; 3.7 to 12.5)	19/281 (6.8; 4.3 to 10.3)	11/269 (4.1; 2.3 to 7.1)
High	55/1037 (5.3; 4.1 to 6.8)	45/949 (4.7; 3.6 to 6.3)	16/306 (5.2; 3.2 to 8.3)	16/240 (6.7; 4.1 to 10.6)	39/731 (5.3; 3.9 to 7.2)	29/709 (4.1; 2.8 to 5.8)
Other/unknown	3/53 (5.7; 1.9 to 15.4)	3/46 (6.5; 2.2 to 17.5)	0/19 (0.0; 0.0 to 0.2)	0/13 (0.0; 0.0 to 0.2)	3/34 (8.8; 3.0 to 22.9)	3/33 (9.1; 3.1 to 23.5)
Notified for any STI	41/360 (11.4; 8.5 to 15.1)	33/314 (10.5; 7.6 to 14.4)	14/189 (7.4; 4.4 to 12.0)	12/146 (8.2; 4.8 to 13.8)	27/171 (15.8; 11.1 to 22.0)	21/168 (12.5; 8.3 to 18.3)
Notified for chlamydia	22/265 (8.3; 5.5 to 12.2)	17/227 (7.5; 4.7 to 11.7)	8/144 (5.6; 2.8 to 10.6)	7/108 (6.5; 3.2 to 12.8)	14/121 (11.6; 7.0 to 18.4)	10/119 (8.4; 4.6 to 14.8)
Notified for gonorrhoea	21/47 (44.7; 31.4 to 58.8)	17/43 (39.5; 26.4 to 54.4)	7/19 (36.8; 19.1 to 59.9)	6/15 (40.0; 19.8 to 64.2)	14/28 (50.0; 32.6 to 67.4)	11/28 (39.3; 23.5 to 57.6)
Any STI-related complaints	55/665 (8.3; 6.4 to 10.6)	37/608 (6.1; 4.4 to 8.3)	17/195 (8.7; 5.5 to 13.5)	12/148 (8.1; 4.7 to 13.6)	38/470 (8.1; 5.9 to 10.9)	25/460 (5.4; 3.7 to 7.9)
Number of sex partners in the last 6 months						
0	1/19 (5.3; 0.9 to 24.6)	1/15 (6.7; 1.8 to 29.8)	0/6 (0.0; 0.0 to 3.9)	0/5 (0.0; 0.0 to 43.4)	1/13 (7.7; 1.3 to 33.3)	1/10 (10.0; 2.8 to 40.4)
1	8/445 (1.8; 0.9 to 3.5)	6/401 (1.5; 0.7 to 3.2)	4/122 (3.3; 1.3 to 8.1)	4/94 (4.3; 0.0 to 10.4)	4/323 (1.2; 0.4 to 3.1)	2/307 (0.7; 0.0 to 2.3)
2	22/362 (6.1; 4.0 to 9.0)	12/331 (3.6; 2.1 to 6.2)	7/102 (6.9; 3.3 to 13.5)	5/80 (6.2; 0.0 to 13.8)	15/260 (5.8; 3.5 to 9.3)	7/251 (2.8; 1.4 to 5.6)
3–5	42/556 (7.6; 5.6 to 10.0)	32/487 (6.6; 4.7 to 9.1)	14/219 (6.4; 3.8 to 10.4)	11/159 (6.9; 0.0 to 11.9)	28/337 (8.3; 5.8 to 11.7)	21/328 (6.4; 4.2 to 9.6)
6–10	22/185 (11.9; 8.0 to 17.3)	16/161 (9.9; 6.2 to 15.5)	9/96 (9.4; 5.0 to 16.9)	5/72 (6.9; 0.0 to 15.2)	13/89 (14.6; 8.7 to 23.4)	11/89 (12.4; 7.0 to 20.7)
≥10	3/39 (7.7; 2.7 to 20.3)	2/35 (5.7; 1.6 to 18.6)	2/14 (14.3; 4.0 to 39.9)	2/11 (18.2; 0.0 to 47.7)	1/25 (4.0; 0.7 to 19.5)	0/24 (0.0; 0.0 to 13.8)
Unknown	5/64 (7.8; 3.4 to 17.0)	4/62 (6.5; 2.5 to 15.4)	0/1 (0.0; 0.0 to 0.8)	0/1 (0.0; 0.0 to 79.3)	5/63 (7.9; 3.4 to 17.2)	4/61 (6.6; 2.6 to 15.7)
Sex worker	5/70 (7.1; 3.1 to 15.6)	3/70 (4.3; 1.5 to 11.9)	1/3 (33.3; 6.1 to 79.2)	0/3 (0.0; 0.0 to 56.1)	4/67 (6.0; 2.3 to 14.4)	3/67 (4.5; 4.4 to 12.4)

*Educational level: Low—no education, elementary school, (pre-)vocational education. Middle—senior secondary education, pre-university education. High—university of applied sciences, university. MSW, men who have sex with women; STI, sexually transmitted infection.

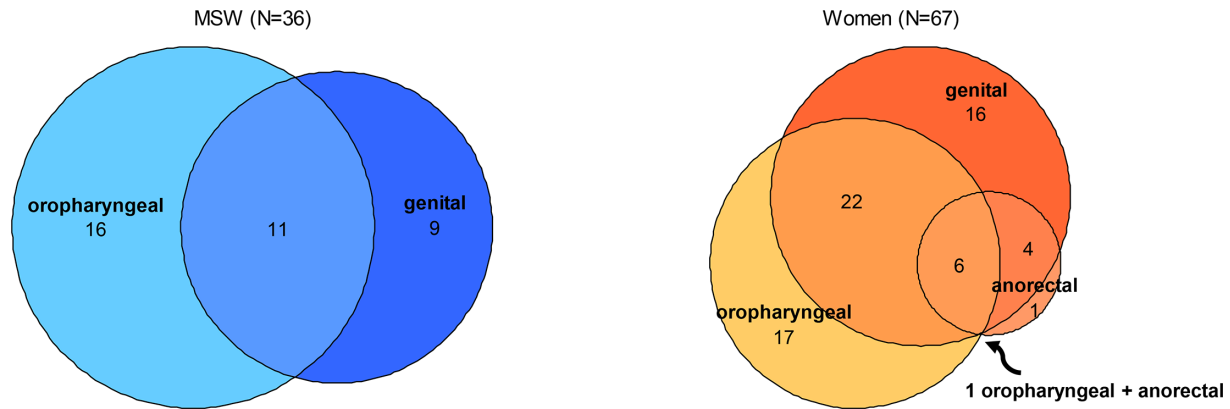


Figure 1 Number of positive gonorrhoea cases per anatomical location among men who have sex with women (MSW) and women.

Gonorrhoea positivity by culture

In total, seven NAAT-positive clients were cultured, either because of missed treatment consultation ($n=3$) or direct treatment ($n=4$). These seven clients accounted for nine missing cultures; 5.6% ($n=4/68$) of the urogenital cultures were missing and 6.8% ($n=5/73$) of the oropharyngeal site. In MSW, 83.3% ($n=15/18$, 2 lacking) urethral cultures tested positive, while 39.1% ($n=9/23$, 4 lacking) of the oral cultures yielded positive results. Among women, 56.5% ($n=26/46$, 2 lacking) of vaginal cultures conducted were positive, while 35.5% ($n=16/45$, 1 lacking) of oral cultures were positive. Of 16 NAAT-positive MSW with isolated oral gonorrhoea, 33.3% ($n=5/15$, 1 lacking) were cultured positive, as compared with 17.6% ($n=3/17$, 0 lacking) positive cultures among women with isolated oral gonorrhoea.

The median time between NAAT and culture sampling was 6 days (min 0 day, max 25 days, IQR 4–8 days). Lower Ct values were associated with higher culture positivity (online supplemental figure 1). No difference in Ct values was observed between individuals with and without STI-related complaints, nor across various time intervals between NAAT and culture sampling.

Validation with opa gene-based PCR and/or GeneXpert

Figure 2 outlines the flow chart of MSW and women who tested positive for oropharyngeal gonorrhoea with the cobas NAAT, validated by opa gene-based PCR and GeneXpert. Among MSW, two out of the 27 samples (7.4%) could not be confirmed, both of which were isolated oropharyngeal samples. This yields an oropharyngeal gonorrhoea positivity rate of 5.9% (95% CI 4.0% to 8.6%) among confirmed cases. Among women, five out of 46 (10.8%) oral samples could not be confirmed, with three of them being isolated oropharyngeal cases. The oropharyngeal gonorrhoea positivity rate based on confirmed cases was 3.9% (95% CI 2.8% to 5.2%) for women.

DISCUSSION

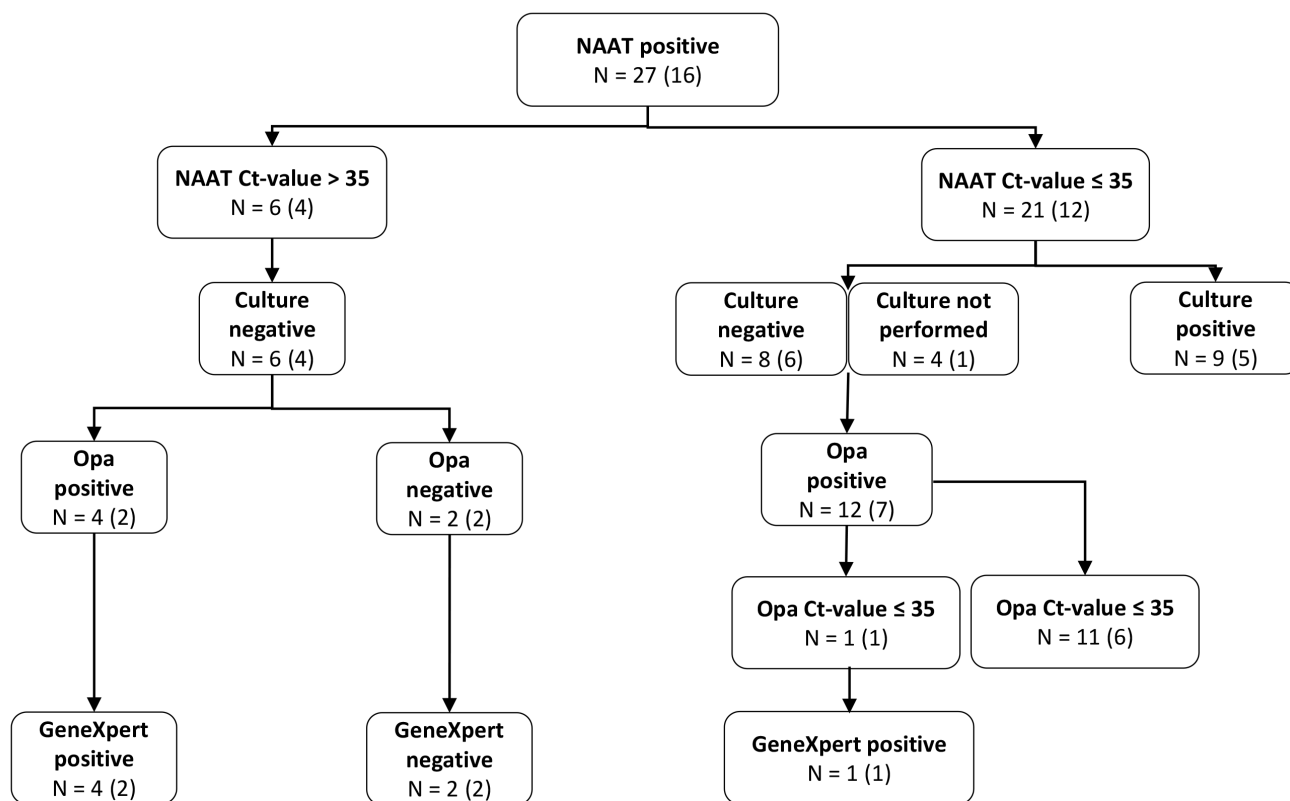
This cross-sectional study assessed the detection rate and potential underdiagnosis of oropharyngeal gonorrhoea, focusing on MSW and women. Among MSW, the overall gonorrhoea detection rate increased from 3.6% (regular testing) to 6.4% (extended oropharyngeal testing). At the oropharyngeal site, the detection rate was 6.4%. A notable proportion (44.4%) of all gonorrhoea cases were isolated in the pharynx. Of the oropharyngeal infections among MSW, 39.1% yielded positive cultures, and among isolated oropharyngeal infections this was 33.3%. Among women, the overall gonorrhoea detection rate remained

6.0% despite additional oropharyngeal testing. The oropharyngeal detection rate was 4.3%, with 35.5% of the oropharyngeal cultures and 17.6% of the isolated oropharyngeal cultures testing positive. We used opa gene-based PCR assay and GeneXpert to confirm the presence of gonorrhoea, finding a small proportion false positives (7.4% among MSW and 10.8% among women). This resulted in a confirmed oropharyngeal gonorrhoea positivity rate of 5.9% among MSW and 3.9% among women.

The notable rise in gonorrhoea detection rate on extending oropharyngeal testing in MSW highlights underdiagnosis within this population under current testing protocols. The oropharyngeal detection rate among MSW was even higher than that among women, for which there is no clear explanation, as systematic oral testing of our MSW population had not been conducted previously. Women are typically routinely tested for oral gonorrhoea due to reporting oral sex (95% report oral sex); their inclusion in expanding testing did not notably impact detection rates or treatment strategies. Recent studies at SHCs in Australia and the USA have shown that oropharyngeal gonorrhoea is common among women and MSW who are notified for gonorrhoea.^{17 18} Chow *et al* observed oropharyngeal gonorrhoea detection rates between 18% (MSW) and 46% (women).¹⁷ Similarly, McLaughlin *et al* identified that around 30% of gonorrhoea contacts had a gonorrhoea infection at the pharynx.¹⁸ Although our overall detection rate among SHC visitors was much lower than these studies, our detection rate of 40% among notified women and MSW was comparable. Additionally, in line with these studies, we observed a high proportion of isolated oropharyngeal infections. Chow *et al* found among notified gonorrhoea contacts that 89% of MSW and 40% of women had isolated oral infections.¹⁷ Although proportions are not specifically for gonorrhoea contacts, they were more comparable with McLaughlin *et al* (44% vs 36% in MSW and 25% vs 19% in women).¹⁸

The contribution of oropharyngeal gonorrhoea infections to transmission is subject to ongoing debate, with a specific emphasis on the role of kissing.^{10–16} The high proportion of isolated infections in our study and previous studies, alongside the surge in gonorrhoea infections since 2022 in the Netherlands and other European countries—particularly among young heterosexual individuals^{2–5} and most pronounced orally¹—has sparked inquiries into the potential significance of the pharyngeal reservoir in transmission dynamics. Mathematical model studies among MSM have suggested that pharyngeal infections could contribute to onward transmission.^{21 22} The extent hereof among heterosexual individuals is understudied. MSW are not routinely tested for oropharyngeal infections, resulting in a lack

a MSW



b Women

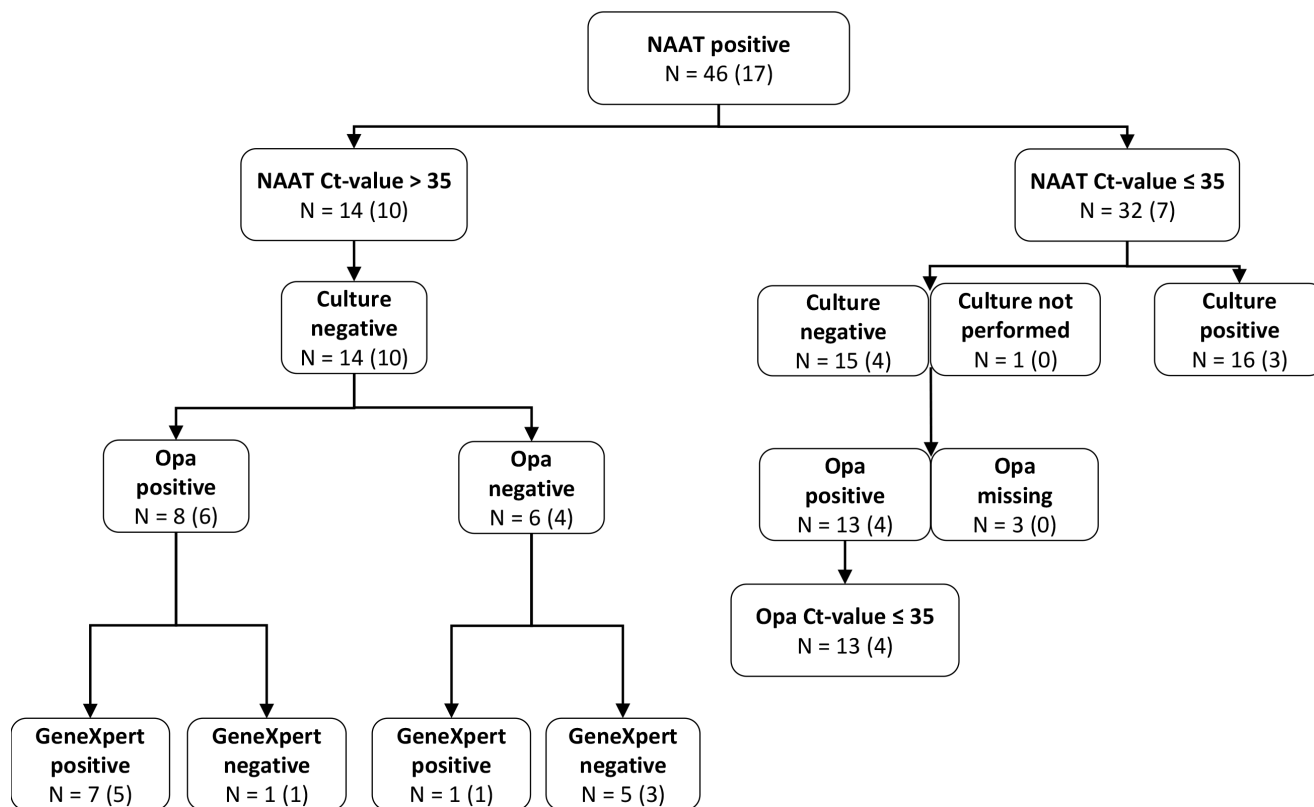


Figure 2 Overview of initial cobas NAAT-positive samples at the oropharyngeal site (with isolated samples) cultured and validated with opa gene-based PCR and GeneXpert: (a) MSW and (b) women. Ct, cycle threshold; MSW, men who have sex with women; NAAT, nucleic acid amplification test; Opa, opa gene-based PCR.

of comprehensive prevalence data for modelling studies. Modelling studies involving heterosexual individuals are likely necessary before any adjustments to testing policies in the Netherlands will be implemented. Currently, the Netherlands is cautious regarding oral testing, as oral gonorrhoea is not considered to play a major role in transmission and in the context of antibiotic resistance.

Our study provides valuable input for mathematical modelling studies that examine heterosexual transmission dynamics. Moreover, additional behavioural data are imperative for these transmission models. Notably, kissing and certain forms of oral sex, such as cunnilingus, are not assessed at SHC in the Netherlands, nor are they commonly assessed in clinics elsewhere. Our study may serve as a first step towards documenting oral sex practices for all SHC clients in the Netherlands, not just for women and MSM. Almost everyone kisses,¹¹ making its reporting of limited value in understanding transmission dynamics. However, reporting specific practices such as cunnilingus may provide additional valuable insights. Even with behavioural data, it remains a major challenge to differentiate the impact of various behaviours in transmission due to their overlap in real-life setting.

In addition to providing prevalence estimates suitable for mathematical models, this study has shed light on the viability of gonorrhoea in the pharynx. Viability is an important factor for comprehensive understanding of its impact on transmission. The cobas NAAT test, used for diagnosis and treatment at the SHC, is superior to culture in organism detection, but may also detect DNA from non-viable NG. Consequently, not all identified NG are necessarily active, potentially leading to unnecessary treatment and fostering antimicrobial resistance. In the Netherlands, gonorrhoea samples are cultured prior to treatment to assess antibiotic susceptibility for surveillance purposes by a part of the SHCs.²³ We used these culture results to detect viable organisms. Although urogenital cultures showed higher culture positivity rates (83% in MSW and 57% in women), we found remarkable numbers of positive oral cultures (39% in MSW and 35% in women). Among those with an isolated oral infection, fewer cultures tested positive (33% in MSW and 18% in women). To our knowledge, no other studies also included culture results.

For confirmation purposes, our study extended the laboratory analysis using opa gene-based PCR assay and GeneXpert platform. Among MSW, we identified a lower proportion of false positives of oropharyngeal gonorrhoea (7.4%) compared with women (10.8%). Consequently, the confirmed oropharyngeal gonorrhoea positivity rate was somewhat lower (5.9% among MSW and 3.9% among women) compared with the positivity based solely on cobas NAAT (6.4% among MSW and 4.3% among women). Of MSW with gonorrhoea, 69% (n=25/36) had a confirmed oral infection; in women, this was 61% (n=41/67). The extended confirmation process we implemented in our study is unlikely to become part of regular practice, as it is costly and the proportion of false positives was relatively low.

Strengths and limitations

A notable strength of our study is the retrospective validation of oropharyngeal gonorrhoea samples, which allowed us to exclude false positives and provide a more accurate estimate of the true prevalence of oropharyngeal gonorrhoea. Additionally, we reported culture results and were able to confirm viable gonorrhoea infections in 39% of NAAT-positive MSW and in 35% of NAAT-positive women, including cases of isolated pharyngeal gonorrhoea. This is significant because culture confirmation is essential for understanding transmission dynamics and

addressing treatment failures in pharyngeal infections.^{24–26} The lower percentage of positive cultures at pharyngeal site compared with urogenital sites in our study is also observed by others.^{1,27} In addition, culture sensitivity is known to be around 50%.²⁸

Our study had also limitations. First, while we validated the oropharyngeal gonorrhoea NAAT-positive samples, we only validated the positive sample and not the negative ones. Ideally, every sample should be validated. Second, we did not repeat the NAAT test at the treatment consultation. This limited our ability to determine whether individuals who initially tested NAAT positive for gonorrhoea remained positive via NAAT and/or culture at time of treatment. It is known that gonorrhoea can spontaneously clear without antibiotic treatment, also within a timespan of a week. Reported clearance rates range from 11% to 42%, with a median clearance time of 10 days reported in a randomised controlled trial by Mensforth *et al.*^{10,29} Most clients in our study were treated within 1 week after their test consultation. Although we observed a relatively high prevalence of oropharyngeal gonorrhoea, the potential impact on transmission dynamics may be influenced by spontaneous clearance. Third, variability in swabbing methods between clients, with some individuals self-swabbing while others were swabbed by a nurse, could have impacted the detection of gonorrhoea. This inconsistency in swabbing methods is potentially affecting the accuracy of gonorrhoea detection. However, previous studies have shown that self-obtained swabs are non-inferior to provider-performed swabs.³⁰ Lastly, our prevalence estimates may have limited generalisability as they are based on data from a single SHC in Rotterdam and may not reflect other regions. Nevertheless, we believe our results indicate that underdiagnosis of gonorrhoea occurs when not all anatomical locations are tested, a finding likely applicable elsewhere since MSW are more selectively tested.

CONCLUSIONS

Our study shows that the current testing policy leads to underdiagnosis of gonorrhoea. A significant proportion of gonorrhoea infections in our study were isolated in the oropharynx, with a majority being confirmed and over one-third proven viable. However, the impact on gonorrhoea transmission dynamics remains unclear. This study highlights the importance of further research in this area to inform comprehensive prevention and control strategies. This is particularly pertinent given the recent surge in gonorrhoea among MSW and women in the Netherlands and elsewhere in Europe.

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7:458 in the National Central Committee for Human Studies (www.ccmo.nl) and in the conduct of good behaviour in research (www.federa.org). Clients of the SHC consent that surveillance data and laboratory results are used for research. The study was conducted in accordance with the Declaration of Helsinki.

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