Evaluation of Self-Collected Versus Clinician-Collected Swabs for the Detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* Pharyngeal Infection Among Men Who Have Sex With Men

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Abstract: We evaluated self-sampling to detect pharyngeal *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) infection among men who have sex with men attending a San Francisco STD clinic. The prevalence of pharyngeal NG and CT infection was 6.7% (32/480) and 1.3% (6/480), respectively. The percent agreement between self-collected and clinician-collected NG and CT specimens using nucleic acid amplification testing was 96.6% with a κ of 0.766 (95% confidence interval: 0.653–0.879) and 99.4% with a κ of 0.766 (95% confidence interval: 0.502–1.000), respectively. Acceptability was high among participants.

Chlamydia trachomatis (CT) and *Neisseria gonorrhoeae* (NG) are highly prevalent curable sexually transmitted infections (STIs) that are associated with significant adverse reproductive health sequelae among men and women.[1] In the United States, men who have sex with men (MSM) constitute a group at high risk for CT and NG infections.[2] Both pathogens can infect the pharynx. Studies have reported prevalences of pharyngeal infection among MSM ranging from 1% to 2% for CT and 3% to 9% for NG.[3–8] The pharynx can be the only site of infection[9] and, as such, might be an important reservoir for further transmission to genital sites.[6,10] Because pharyngeal infections are largely asymptomatic, accurate and acceptable pharyngeal diagnostics are critical to STI control efforts.

Most public health laboratories in the United States have adopted nucleic acid amplification tests (NAATs) for CT and NG detection,[11] which exhibit high sensitivity compared to culture or enzyme immunoassay for diagnosis at genital sites.[12–14] Other studies have demonstrated high sensitivity[15] but varied specificity[8,16] of NAATs for CT and NG diagnosis in the rectum and pharynx. Those assays are not cleared by the Food and Drug Administration for testing rectal or pharyngeal specimens, although many laboratories have conducted internal validation studies and offer diagnostic testing.[1]

The development and availability of self-collection methods using molecular diagnostics have enabled better access to sexual health services in nonclinical settings, including Internet-based testing programs and home sampling.[17–19] Self-sampling for STI detection among women using vaginal swabs[18] and men using rectal swabs[20] has been found to be both feasible and acceptable. Similarly, a recent evaluation among MSM in the United Kingdom showed high levels of acceptability[20] as well as high sensitivity and specificity of self-taken pharyngeal swabs for CT and NG detection.[21] To date, no studies have evaluated the performance of pharyngeal self-sampling in the United States. In this study, we evaluated the acceptability and performance of self-collected versus clinician-collected specimens for the detection of pharyngeal CT and NG infection using NAATs.

Between March and May 2009, subjects were recruited from San Francisco's municipal STD clinic, San Francisco City Clinic, during a routine clinic visit. Eligible individuals included English-speaking MSM undergoing testing for CT and NG where pharyngeal swab collection was a component of their standard of care. Per standard clinic protocol, all MSM who report performing fellatio in the past 2 weeks were tested for pharyngeal CT and NG infection. Verbal informed consent was obtained. Study subjects did not receive any reimbursement for participation. The University of California San Francisco Committee on Human Research approved the study.

After the clinician collected the pharyngeal specimen, participants collected their own specimen without a clinician present in the examination room. Both specimens were collected using the standard APTIMA unisex collection kit (Gen-Probe, Inc., San Diego, CA). We provided each participant with instructions for self-collection, an accompanying diagram, and a mirror for viewing of the pharynx. Following specimen collection, participants were asked to complete an acceptability questionnaire modeled on the work of Wayal et al.[20] To reduce response bias, we reverse-phrased 3 of the 5 questions asked. Participant rating of acceptability was based on a 5-point scale: 1 = strongly disagree, 2 = disagree, 3 = no preference, 4 = agree, and 5 = strongly agree.

Both specimens were placed into APTIMA unisex swab transport media tubes (Gen-Probe, Inc.) for NAATs using the APTIMA Combo 2 Assay (AC2, Gen-Probe, Inc.). Clinician-collected specimens were shipped within 24 hours to the San Francisco Department of Public Health Laboratory and tested per standard laboratory protocol. Self-collected specimens were stored at room temperature and tested

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TABLE 1. Agreement Between Self-Collected and Clinician-Collected Pharyngeal Swabs for the Detection of *Neisseria gonorrhoeae* Among Men Who Have Sex With Men

	Clinician-Collected		
	Positive	Negative	Total
Self-Collected			
Positive	29	13	42
Negative	3	428	431
Total	32	441	473*
Percentage agreement: 96.6%			
Kappa: 0.766 (95% CI: 0.653–0.879)			

*Seven invalid or equivocal specimens excluded from analysis.

within 60 days of collection in accordance with AC2 testing instructions. In compliance with the Clinical Laboratory Improvement Act, the Public Health Laboratory internally verified the use of AC2 on the automated TIGRIS platform for rectal and pharyngeal specimens in 2005 and currently uses AC2 for dual detection of NG and CT at those sites. Study participants received test results from the clinician-collected specimens only.

The percent agreement and κ values between self-collected and clinician-collected test results were calculated. Participant data were linked to other test results from that clinic visit to analyze discordant results. Descriptive statistics from the acceptability questionnaire were examined.

Overall, 480 MSM participated, 55.2% (480/870) of the total MSM tested for pharyngeal NG or CT during the study period. The prevalence of pharyngeal NG and CT infection based on the clinician-collected specimen was 6.7% (32/480) and 1.3% (6/480), respectively. Among nonstudy participants tested during the same period, the prevalence of pharyngeal NG and CT infection was 5.4% (21/390) and 1.0% (4/388), respectively, with no significant difference in NG or CT prevalence found between participants and nonparticipants ($P = 0.26$ and $P = 0.51$), respectively.

Among pharyngeal NG specimens, the percent agreement between self-collected and clinician-collected swabs was 96.6%, and the κ was 0.766 (95% confidence interval: 0.653–0.879) (Table 1). Among pharyngeal CT specimens, the percent agreement between self-collected and clinician-collected swabs was 99.4%, and the κ was 0.766 (95% confidence interval: 0.502–1.000) (Table 2). There were no cases of dual pharyngeal CT and NG infection. Five self-collected and 2 clinician-collected specimens had an invalid or equivocal test result for NG. Those specimens were retested and had a second invalid or equivocal result, and thus were excluded from the analysis.

Of the 13 study participants who had a clinician-negative, self-collected positive pharyngeal NG specimen, 5 had a urethral and/or rectal NG coinfection, 2 had equivocal test results for urethral and/or rectal NG infection, and 6 had no concurrent NG infections. Of the 3 participants who had a clinician-positive, self-collected negative pharyngeal NG specimen, 1 had a positive urethral and/or rectal NG coinfection, 1 had an equivocal test result for urethral and/or rectal NG infection, and 1 had no concurrent NG infections. Of the 2 participants who had a clinician-negative, self-collected positive pharyngeal CT specimen, 1 had a concurrent rectal CT infection.

We received acceptability questionnaires from 471/480 study participants (98%). Overall, participants expressed a high level of acceptance of self-sampling as shown in Table 3. Most participants (92%) expressed willingness to self-collect a pharyngeal specimen at home. Given an option between clinician collection and self-collection, 54% of participants expressed no preference, whereas a few more preferred self-collection. The majority of participants agreed or strongly agreed that instructions were easy to follow (89%) and that the specimen was easy to self-collect (80%). A few participants expressed some discomfort with self collection, but the overall level of acceptability remained high (average score = 2.64). Among those who expressed difficulty or self-reported problems with specimen collection in the questionnaire, we found no significant differences in test results by method of specimen collection (data not shown).

This study of self-sampling for the detection of pharyngeal NG and CT infection among MSM in San Francisco showed excellent agreement[22] between self-collected and clinician-collected specimens using NAATs. Among those who agreed to participate in the study, acceptability was high. Consistent with these findings, previous studies have shown self-sampling to be acceptable and feasible using various non-invasive collection methods, including self-taken vaginal,[18] as well as pharyngeal and rectal swabs.[21]

Among asymptomatic MSM in the United Kingdom, Alexander et al. observed high sensitivity but a statistically significant difference in specificity of self-taken compared to nurse-taken pharyngeal specimens.[21] Among patients who had a false-positive self-collected pharyngeal specimen, 90.9% (10/

TABLE 2. Agreement Between Self-Collected and Clinician-Collected Pharyngeal Swabs for the Detection of *Chlamydia trachomatis* Among Men Who Have Sex With Men

	Clinician-Collected		
	Positive	Negative	Total
Self-Collected			
Positive	5	2	7
Negative	1	465	466
Total	6	467	473*
Percentage agreement: 99.4%			
Kappa: 0.766 (95% CI: 0.502–1.000)			

*Seven invalid or equivocal specimens excluded from analysis.

TABLE 3. Acceptability Scores of Self-Sampling for Pharyngeal Swab Collection Among Men Who Have Sex With Men—San Francisco City Clinic, 2009

Acceptability Measure	Average Score*
Willing to self-collect at home	4.31
Prefer [self-collection]†	3.05
Instructions easy to follow	4.25
[Easy]† to self-collect throat swab	4.03
[Comfortable]† to self-collect throat swab	2.64

*Range 1–5, 1 = strongly disagree, 5 = strongly agree.
†Items in brackets were reverse-phrased in the questionnaire to reduce response bias.
Questionnaire modeled after Wayal et al.[20]

11) had a concurrent NG infection at the urethra and/or rectum. In our evaluation, we observed a lower but not inconsequential rate of coinfection at a different anatomical site: 38.5% (5/13) of patients with self-taken NG positive, clinician-negative pharyngeal results had NG infection elsewhere. Our written instructions did not ask patients explicitly to wash their hands before collection, and as such, contamination of collection materials when handling specimens could account for our finding. Those observations suggest that the risk of potential contamination and false-positive site-specific infections should be discussed with patients before self collection.[23] Further studies are needed to determine the role of sampling technique and how to reduce the risk of false-positive site-specific test results among persons who self-collect specimens tested with highly sensitive NAATs.

Our study had certain limitations. Due to the low prevalence of pharyngeal CT infection, the precision of κ estimates between self-collected and clinician-collected pharyngeal specimens was low; however, the lower bounds of the 95% confidence limits for the κ estimates for both CT and NG are considered good agreement by standard rubrics.[22] We were not able to record how many MSM attending the clinic were offered to participate in the study, and thus we lacked data on enrollment percentages or reasons for nonparticipation. We might have overestimated the proportion of those declining to participate, given the likelihood that not all patients were offered enrollment in a busy clinic setting. Our data suggest that those who chose not to participate were just as likely to be diagnosed with pharyngeal NG or CT infection; however, it is possible that refusal to participate in the study was a defacto statement of nonacceptance. To simplify clinic patient flow, the order in which the clinician and self-sampling specimens were collected was not randomized. Self-collected specimens were stored at room temperature and tested within 60 days of collection as per AC2 protocol. Given the fact that the study swab was collected second and stored for a longer period than the clinician swab, the study might be biased toward lower detection in the study swabs, and the observed measure of sensitivity might be underestimated. Although San Francisco is a unique urban environment and this study was conducted among MSM, we have no reason to believe the findings of our analysis would not be generalizable to other populations.

Various self-sampling methods, including self-collected vaginal and rectal swabs and patient-collected urine specimens, have improved access to sexual health services among hard-to-reach populations.[19] Similarly, self-collected pharyngeal swabs might serve as an alternative to clinic-based testing, allowing public health efforts to continue exploring nonclinic-based settings such as street fairs, Internet-based programs, home sampling, and community centers.[24] Additional studies to replicate our findings and to demonstrate the impact of pharyngeal screening on the community-level transmission of CT and NG infection among MSM and other high-risk populations are needed.

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