Three-site screening for sexually transmitted infections in men who have sex with men using online self-testing in an English sexual health service

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**Abstract**

**Objectives:** Among men who have sex with men (MSM) in the United Kingdom (UK), chlamydia (CT) and gonorrhoea (NG) infections commonly occur asymptomatically at extragenital sites. Therefore, MSM seeking sexual health services are offered three-site (oropharyngeal, rectal, and urogenital) STI screening. To increase access to screening, some UK sexual health services enable asymptomatic service users to order free STI screening kits online for self-sampling at home. We sought to assess prevalence of overall and extragenital CT/NG infection amongst asymptomatic MSM who used online self-testing in Hampshire, UK.

**Methods:** We assessed prevalence of CT/NG infections from non-pooled samples amongst asymptomatic cisgender MSM using an administrative database with results from 5,601 STI screening kits returned between 20/12/2016-31/01/2020. We compared number of diagnoses of extragenital infection with urogenital results of the same individuals to determine prevalence of infection that would have been missed with urine testing alone.

**Results:** Amongst 5051 valid CT and 5040 valid NG asymptomatic test results, overall prevalence was 5.9% (298/5051) and 4.5% (228/5040), respectively. Amongst MSM with asymptomatic CT, 71.8% (214/298) had extragenital infection only, *Χ*2 (1, *N*=298) =56.71, *p*<0.001. Amongst those with asymptomatic NG, 89.9% (205/228) had extragenital infection only, *Χ*2 (1, *N*=228) =145.281, *p*<0.001.

**Conclusions:** Overall, most CT/NG infections amongst asymptomatic MSM who used online self-testing were extragenital. Given this and the likelihood of onward transmission from asymptomatic infection, it is recommended that three-site testing remain standard for MSM and free screening services be expanded in easily accessible ways.

**Key Words:** Gonorrhoea; Chlamydia; STI; Screening; Online; MSM; Extragenital; Asymptomatic; Gay and Bisexual Men

**Key Messages:**

1. The vast majority of asymptomatic Chlamydia (CT) and Gonorrhoea (NG) infections among men who have sex with men (MSM) in Hampshire, UK occur extragenitally without concurrent infection of the urethra.

2. Three-site testing should remain the standard for MSM and free screening services should be expanded in easily accessible ways.

Men who have sex with men (MSM) are more likely to be diagnosed with chlamydia (CT) and gonorrhoea (NG) than the general population.1 The majority of CT/NG infections among MSM are asymptomatic and symptoms vary by anatomical site: urethral infection is predominantly symptomatic, whereas most rectal and oropharyngeal infections are asymptomatic.2,3 Consequently, MSM who engage in oral and anal sex may be more likely than men who do not engage in these behaviours, or who have vaginal sex only, to acquire an asymptomatic infection.

The frequently asymptomatic nature of CT/NG means that infections are often undiagnosed unless the specific sites of infection are screened.2,3 This can be problematic as CT/NG infection may lead to onward transmission and long-term health complications such as infertility.2,4 The American STD Surveillance Network reported that amongst 21,994 MSM attending 44,104 clinic visits, 71.8% of rectal and 73.8% of oral NG infections would have been missed with urogenital testing alone, as would 88.3% and 92.2% of rectal and pharyngeal CT infections, respectively.3

Several behavioural factors may contribute to higher population diagnosis rates among MSM. First, MSM report more sexual partners, more new partners annually, and more concurrent partnerships, resulting in larger, interconnected sexual networks.5 Second, they are more likely to engage in behaviours associated with increased STI risk such as receptive and insertive anal sex, anal sex versatility, group sex, and chemsex.5,6 Third, condom use amongst MSM has decreased, likely due to greater use of HIV prevention measures such as Treatment as Prevention, U=U, and pre-exposure prophylaxis (PrEP).7 Fourth, MSM, particularly those living with HIV and those with multiple partners, are encouraged to test frequently for STIs and screening is required for access to PrEP.8 Finally, increased rates of STIs, including HIV, amongst MSM are syndemic and influenced by the interactions of many factors, including higher rates of mental health and substance misuse problems and poor access to health services.9

Among MSM, regular urine, oropharyngeal, and rectal STI screening is recommended every three months for individuals engaging in condomless sex with new or casual partners.1,8 To improve access and engagement, several NHS services now offer free online STI testing. In Hampshire, STI test kits can be ordered online through NHS Solent Sexual Health Service (<https://letstalkaboutit.nhs.uk>). Testing kits for MSM contain collection material for urine and pharyngeal and anorectal swabs.

Given the associated burden of sampling on individuals and extra costs to services, it is important to assess the value of extra-genital sampling. We investigated the prevalence of urogenital, pharyngeal, and rectal CT and NG in all STI self-screening kits returned to Solent Sexual Health Service by asymptomatic, cisgender MSM over three years (20/12/2016-31/01/2020). We also examined extragenital positivity amongst individuals with negative urine screens to determine what proportion of infection would have been missed without three-site testing.

**METHOD**

Data were from an NHS database of self-test STI kit results ordered using the above website. During the ordering process, anyone who reported current STI symptoms, being a known contact of someone diagnosed with an STI in the past three months, recent sex with someone from a country with high HIV prevalence, injection drug use (self or partner), transgender identity, or transactional sex was unable to order online and was referred to in-clinic testing. Self-test kits for cisgender men who reported having at least one male sexual partner included collection material and instructions for urine and throat and rectal swabs (for CT/NG), finger-prick blood samples, and a Freepost envelope. Returned kits were tested for CT/NG infection with the Aptima Combo 2 Assay Nucleic Acid Amplification Test (NAAT). Results were sent approximately seven days later via text message. Study procedures were approved by Solent NHS Trust Clinical Governance and the University of Southampton research ethics committee.

## **Data Analysis**

Data analysis was conducted on an anonymized dataset containing results from 5601 test kits from asymptomatic, cisgender men who reported male sexual partners. Urine, throat, and rectal CT and NG test results were coded to identify positive, negative, and failed, invalid, or inconclusive results. Descriptive statistics were performed using SPSS to determine prevalence of CT and NG at each testing site. Amongst those with a positive diagnosis who had valid tests at all three sites, comparisons were made using Chi-squared analysis between extragenital positivity only vs. urine positivity (with or without extragenital positivity).

**RESULTS**

Of 5061 returned kits, 5051 had valid samples at all sites for CT and 5040 had valid samples at all sites for NG (most invalid samples were because the sample for a specific site was not returned). Sample age range was 15-91 years old (Mean=30.7, Median=27.0, SD=11.0).

The prevalence of asymptomatic CT across all sites was 5.9% (298/5051). The most common infection site was the rectum (215/5051, 4.26%), followed by the urethra (84/5051, 1.66%), and throat (44/5051, 0.87%) (See Table 1). 256 individuals demonstrated single site infection (174 rectum, 59 urine, 23 throat), 39 two-site co-infection (21 rectum/urine, 17 throat/rectum, 1 throat/urine), and 3 three-site co-infection (rectum/throat/urine). Most asymptomatic CT infections were extragenital only (214/298, 71.8%) and they were significantly more likely to be extragenital only as compared to in the urogenital tract (with or without co-infection), *Χ*2 (1, *N*= 298) =56.71, *p*<0.001.

The prevalence of asymptomatic NG across all sites was 4.5% (228/5040). The most common infection site was the throat (143/5040, 2.83%), followed by the rectum (113/5040, 2.24%), and urethra (23/5040, 0.46%) (See Table 1). 183 individuals demonstrated single site infection (100 throat, 74 rectum, 9 urine), 39 two-site co-infection (31 throat/rectum, 6 throat/urine, 2 rectum/urine), and 6 three-site co-infection (rectum/throat/urine). Most asymptomatic NG infections were extragenital only (205/228, 89.9%) and they were significantly more likely to be extragenital only as compared to in the urogenital tract (with or without co-infection), *Χ*2 (1, *N*= 228) =145.281, *p*<0.001.

**DISCUSSION**

Amongst asymptomatic, cisgender men reporting male sexual partners, prevalence of CT and NG infection was 5.9% and 4.5%, respectively. Prevalence varied by anatomical site: asymptomatic CT was most prevalent in the rectum (4.3%), whereas asymptomatic NG was most prevalent in the throat (2.8%). The vast majority of asymptomatic CT and NG infections were found extragenitally, without infection of the urethra (71.8% for CT, 89.9% for NG); thus, without extragenital screening, these infections would have been undiagnosed and consequently untreated.

 Our results provide further support for screening asymptomatic MSM at extragenital sites.3 However, three-site screening carries additional burden for the individual and increased financial costs for the service. One cost-effective solution may be to pool samples from tested sites, although reduced sensitivity, particularly for pharyngeal infections, has been observed.4 Alternatively, given very low prevalence of asymptomatic, single-site urogenital infection (CT:23/5051, 0.45%; NG:9/5040, 0.18%), urogenital screening may be less important than extragenital screening for asymptomatic MSM. Our findings highlight the need for further research on urethral screening for CT/NG amongst asymptomatic MSM, including health economic modelling which compares three-site screening with extragenital screening only, while adjusting for costs associated with future burden of disease and differences in prevalence of asymptomatic urethral NG and CT infection.

 A further challenge of three-site testing is the ongoing threat of antimicrobial resistance which may be perpetuated through enhanced screening and associated greater use of antibiotics.2 We argue that reduced screening is not reasonable, given known risks of onward transmission and persistent NG/CT infection,2-4 but that repeat testing of infected sites to establish persistence of infection should be considered prior to antibiotic administration. CT and NG can demonstrate spontaneous clearance. Amongst MSM, with a test/retest time between 3-35 days, CT clearance has been reported for 4.0% of anorectal infections and 80.0% of oropharyngeal infections and NG clearance for 66.7% of urogenital infections, 22.2% of anorectal infections, and 30.8% of oropharyngeal infections.10 Given this, and until additional effective antibiotics are developed, it may be necessary to implement re-testing of infected but asymptomatic sites prior to treatment. Should this approach be adopted, appropriate counselling of patients will be necessary to reduce the risk of onward transmission.

Limitations of this study should be noted. Firstly, data were only from asymptomatic MSM who ordered self-screening kits online. Thus, these results are not generalisable to MSM who present with NG/CT symptoms or those who would not choose self-testing. Second, when ordering online, individuals self-report any symptoms. Some symptomatic individuals may have falsely indicated no symptoms to obtain a screening kit online and avoid a visit to their GP/sexual health clinic. However, given the very low prevalence of urogenital CT/NG in this sample (which are frequently symptomatic if present), we think it is unlikely this greatly affected our findings. Lastly, because the online STI screening program was anonymous, it was not possible to identify participants who may have ordered multiple kits over the three-year period. However, all positive cases would have been prescribed antibiotics, and as such, subsequent diagnoses most likely indicate new repeat infections rather than continuous long-term infection.

**Conclusion**

Using a large clinical administrative database, we found high prevalence of CT and NG infection at extragenital sites without concurrent urethral infection in asymptomatic cisgender MSM. This provides further UK-specific support for three-site screening in this population. Sexual health services should implement or continue to offer free three-site screening to asymptomatic MSM to prevent onward spread and future burden of disease.

**Competing Interests:** Heather Armstrong is on the Editorial Board of BMJ STI.

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Table 1. Prevalence of asymptomatic CT and NG among cisgender MSM who self-test online

|  |  |  |
| --- | --- | --- |
|  | CT | NG |
|  | N | Positive Cases | Prevalence | N | Positive Cases | Prevalence |
| Overall | 5051 | 298 | 5.9% | 5040 | 228 | 4.5% |
| Urine | 5051 | 84 | 1.7% | 5040 | 23 | 0.5% |
| Throat | 5051 | 44 | 0.9% | 5040 | 143 | 2.8% |
| Rectum | 5051 | 215 | 4.3% | 5040 | 113 | 2.2% |
| Genital (with or without co-infection) | 298 | 84 | 28.2% | 228 | 23 | 10.1% |
| Extragenital only | 298 | 214 | 71.8% | 228 | 205 | 89.9% |

Contributor Statement

Gideon Charin conducted the data analysis and wrote the first version of the manuscript. He also contributed to and approved revisions for the final version.

Ynez Symonds oversees the STI screening program and conceptualised the research. She provided support for data analysis and contributed to and approved revisions for the final version.

Clare Scholfield oversees the STI screening program and conceptualised the research. She provided support for data analysis and contributed to and approved revisions for the final version.

Cynthia A. Graham provided significant contributions to the interpretation of the data. She also provided substantial revisions, and approval, for the final version.

Heather L. Armstrong conceptualised the research, conducted the data analysis, and co-wrote the final manuscript. She has reviewed and approved all revisions for the final version.