What Is the Optimal Testing Strategy for Oropharyngeal Neisseria gonorrhoeae in Men Who Have Sex With Men? Comparing Selective Testing Versus Routine Universal Testing From Dutch Sexually Transmitted Infection Clinic Data (2008-2017)

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What Is the Optimal Testing Strategy for Oropharyngeal *Neisseria gonorrhoeae* in Men Who Have Sex With Men? Comparing Selective Testing Versus Routine Universal Testing From Dutch Sexually Transmitted Infection Clinic Data (2008–2017)

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Background. Most oropharyngeal *Neisseria gonorrhoeae* infections are asymptomatic, and many infections remain undetected, creating a reservoir for ongoing transmission and potential drug resistance. It is unclear what the optimal testing policy is in men who have sex with men (MSM), as routine universal testing data are lacking.

Methods. Surveillance data from all Dutch sexually transmitted infection (STI) clinics between 2008 and 2017 were used (N = 271 242 consultations). Oropharyngeal testing policy was defined as routine universal testing when ≥85% of consultations included oropharyngeal testing or as selective testing (<85% tested). Independent risk factors for oropharyngeal *N. gonorrhoeae* were assessed among MSM routinely universally screened using backward multivariable logistic regression analyses.

Results. Routine universal testing was performed in 90% (238 619/265 127) of consultations. Prevalence was higher using routine universal testing (5.5%; 95% CI, 5.4–5.6; 12 769/233 476) than with selective testing (4.7%; 95% CI, 4.4–5.0; 799/17 079; $P < .001$). Proportions of oropharyngeal-only infections were 55% and 47%, respectively. Independent risk factors were age <31 years (OR, 2.1; 95% CI, 1.9–2.3), age 31–43 years (OR, 1.7; 95% CI, 1.6–1.9, compared with >43 years), being notified for any STI (OR, 2.0; 95% CI, 1.9–2.1), concurrent urogenital *N. gonorrhoeae* (OR, 2.4; 95% CI, 2.1–2.7), and concurrent anorectal *N. gonorrhoeae* (OR, 11.4; 95% CI, 10.6–12.3). When using any of the risk factors age, notified, or oral sex as testing indicators, 98.4% (81 022/82 332) of MSM would be tested, finding 99.5% (4814/4838) of infections.

Conclusions. Routine universal testing detected more oropharyngeal *N. gonorrhoeae* infections than selective testing, of which more than half would be oropharyngeal only. Using independent risk factors as testing indicator is not specific. Therefore, routine universal oropharyngeal testing in MSM is feasible and warranted, as currently advised in most guidelines.

Keywords. MSM; oropharyngeal; *Neisseria gonorrhoeae*; oral; testing policy.

Neisseria gonorrhoeae infections pose a public health challenge. If left untreated, *N. gonorrhoeae* infections can lead to complications and enhanced human immunodeficiency virus (HIV) transmission [1]. Men who have sex with men (MSM) are disproportionally affected by *N. gonorrhoeae* infections. Epidemiological studies show that the majority of *N. gonorrhoeae* infections in MSM are extra-genital [2, 3]. The main driver for *N. gonorrhoeae* transmission in sexually active MSM is yet unknown; however, the pharynx is a common reservoir for *N. gonorrhoeae*, which could enable ongoing transmission [4–7]. Several studies showed that unprotected oral intercourse can lead to urethral *N. gonorrhoeae* infections in MSM [8–10]. In one-third of MSM with a urethral *N. gonorrhoeae* infection, the oropharynx was reported to be the only site of exposure [8]. Unprotected receptive oral sex is a common sexual technique in MSM; studies from the United States and Australia showed that 75–91% of MSM reported unprotected receptive oral sex in the past 6 months [11, 12] compared with 36% for unprotected receptive anal sex [12]. About one-third of the diagnosed *N. gonorrhoeae* infections are oropharyngeal only (29%)—that is, without concurrent urogenital or anorectal infection [13, 14]. Detection and treatment of oropharyngeal-only gonorrhoea infections are crucial, as these

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infections would not be coincidentally treated with urogenital or anorectal infections. Oropharyngeal infections could play a major role in transmission due to their asymptomatic nature, in contrast to urogenital infections [4, 7]. Therefore, their detection depends on testing policy and testing practice. The Centers for Disease Control and Prevention (CDC) in the United States recommends selective oropharyngeal *N. gonorrhoeae* testing in MSM who have had receptive oral intercourse, regardless of condom use during exposure in the 2015 CDC Sexually Transmitted Diseases Treatment Guidelines [15]. Testing and positivity at extra-genital sites have significantly increased in the United States in the past years [16]. Dutch sexual health clinics are publicly funded, serving a high-risk population including young people aged 24 years or younger, MSM, and individuals who were notified for sexually transmitted infections (STIs) [3]. Since recent years, the United Kingdom, Australia, and the Netherlands recommend routine universal oropharyngeal testing in MSM [17, 18].

However, it is unknown whether and how many oropharyngeal *N. gonorrhoeae* infections are missed using a selective testing policy practice, and whether routine universal testing is feasible and implemented in practice. This hampers a proper evaluation of current testing guidelines and practices. To identify what is the most optimal testing practice for *N. gonorrhoeae* in MSM, there is a need for current data on the prevalence and anatomical site distribution of *N. gonorrhoeae* at all 3 anatomical sites among routinely universally tested MSM. Previous studies often used a selection of MSM who were tested at all 3 anatomical sites [13, 19], and it is likely that infections were missed in the oropharyngeal-untested MSM. If oropharyngeal infections are currently missed, and most of these infections would be oropharyngeal only, this could have major consequences for transmission at the population level. Moreover, oropharyngeal *N. gonorrhoeae* infections become more important since the emergence of drug-resistant strains [20]. The oropharyngeal site provides an enabling environment for horizontal transfer of genes from commensal *Neisseria* and other bacterial species to *N. gonorrhoeae*. Also, treatment failure is most likely to occur at the oropharyngeal site [21].

In order to identify the optimal testing strategy for oropharyngeal *N. gonorrhoeae* in MSM, and thereby to optimize gonorrhoea control, we compared selective oropharyngeal testing with routine universal oropharyngeal testing to assess the proportion of infections missed using selective testing using data from all Dutch sexual health clinics. Additionally, we assessed the anatomical site distribution and independent risk factors for oropharyngeal and oropharyngeal-only *N. gonorrhoeae* among routinely universally tested MSM.

METHODS

Study Population

In this retrospective study, coded surveillance consultations from all sexual health clinics in the Netherlands were obtained from the National Institute for Public Health and the Environment (RIVM). All consultations with at least 1 *N. gonorrhoeae* test between 2008 and 2017 were included in the analyses (N = 271 242). The STI clinic consultation data used in this study included sociodemographic characteristics, sexual behavior in the past 6 months, self-reported symptoms, and STI diagnoses. Data on self-reported oral sex were available from 2016. The data were collected through an electronic patient registry. Men who have sex with men were defined as men who had sex with at least 1 man in the past 6 months. According to the Dutch guidelines, there is no extra-genital test indication for heterosexual men [22]. Therefore, consultations in men with missing data on sexual preference (n = 912; 0.1% of all consultations in men) were categorized into MSM when an anorectal or oropharyngeal *N. gonorrhoeae* test was performed (n = 444) and into heterosexual men in the absence of anorectal and oropharyngeal testing (n = 468). Incidental testing was defined as less than 5% of MSM tested oropharyngeally per clinic per year. The proportion of incidental testing was low (0.1%; n = 385) and is not presented in this paper. In total, 265 127 MSM consultations from 1 decade were included in the analyses (Figure 1).

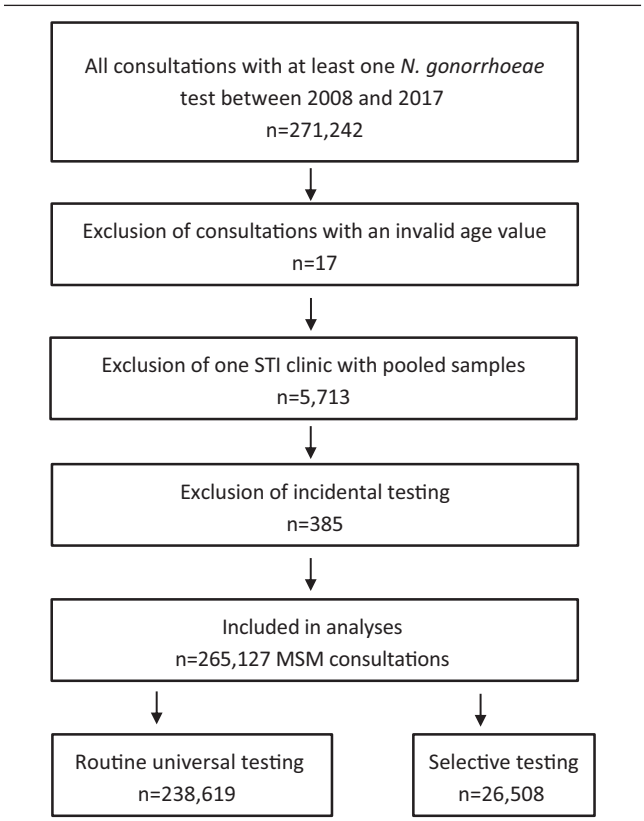

Figure 1. Flow chart of the study population. Abbreviations: MSM, men who have sex with men; *N. gonorrhoeae, Neisseria gonorrhoeae*; STI, sexually transmitted infection.

Routine Clinic Procedures

All MSM were tested for gonorrhoea at the urogenital site. Before 2015, the Dutch guidelines advocated selective testing on indication for oropharyngeal and anorectal gonorrhea—that is, testing after the self-report of receptive unprotected intercourse or symptoms. Since 2015, routine universal oropharyngeal and anorectal testing for MSM is recommended in the Netherlands [22, 23]. In all but 106 (0.04%) consultations, *Chlamydia trachomatis* was also tested for according to the same guidelines as described above for *N. gonorrhoeae*. *N. gonorrhoeae* prevalence was defined based on at least 1 positive test, either a nucleic acid amplification test (NAAT) or a Gram stain. Although commercial *N. gonorrhoeae* assays are not yet licensed to test oropharyngeal specimens at the time of this study's data collection, NAATs have been shown to have twice the sensitivity compared with culture [21]. Performance characteristics might vary by assay. All but 1 STI clinic only used NAAT for diagnoses. One large STI clinic (about one-third of all Dutch tests) also used a Gram stain and culture in about one-fifth of their urogenital and anorectal diagnoses. Guidelines advocate that all MSM should be tested for syphilis and HIV [22, 23]. In practice, this was 99.5% (n = 263 928). Specimens were tested in regional laboratories using different diagnostic assays. All tests were performed according to the manufacturers' protocol.

Statistical Analyses

The primary outcome was oropharyngeal *N. gonorrhoeae* prevalence. This was calculated by dividing the number of positive tests by the total number of tests, multiplied by 100 for all anatomical sites. The secondary outcome was the anatomical site distribution of *N. gonorrhoeae*, defined as oropharyngeal-only versus oropharyngeal infection with concurrent urogenital and/or anorectal infection. The testing procedure—that is, routine universal or selective—was the main predictor variable. The classification of the testing policy was solely based on the proportion of MSM that were tested oropharyngeally. Reasons for oropharyngeal testing, such as sexual risk behavior or symptoms, were not taken into account as this study evaluates clinical practice. Routine universal testing was defined as 85% or more of MSM tested oropharyngeally per clinic per calendar year, starting in January. For example, if an STI clinic changed from selective testing to routine universal testing in July 2010 with coverage of 95% who were oropharyngeally tested, all consultations in 2010 will be set to selective testing, and in 2011 all consultations will be set to routine universal. Selective testing was defined as 5–85% of MSM tested oropharyngeally per clinic per calendar year. We did not observe a switch from routine universal testing to selective testing in the data. Univariable and multivariable generalized estimating equation (GEE) analyses were used to identify determinants independently associated with oropharyngeal and oropharyngeal-only *N. gonorrhoeae*. GEE analyses adjusts for repeated measures of individuals. Data of MSM who were routinely universally tested in 2016–2017 were used, as the variable "oral sex" and a coded personal identifier were available from 2016. The variables tested were age (<31 years, 31–43 years, and >43 years; based on tertiles), ethnicity (Western, non-Western), number of sex partners in the past 6 months (<4, 4–8, and >8; based on tertiles), reporting commercial sex work, reporting swinging, being notified for an STI by an (ex) partner (partner notification), condom use during last ano-genital sexual contact (insertive or receptive), reporting any symptoms, concurrent STI, and year of testing. All analyses were adjusted for STI clinic region (n = 8). Variables that were associated with the outcomes in univariable analyses ($P < .05$) were included in the multivariable model. Stepwise backward selection based on the authors' expertise was used to construct the multivariable model. Analyses were performed using SPSS software version 21.0.0 (IBM). Because the retrospective coded data originated from standard care and were analyzed anonymously, neither a full ethical review nor informed consent for data analysis was needed, as confirmed and approved by the Medical Ethical Committee of Maastricht University (METC 11-4-108).

RESULTS

Characteristics of the Study Population

The median age of the MSM was 36 years (interquartile range [IQR], 27–47 years), and the majority had Western ethnicity (76.7%; 203 469/243 612). Men who have sex with men reported a median of 5 sex partners in the past 6 months (IQR, 3–10). *N. gonorrhoeae* prevalence at any anatomical site was 9.6% (25 340/265 127); for *C. trachomatis* this was 10.0% (26 621/265 021). *C. trachomatis/N. gonorrhoeae* coinfection was present in 2.0% (5400/265 127) of consultations. The characteristics of the study population are described in Table 1.

Routine Universal Testing Versus Selective Testing

Routine universal oropharyngeal testing was performed in 90% (238 619/265 127) of all MSM consultations. Among MSM routinely universally tested, oropharyngeal testing was performed in 88.0–99.7% (mean, 97.8%) of consultations per STI clinic year. For selective testing this was between 8.1% and 83.7% (mean, 64.4%). The proportion of routine universal testing was larger after this was advocated in the 2015 guidelines compared with 2008–2014 (97.7% [114 599/117 053] vs 83.8% [124 020/148 074]; $P < .001$). Oropharyngeal *N. gonorrhoeae* prevalence was higher using routine universal testing (5.5%; 95% confidence interval [CI], 5.4–5.6%; 12 769/233 476) compared with selective testing (4.7%; 95% CI, 4.4–5.0%; 799/17 079; $P < .001$).

Anatomical Site Distribution

The majority of oropharyngeal *N. gonorrhoeae* infections in MSM were oropharyngeal only (54.8%; 7436/13 568)—that

Table 1. Characteristics of the Study Population

	Selective Testing: Total n = 26 508; n Tested = 17 079 (64%)	Routine Universal Screening: Total n = 238 619; n Tested = 233 476 (98%)
Age		
<31 years	35.3 (9346)	34.5 (82 304)
31–43 years	30.4 (8048)	32.8 (78 320)
>43 years	34.4 (9114)	32.7 (77 995)
Non-Western ethnicity	6.1 (1604)	16.2 (38 539)
Number of sex partners		
<4	41.1 (10 883)	31.7 (75 697)
4–8	28.5 (7546)	31.2 (74 453)
>8	30.5 (8076)	32.2 (76 895)
Commercial sex work	1.5 (409)	1.5 (3654)
Swinger[a]	9.2 (2442)	3.2 (7753)
Notified for STI	15.0 (3976)	18.7 (44 503)
Condom use during last anogenital sexual contact	30.9 (8188)	30.8 (73 524)
Oral sex[b]	91.1 (481)	93.5 (78 095)
Symptoms	20.7 (5491)	24.1 (57 623)
Chlamydia trachomatis		
Urogenital test	99.1 (26 264)	99.7 (237 798)
Urogenital positive	2.7 (710)	2.7 (6067)
Anorectal test	64.2 (17 021)	89.3 (213 003)
Anorectal positive	6.3 (1077)	6.6 (13 759)
Any site positive	9.6 (2556)	10.1 (24 065)
Neisseria gonorrhoeae		
Urogenital test	92.2 (26 290)	92.7 (221 087)
Urogenital positive	3.6 (955)	3.5 (8438)
Anorectal test	64.6 (17 123)	87.2 (208 118)
Anorectal positive	10.2 (1736)	8.0 (17 103)
Any site positive	7.3 (1930)	9.8 (23 410)
HIV		
Untested	4.4 (1158)	1.9 (4439)
Negative	86.6 (22 967)	82.0 (195 588)
Known positive	7.5 (2001)	15.1 (36 129)
First positive test	1.4 (382)	1.0 (2463)
Syphilis		
Untested	0.9 (243)	0.4 (956)
Negative	96.7 (25 625)	96.9 (231 212)
Positive	2.4 (640)	2.7 (6451)

Data are presented as % (n).

Abbreviations: HIV, human immunodeficiency virus; MSM, men who have sex with men; STI, sexually transmitted infection.

[a]Swingers were defined as part of a male–female couple who had sex as a couple with other male–female couples and their self-identified heterosexual sex partners. These individuals were classified as MSM as they reported male–male sex in the past 6 months.

[b]Data on oral sex were only available for 2016 and 2017.

is, without concurrent urogenital or anorectal *N. gonorrhoeae* infection. The proportion oropharyngeal-only infections was larger in routinely universally tested MSM compared with selectively tested MSM ($P < .001$) (Figure 2).

Independent Risk Factors for Oropharyngeal *N. Gonorrhoeae*

Using consultations from 2016 and 2017 among routinely universally tested MSM (n = 83 549), independent risk factors for oropharyngeal *N. gonorrhoeae* were young age, being notified

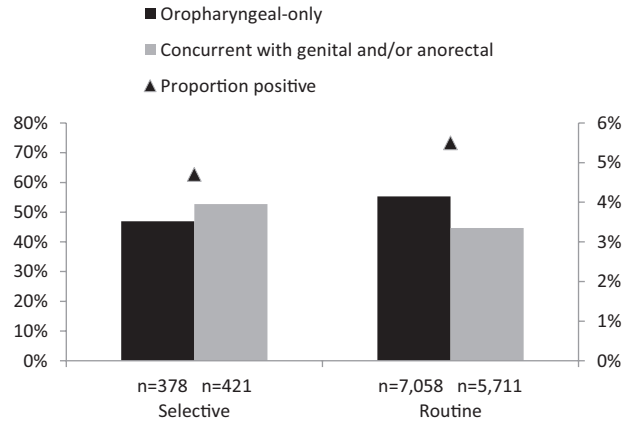

Figure 2. Anatomical site distribution of oropharyngeal *Neisseria gonorrhoeae* in MSM stratified by testing policy: selective testing or routine universal testing. Concurrent infections among the selectively tested MSM were as follows; urogenital, 28.0% (118/421); anorectal, 47.0% (198/421); and both urogenital and anorectal, 25.0% (105/421). For MSM routinely universally tested this was 12.6% (720/5711), 61.2% (3493/5711), and 26.2% (1498/5711), respectively. Abbreviation: MSM, men who have sex with men.

for STI, having concurrent urogenital *N. gonorrhoeae*, and having concurrent anorectal *N. gonorrhoeae*. The risk was lower in MSM with HIV compared with MSM who tested negative for HIV (Table 2).

Independent Risk Factors for Oropharyngeal-only *N. Gonorrhoeae*

Using consultations from 2016–2017 among routinely universally tested MSM, independent risk factors for oropharyngeal-only *N. gonorrhoeae* were older age and condom use during the last ano-genital sexual contact. Protective factors were being known HIV positive, being newly diagnosed with HIV compared with testing HIV negative, reporting symptoms, being notified, or having concurrent anorectal *C. trachomatis* infection (Table 2).

Testing Scenarios

Testing scenarios were compared using consultations from routinely universally tested MSM between 2016 and 2017. When only testing MSM who reported oral sex in the past 6 months, the total tested population would be 94.1% (n = 77 461) of all MSM, finding 98.7% (4675/4838) of all oropharyngeal infections. A total of 163 of 4838 (3.3%) oropharyngeal *N. gonorrhoeae* infections would be missed (ie, 60/4838; 1.2%) from MSM who did not report oral sex and 103 if 4838 (2.1%) from MSM with missing data on oral sex. Of the 163 missed infections, 52–62% (31/60 and 63/103) were oropharyngeal-only infections, respectively. When using the independently associated factors for oropharyngeal *N. gonorrhoeae* as testing indicators, up to 98.4% (81 022/82 332) of MSM would be tested, finding up to 99.5% (4814/4838) of oropharyngeal *N. gonorrhoeae* infections. When using the independently associated factors for oropharyngeal-only *N. gonorrhoeae* as testing indicators, up to

Table 2. Risk Factors for Oropharyngeal and Oropharyngeal-only *Neisseria gonorrhoeae* in Men Who Have Sex With Men Routinely Universally Tested Between 2016 and 2017 Using Generalized Estimating Equation Analyses

	Oropharyngeal *N. gonorrhoeae* Positive (n = 4383; 5.9%)			Oropharyngeal-Only *N. gonorrhoeae* Positive (n = 2423; 2.9%)		
	% (n)	OR (95% CI)	Adjusted OR (95% CI)	% (n)	OR (95% CI)	Adjusted OR (95% CI)
Age						
<31 years	7.8 (2430)	2.4 (2.2–2.6)	2.2 (2.0–2.4)	1.9 (494)	1	1
31–43 years	6.1 (1510)	1.8 (1.7–2.0)	1.8 (1.6–1.9)	3.2 (804)	1.8 (1.6–2.0)	1.8 (1.6–2.0)
>43 years	3.4 (898)	1	1	3.6 (1125)	2.0 (1.8–2.2)	2.1 (1.9–2.4)
Number of sex partners						
<4	4.5 (1137)	1	1	2.1 (523)	1	1
4–8	5.8 (1638)	1.3 (1.2–1.4)	1.3 (1.2–1.4)	2.9 (828)	1.4 (1.3–1.6)	1.4 (1.3–1.6)
>8	7.1 (2063)	1.6 (1.5–1.7)	1.6 (1.5–1.7)	3.7 (1072)	1.8 (1.6–2.0)	1.9 (1.7–2.2)
Notified for STI	10.6 (1768)	2.4 (2.3–2.6)	2.0 (1.8–2.1)	4.9 (816)	2.1 (1.9–2.2)	2.1 (1.9–2.3)
Condom use during last anogenital sexual contact				3.4 (1006)	1.3 (1.2–1.4)	1.2 (1.1–1.3)
Oral sex	6.0 (4675)	2.2 (1.7–2.9)	1.8 (1.4–2.4)	3.0 (2334)	2.1 (1.5–3.1)	1.9 (1.3–2.7)
Symptoms	9.9 (1698)	2.2 (2.0–2.3)	ns	2.9 (505)	ns	na
Chlamydia trachomatis[a]						
Urogenital	8.8 (228)	1.6 (1.4–1.8)	ns	3.2 (982)	ns	na
Anorectal	10.7 (630)	2.0 (1.9–2.2)	ns	3.2 (82)	ns	na
Oropharyngeal	13.4 (113)	2.5 (2.0–3.0)	1.6 (1.2–2.0)	4.9 (41)	ns	na
N. gonorrhoeae[a]						
Urogenital	36.3 (853)	10.9 (9.9–11.9)	2.4 (2.1–2.8)	na	na	na
Anorectal	36.0 (2211)	15.8 (14.8–16.9)	11.0 (10.1–12.0)	na	na	na
HIV						
Negative	5.7 (4030)	1	1	3.0 (2121)	1	1
Known positive	6.6 (699)	1.2 (1.1–1.3)	0.8 (.7–.8)	2.5 (264)	0.8 (.7–.9)	0.8 (.7–.9)
First positive test	10.3 (52)	1.9 (1.4–2.5)	0.9 (.6–1.2)	3.2 (16)	1.1 (.6–1.7)	0.7 (.4–1.3)

N = 83 549; total tested oropharyngeally, n = 82 332 (98.5%).
Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; na, not assessed; ns, nonsignificant; OR, odds ratio; STI, sexually transmitted infection.
[a]Compared with tested negative.

77.1% (63 454/82 332) of MSM would be tested, finding up to 74.8% (1813/2423) of oropharyngeal-only *N. gonorrhoeae* infections (Table 3).

DISCUSSION

We studied the optimal testing strategy for oropharyngeal *N. gonorrhoeae* in a very large cohort of MSM, comparing routine universal testing with selective testing. Oropharyngeal *N. gonorrhoeae* positivity was higher using routine universal testing. Therefore, selective testing proved to be a suboptimal control strategy for oropharyngeal *N. gonorrhoeae* in MSM, as it would miss a substantial proportion of infections. Moreover, over half of all these missed infections would be oropharyngeal only. These infections would not be coincidentally treated with a concurrent urogenital or anorectal *N. gonorrhoeae* infection. In routinely universally tested MSM, being young and being notified were independent risk factors that could be used as a testing indicators. Oral sex was not independently associated, and almost all MSM reported this behavior (94%). Testing based on independent risk factors or based on risk behavior (oral sex) would not be specific enough, as it requires almost all MSM to be tested without diagnosing all oropharyngeal *N. gonorrhoeae* infections. Therefore, routine universal oropharyngeal testing in MSM is warranted and feasible, as 98% of MSM were tested at the oropharyngeal site.

The results of this study are in line with the Dutch testing guidelines for sexual health clinics, which advocate routine universal oropharyngeal testing in MSM since 2015 [18]. This is in accordance with other countries such as Australia and the United Kingdom [17, 24] and previous studies promoting increased testing [4, 7, 10]. However, not all countries recommend routine universal oropharyngeal testing in MSM [15]. There are several reasons for oropharyngeal testing for *N. gonorrhoeae*, such as limiting transmission and reducing opportunity for horizontal gene transfer, which occurs mainly at the oropharyngeal site as other *Neisseria* species reside here. Rapid detection after exposure is facilitated by using highly sensitive NAAT, although formal Food and Drug Administration clearance for oropharyngeal testing is still lacking. However, there are some comments whether enhanced testing lowers *N. gonorrhoeae* prevalence [25] and outweighs the development of resistance. Moreover, cost-effectiveness studies for oropharyngeal testing are lacking at the time of this study's data collection [26]. A modeling study stated that enhanced testing only yields a

Table 3. Different Testing Scenarios for Oropharyngeal and Oropharyngeal-only *Neisseria gonorrhoeae* Using the Variable Oral Sex and Independently Associated Variables Identified by Multivariable Generalized Estimating Equation Analyses in Routinely Universally Screened Men Who Have Sex With Men

All oropharyngeal *N. gonorrhoeae*	Tested n = 82 332 n (%)	Positive n = 4 838 n (%)	Missed oropharyngeal infections n (%)
Age			
≤43 years	55 961 (68.0)	3940 (81.4)	18.6 (898)
Notified for STI[a]			
Yes	16 613 (20.2)	1768 (36.6)	63.4 (3.064)
Oral sex[b]			
Yes	77 461 (94.1)	4675 (98.7)	60 (1.3)
One or more of the above-mentioned criteria	81 022 (98.4)	4814 (99.5)	24 (0.5)
Oropharyngeal-only *N. gonorrhoeae*	**Tested n = 82 332 n (%)**	**Positive n=2423 n (%)**	**Missed oropharyngeal-only infections n (%)**
Age			
≥31 years	51 169 (62.0)	1298 (53.6)	1125 (46.4)
Condom use during last anogenital sexual contact			
Yes	29 897 (36.0)	1003 (43.1)	1325 (56.9)
One or more of the above-mentioned criteria	63 454 (77.1)	1813 (74.8)	610 (25.2)

Data are presented as n (%).

Abbreviation: STI, sexually transmitted infection.

[a]Data were missing for 61 consultations (0.1%).

[b]Data were missing for 2718 consultations (3.3%).

small decline in prevalence, and that this does not counter the microbial resistance [27]. Other studies found that the bacterial load of oropharyngeal *N. gonorrhoeae* is lower compared with that at the urogenital and anorectal site [28–30], and samples with lower bacterial load are found to naturally clear more often compared with higher load samples [30]. However, two-thirds of oropharyngeal *N. gonorrhoeae* infections remained positive between testing and treatment [30], indicating the transmission potential of these infections. For public health gain, treatment is required in these infections to halt transmission. Also, despite the one-third clearance, transmission could have taken place between testing and treatment, given the easy/high transmission of *N. gonorrhoeae* between sex partners, and the overall high number of reported sex partners of MSM. The treatment efficacy of oropharyngeal *N. gonorrhoeae* has been questioned, as it was less effective compared with that at other anatomical sites [31–33].

Strengths of our study are the use of national surveillance data and the occurrence of different testing scenarios in different sexual health clinics. A very large number of MSM were included, covering sexual health clinics in the whole country. Also, a large number of MSM receiving routine universal oropharyngeal testing were included, making the findings of the study robust and highly representative of and generalizable to the population of MSM who visit STI clinics or sexual health clinics.

The study also had some limitations. We could not rule out the possibility of false positives in the study. It is unknown whether increased oropharyngeal testing, such as implementing routine universal testing, could lead to an increased number of false positives. False-positive results could be a problem in low-endemic populations. However, the population prevalence of oropharyngeal *N. gonorrhoeae* was substantial, and most manufacturers' protocols do not advocate confirmatory testing for oropharyngeal *N. gonorrhoeae*. Possibly, risk factors for oropharyngeal *N. gonorrhoeae* were missed, as not all hypothesized routes of transmission were included as variables in our dataset. For example, rimming [4], kissing [11, 34], and the use of saliva as a lubricant [11, 35, 36] have been suggested as transmission routes. A study from Australia found that specific sexual practices such as tongue kissing were not associated with oropharyngeal *N. gonorrhoeae* after adjusting for the number of casual partners [34]. We did not find an association between the total number of sexual partners and oropharyngeal *N. gonorrhoeae*, but we could not distinguish between casual and regular sexual partners. Risk factors for oropharyngeal infections differed from risk factors for oropharyngeal-only infections. For example, using a condom during the last ano-genital sexual contact was associated with oropharyngeal-only infections but not with oropharyngeal infections. If condoms were only used during genital-anal intercourse, and not during oral intercourse, this would result in more oropharyngeal-only infections. We found that being HIV positive or reporting symptoms had a small protective effect on oropharyngeal infections and being HIV positive on oropharyngeal-only infections. Explanations for this can be repeat testing of MSM who are positive for HIV, a higher proportion of concurrent genital and anorectal *N. gonorrhoeae* in MSM who are positive for HIV, and the fact that the majority of reported symptoms will likely be urogenital symptoms.

Last, the 85% cutoff to define routine universal testing was based on empirical study data and the authors' expertise, as there is no standardization available. Results could be different when using a different cutoff. Also, clinic calendar years were used to define the testing policy instead of using clinic calendar months. This could lead to misclassification in the calendar year of switching from selective to routine testing, as the whole year would be classified as selective testing. However, the implementation of this misclassification would be minimal as it goes both ways. Moreover, the implementation of a testing policy usually takes longer than 1 month, and using calendar years provides a more stable estimate of the implemented testing policy without monthly fluctuations. In reality, this possible bias is small as only 74% (20/27) of STI clinics proved to change from selective to routine universal and no STI clinic switched, which means there were only 20 changes in 270 clinic years (7.4% of all clinic years).

In conclusion, oropharyngeal infections have been proposed to play a major role in the ongoing transmission of *N. gonorrhoeae*. With regard to the rising incidence of *N. gonorrhoeae* infections, it is imperative to detect and treat oropharyngeal infections. This study informs on the optimal testing strategy for oropharyngeal *N. gonorrhoeae* in MSM by recommending routine universal testing instead of selective testing, as oropharyngeal *N. gonorrhoeae* prevalence was higher using routine universal testing. Moreover, half of the infections were oropharyngeal only and would therefore not be coincidentally treated with a urogenital or anorectal infection if not routinely tested for.

Notes

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