Swab-yourself trial with economic monitoring and testing for infections collectively (SYSTEMATIC): Part 1. A diagnostic accuracy, and cost-effectiveness, study comparing clinician-taken versus self-taken rectal and pharyngeal samples for the diagnosis of gonorrhoea and chlamydia

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Summary of main points (40 words)

Extragenital self-sampling for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* is frequently undertaken despite no robust evidence of its efficacy. This randomised, powered, study found no difference in diagnostic accuracy between clinician, and self-taken, rectal and pharyngeal samples for diagnosing these infections.

Word count is 3017 (however on page 6 there is the reference to SYSTEMATIC Part 2 which is written in full and is 55 words)

Abstract

Background:

Urogenital testing misses extragenital *Neisseria gonorrhoeae* (NG) and *Chlamydia trachomatis* (CT). Extragenital self-sampling is frequently undertaken despite no robust RCT evidence of efficacy. We compared clinician-taken rectal and pharyngeal samples with self-taken samples for diagnostic accuracy and cost in MSM and females.

Methods:

Prospective, convenience, sample in UK sexual health clinic. Randomised order of clinician and self-samples from pharynx and rectum, plus first catch urine (MSM) and vulvovaginal swabs (females), for NG/CT detection.

Results:

Of 1793 participants (1284 females, 509 MSM), 116 had NG detected (75 urogenital site, 83 rectum, 72 pharynx); 9.4% infected females and 67.3% MSM were urogenital negative. 276 had CT detected (217 urogenital site, 249 rectum, 63 pharynx); 13.1% infected females and 71.8% MSM were urogenital negative. Sexual history did not identify those with rectal infections. Clinician-rectal and self-rectal positive percent agreements (PPA) for NG detection were 92.8% and 97.6%; clinician-rectal, and self-rectal PPA for CT detection were 95.6% and 97.2%. There was no difference in diagnostic accuracy between clinician and self-taken samples.

Clinicians performed swabs quicker than participants so costs were lower. However, in asymptomatic people, non-qualified clinicians would oversee self-swabbing and these costs would be lower than clinician's.

Conclusions:

There was no difference in diagnostic accuracy of clinician compared with self-taken extragenital samples. Sexual history did not identify those with rectal infections so individuals should have extragenital clinician, or self-taken, samples. Clinician swabs cost less than self-swabs but in asymptomatic people, or doing home sampling, their costs would be lower than clinician swabs.

Trial Registration: ClinicalTrials.gov NCT02371109

Background

Neisseria gonorrhoeae (NG) and *Chlamydia trachomatis* (CT) are the two most common bacterial sexually transmitted infections (STIs) in the world[1]. Both infections can be asymptomatic in males and females, but may lead to serious sequelae if untreated[2,3]. Hence increased provision of community screening, and internet ordered postal screening kits, for asymptomatic NG and CT has been adopted, using self-taken vulvovaginal swabs (VVS) in females and first-catch urine samples (FCU) in males for nucleic acid amplification testing (NAAT)[4,5].

Both infections can infect the rectum and pharynx (extragenital sites), usually with no symptoms. Infections may be present in one of, or both, the urogenital and extragenital sites. Unless all anatomical sites are tested, some infections may be missed.

Many community testing programmes do not include extragenital samples as historically clinicians have taken these[4], yet the majority of NG and CT infections in men who have sex with men (MSM) are extragenital[6]. Identifying, and treating, extragenital infections is important for preventing complications and may improve control of gonorrhoea and chlamydia. Pharyngeal infections in MSM and females can be transmitted to the male urethra through oral-penile sex[7,8], pharyngeal NG may be transmitted to the rectum in MSM by using saliva as a lubricant for anal sex[9], and rectal infections in females may be autoinoculated to urogenital sites[10,11].

Most guidelines suggest extragenital testing in MSM and females should be based on reported receptive anal and giving oral sex[2,3,12,13]. However, universal extragenital sampling is being recommended by many as extragenital infections are frequently found in those not disclosing anal and oral sex[14-18].

Self-taken samples are preferred by most people[19], and can be performed outside healthcare facilities. Using self-taken swabs from extragenital sites would enable extragenital testing in community settings and by postal-testing.

Experience of self-taken extragenital swabs to detect NG and CT, is increasing but published evidence of their efficacy is limited to five studies comparing self-taken with clinician-taken swabs[20-24]. Four studies assessed rectal swabs[20-23], and three assessed pharyngeal swabs in MSM[20,23,24]; one assessed rectal swabs in females[21] and none have assessed pharyngeal swabs in females. No appropriately powered trial, with randomised order of clinician versus self-taken extragenital swabs, in MSM or females has been performed.

We therefore performed a study comparing clinician-taken versus self-taken rectal and pharyngeal swabs for the diagnosis of gonorrhoea and chlamydia in females and MSM. We also compared the cost-effectiveness and cost per infection found.

Methods

Participants

A prospective, convenience, sample of females and MSM, 16 years or over presenting to Leeds Sexual Health's central clinic between January 2015 and September 2016. Those wishing to be tested for NG and CT, and willing to perform self-taken swabs in addition to standard clinician performed swabs, were invited to participate. Antibiotics taken in the preceding 28 days and/or rectal symptoms (necessitating an examination with clinician swabs using a proctoscope) were exclusion criteria. Written consent was obtained with inclusion allowed only once to prevent learning bias.

Details of age, sex, and urogenital symptoms suggestive of a bacterial STI were collected. A detailed sexual history was recorded, including all sites of sexual exposure and condom use.

Test samples, randomisation and blinding

Participants had three sets of samples: 1. Clinician-taken rectal and pharyngeal swabs analysed separately (Clinician); 2. Self-taken rectal, pharyngeal and VVS/FCU analysed separately (Self); 3. Self-taken rectal, pharyngeal and VVS/FCU analysed as a pooled specimen (Pooled). Other routine samples were collected as clinically indicated. This paper reports the results of the clinician compared with the self-taken extragenital samples. The results of the pooled samples are described elsewhere [Wilson JD, Wallace HE, Loftus-Keeling M, et al. Swab-yourself trial with economic monitoring and testing for infections collectively (SYSTEMATIC): Part 2. A diagnostic accuracy, and cost-effectiveness, study comparing rectal, pharyngeal and urogenital specimens analysed separately, versus as a pooled specimen, for the diagnosis of gonorrhoea and chlamydia. Submitted to Clin Infect Dis with this paper].

Participants were given written and pictorial instructions on swab-taking and insertion into the NAAT specimen containers, with mirrors to aid pharyngeal sampling. Clinician rectal swabs were taken without a proctoscope as per routine clinical practice in those without rectal symptoms.

To minimise learning bias, or any impact of order on NAAT performance, the order of self and clinician swabs, and of self-swabs for pooling and for separate analysis, was randomised using computer generated simple randomisation in advance of the study. Randomisation was done separately for females and MSM to ensure approximately equal numbers of sample order in each group. The order was revealed to the researcher and participant, after consent, using a sealed envelope allocated to the study number.

All patients attending Leeds Sexual Health have a unique clinic identification code. This code was used on clinician and self-taken rectal and pharyngeal samples with the first taken labelled A and second labelled B. Laboratory staff were blinded to whether A and B were clinician or self-samples.

Microbiological analysis

Microbiological analyses were performed in the Department of Microbiology, Leeds General Infirmary, by accredited laboratory personnel. The samples were tested for NG and CT using Aptima Combo 2 (AC2) according to manufacturer's instructions (Hologic, San Diego, USA). AC2 were positive, equivocal or negative for NG and CT. Positive and equivocal results were considered likely positive. To ensure high negative percent agreement (NPA), positive or equivocal tests were tested further using Aptima-GC or Aptima-CT. Samples were classed as positive if AC2 and confirmatory test positive. Equivocal AC2 samples positive on confirmatory tests were only classed as positive if a second AC2 was also positive. An equivocal or positive AC2 assay unconfirmed by Aptima-GC or Aptima-CT was reported as indeterminate. (See supplementary figures 2 and 3).

Some participants had clinician-taken cultures for NG from urogenital and extragenital sites if clinically indicated. Culture results were either positive or negative for NG.

Patient Infected Status and Site Infected Status

The patient infected status (PIS) for gonorrhoea was defined as at least two positive NG NAAT samples (one could be the pooled sample), or a positive NG culture from any site.

The PIS for chlamydia was defined as at least two positive CT NAAT samples (one could be the pooled sample). Indeterminate samples were then categorised as true positive with a positive PIS and false positive with a negative PIS. The site-infected status (SIS) was

defined as at least two positive samples from that site, or one positive site sample and a positive pooled sample.

Sample size and statistical analysis

Clinician sample positive percent agreements (PPA) were assumed to be 99%. PPA of 80% or less for self-samples would be rejected as too low. Fifty NG and CT positive samples would detect a significant difference between PPA of 80% and 99% with 80% power and 95% probability. Recruitment allocation of approximately 2:1 female to MSM was planned based on estimated extragenital infection prevalence, in order to achieve 50 cases of each infection at each site.

The PPA and NPA of clinician and self-samples for the diagnosis of NG and CT were determined using the PIS and SIS and subclassified for sex. Any differences between PPAs in those infected, and NPAs in those without infection, were determined using McNemar's test [25].

Health Economics analysis

Within-study cost-effectiveness analyses following the National Institute of Health and Care Excellence (NICE) recommendations were undertaken from the perspective of the National Health Service (NHS)[26]. Cost and outcome data were combined to produce a deterministic and probabilistic incremental cost-effectiveness ratio (ICER) based on the correct test result from clinician and self-samples. The analyses assumed the estimated cost of performing the tests was £60 and a willingness to pay would not exceed this threshold.

The grade of clinician, any urogenital symptoms, time taken to perform clinician swabs, and the participant's first set of swabs, were recorded. NHS unit costs were taken from a recognised source[27]. Diagnostic kit costs and laboratory processing costs were obtained

from the Department of Microbiology. Swab collection costs were calculated for females and MSM. The analyses used a price year of 2016.

Results

A STARD diagram of participant recruitment is shown in Figure 1. In total 1793 participants (1284 females, 509 MSM) were recruited by 5 NHS clinicians: one consultant (Attending Doctor); one Specialty Registrar (Resident Doctor); two Band 6 Research Nurses (Clinical Nurse Specialists); and one Band 3 Health Care Assistant [HCA] (Nursing Assistant).

In females, the mean age was 25 years (range 16-71; median 23 years); 489 (38.1%) had urogenital symptoms suggestive of a bacterial STI; 1283 (99.9%) had ever received vaginal sex, 595 (46.4%) had ever received anal sex and 1232 (96.0%) had ever given oral sex. In MSM, the mean age was 33 years (range 18-77; median 29 years); 66 (13.0%) had urogenital symptoms suggestive of a bacterial STI; 463 (91.0%) had ever given anal sex, 460 (90.4%) had ever received anal sex, 503 (98.8%) had ever given oral sex, and 506 (99.4%) ever received oral sex.

The numbers completing each sampling order were:

Clinician/Pooled/Self	450
Clinician/Self/Pooled	448
Pooled/Self/Clinician	445
Self/Pooled/Clinician	450

Neisseria gonorrhoea and Chlamydia trachomatis results

The numbers fulfilling the PIS, SIS and sites of infections for NG and CT are shown in Table 1. In females, 6 (9.4%) NG and 31 (13.1%) CT infections were urogenital negative with CT

prevalence higher in rectal samples than VVSs (17% versus 16%). Of the 218 females with rectal infection, only 195 (89%) were VVS positive, whereas of the 206 VVS infections, 195 (95%) were also rectal positive. Disclosing ever having anal sex was not associated with increased risk of rectal NG OR 0.80 (95%CI 0.45-1.43) $p=0.45$; all rectal CT OR 1.18 (95%CI 0.88-1.57) $p=0.26$; or rectal without urogenital CT OR 2.32 (95%CI 0.93-5.78) $p=0.08$. In MSM, 35 (67.3%) NG and 28 (71.8%) CT infections were urogenital negative.

Some results were missing due to errors or samples leaking in transit. For NG these were two VVS, both SIS positive. Three FCU, four clinician-rectal, one self-rectal, three clinician-pharyngeal, and three self-pharyngeal were missing with available samples supporting negative PIS/SIS. For CT these were three FCU (two PIS positive), and five clinician-rectal (one PIS positive). Two VVS, two self-rectal, three clinician-pharyngeal, and three self-pharyngeal were missing with available samples supporting negative PIS/SIS.

A number of results were indeterminate. For NG: three FCU with positive PIS were categorised true positives; two self-rectal swabs with negative PIS categorised false positives; five self-pharyngeal swabs, three categorised true positive, two false positives; one clinician-rectal swab categorised true positive; and two clinician-pharyngeal swabs categorised true positive. For CT: two self-pharyngeal swabs were categorised true positives; three clinician-rectal swabs categorised true positives; and one clinician-pharyngeal swab categorised true positive.

Table 2 shows the PPAs and NPAs of clinician and self-taken rectal and pharyngeal swabs for the detection of NG and CT in all participants, females and MSM. The PPAs of clinician-rectal, and self-rectal swabs for NG detection were 92.8% and 97.6%; and for clinician-rectal, and self-rectal for CT detection were 95.6% and 97.2%. The self-taken rectal and pharyngeal samples identified slightly more true positive cases than the clinician samples, but they also gave more false positive results. However, there was no significant difference

in the diagnostic accuracy of self-taken rectal and pharyngeal samples compared with clinician samples.

Health Economics analysis

Clinicians performed the swabs in an average of 3 minutes irrespective of grade, whereas participants took their swabs in an average of 4 minutes. Females took longer than MSM (4.2 minutes versus 3.7) but clinicians performed the swabs quicker in females (2.9 versus 3.1). Symptomatic participants took longer to take their swabs than those who were asymptomatic (4.3 versus 3.9) and clinicians took longer to perform swabs on those with symptoms versus those without (3.7 versus 2.7).

The results of the cost-effectiveness analysis are shown in Table 3. Total costs of clinician swabs were less than self-swabs in MSM and females. However in those without symptoms, community or clinical practice testing would be overseen by a non-qualified clinician. If self-taken swabs were overseen by a Band 3 HCA, the costs would be lower than clinician swabs in MSM and females. The estimated ICER suggests clinician swabs would cost £923 for MSM and £2054 for females to correctly detect an additional gonorrhoea infection. For detection of chlamydia for MSM costs are lower and effectiveness higher.

Discussion

This is the first adequately powered, randomised, trial comparing the diagnostic accuracy of clinician versus self-taken rectal and pharyngeal swabs for the diagnosis of NG and CT in females and MSM. We demonstrated good concordance between the clinician and self-taken samples with no difference in diagnostic accuracy. There was high PPA and NPA with all swabs. The PPAs of clinician and self-taken swabs were above the recommended 90%[28]. The NPAs for NG and CT detection with all the swabs were over 99%.

If asymptomatic testing in a clinic or community setting is being undertaken self-taken swabs are cheaper than clinician-taken. However, if a person is seen by a qualified clinician, it is cheaper for the clinician to take the swabs unless their time can be used constructively in the patient's care while the patient takes their own swabs. Although we did not evaluate this, in those ordering postal-testing, the time needed for the swab-taking becomes irrelevant and the cost is just that of the kits and swabs.

Limitations of our study are that, although large, this was a single centre study making it less generalisable than a multicentre study. Also, the planned allocation of females to MSM, to achieve 50 cases of each infection at each site, left us with only 39 CT infections in MSM which underpowered the CT sub-analysis in MSM. We assessed only one NAAT so our results cannot necessarily be extrapolated to other NAATs as sensitivities and specificities vary between them[29]. The negative AC2 samples were not retested, so we could have missed some false negative results. However, this is unlikely as each participant had six different samples analysed, with two from each of the rectum and pharynx.

Our definition of true positive samples was conservative. The PIS and SIS required at least two confirmed positive NG or CT NAAT samples, or a positive NG culture. We chose this more stringent definition as Alexander reported a high number of false positive self-taken pharyngeal swabs for NG, possibly due to sample contamination[20]. Such contamination could be from the patient themselves, which would not be of detrimental consequence, however environmental contamination within the sexual health clinics has been described and could be a source of false positive results[30,31]. Our definition contrasts to many other published studies that categorised every confirmed positive sample as true positive[21,23,24] which may have overestimated the sensitivities and specificities in these studies.

To optimise NPA, surfaces were decontaminated before and after each participant. Self-swabbing instructions emphasised reducing environmental contamination by careful hand washing before swab taking, avoiding swab tips touching anything in the environment, and requesting another kit if this happened. Devices were also used to hold transport medium containers. Even with these instructions, there were 10 more false positive self-taken than clinician swabs, indicating that nucleic acid contamination does occur when people are taking their own swabs and clear instructions to minimise this risk need to be given.

To ensure consistency of the clinician swabs, only five clinicians enrolled participants. The two physicians checked each other's technique and then instructed, and initially observed, the non-medical staff in the techniques to be used. Consistent techniques are important as differences in sampling had been shown to affect the isolation rates of gonorrhea by culture[32] but, more recently, probably not by NAAT[33].

In keeping with other studies, we identified high levels of extragenital infections in females[14-17] as well as MSM[6]. In MSM 67.3% of gonorrhoea and 71.8% of chlamydia, and among females 9.4% of gonorrhea and 13.1% of chlamydia, would have been missed by urogenital sampling only. Interestingly the rectum was the most prevalent site for chlamydia infections in females; 23 (11%) had rectal infection without urogenital infection. However, disclosing ever having anal sex was not associated with increased risk of rectal infections. These findings have been reported by others where up to 27% of females had sole rectal infections[15]. Most national[2,3] and international guidelines[12,13] suggest extragenital testing in MSM and females should be based on reported sexual history of receptive anal and giving oral sex. As sexual history did not identify those with rectal infections, our study strongly supports the existing evidence for universal extragenital sampling in both MSM and females undergoing CT and NG testing[14-17].

Pharyngeal gonorrhoea may be transmitted to the rectum in MSM by using saliva as a lubricant for anal sex[9]. Interestingly, our pharyngeal and rectal gonorrhoea prevalence in MSM were identical at 6.7% whereas the urethral prevalence was lower at 3.3%, supporting the oro-rectal transmission hypothesis[9]. Treating extragenital infections prevents complications from gonorrhoea and chlamydia. Although rare, disseminated gonococcal infections are potentially life threatening and occur more frequently from extragenital infections because of lack of symptoms[13]. Azithromycin 1g single dose is frequently used to treat urogenital chlamydia but its estimated efficacy for rectal chlamydia is only 83%[18]. Of the females who were VVS chlamydia positive in our study, 95% were also rectal positive. Approximately 16% would not be cured of undiagnosed rectal infection if VVS tested only, and treated with azithromycin. Persistent rectal infection could lead to repeated urogenital infections due to autoinoculation from the rectum[10,11], with reinfection a recognised contributing factor for tubal infertility[2]. This reinforces recommending universal rectal testing in all females as well as MSM.

In summary, we have demonstrated good concordance between clinician and self-taken samples with no significant difference in diagnostic accuracy. Self-taken swabs were cheaper than clinician-taken if overseen by a non-qualified clinician or performed at home. These findings have important implications for policy makers and providers of STI services as extragenital self-sampling could be used to expand STI testing beyond healthcare facilities to community settings and home-sampling. We found high levels of extragenital infections in females and MSM. A large proportion of these would have been missed by urogenital testing alone. As sexual history does not identify those with extragenital infections, our study strongly supports the existing evidence for universal extragenital sampling in both MSM and females undergoing chlamydia and gonorrhoea testing.

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Conflicts of Interest

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Table 1. The numbers fulfilling the patient infected status, site infected status and sites of infections for gonorrhoea and chlamydia infections in females and MSM

	Gonorrhoea			Chlamydia		
	Females	MSM	Total	Females	MSM	Total
PIS positive	64 (5%)	52 (10.2%)	116 (9%)	237 (18.5%)	39 (7.7%)	276 (15.4%)
SIS urogenital	58 (4.5%)	17 (3.3%)	75 (4.2%)	206 (16.0%)	11 (2.2%)	217 (12.1%)
SIS rectal	49 (3.8%)	34 (6.7%)	83 (4.6%)	218 (17.0%)	31 (6.1%)	249 (13.9%)
SIS pharyngeal	38 (3%)	34 (6.7%)	72 (4%)	58 (4.5%)	5 (1.0%)	63 (3.5%)
Sites infected						
Urogenital +	8	2	10	9	5	14
Rectal -						
Pharyngeal -						
Urogenital +	18	7	25	152	5	157
Rectal +						
Pharyngeal -						
Urogenital +	1	1	2	2	0	2
Rectal -						
Pharyngeal +						
Urogenital +	31	7	38	43	1	44
Rectal +						
Pharyngeal +						
Urogenital -	0	9	9	18	24	42
Rectal +						
Pharyngeal -						

Urogenital -	6	15	21	8	3	11
Rectal -						
Pharyngeal +						
Urogenital -	0	11	11	5	1	6
Rectal +						
Pharyngeal +						

Table 2. Positive percent agreements (PPAs), negative percent agreements (NPAs), true positives, false positives, true negatives, false negatives, of rectal and pharyngeal swabs for the detection of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* in all participants, females and MSM.

	Neisseria gonorrhoeae All Participants 116/1793 (6.5%)					Neisseria gonorrhoeae Females 64/1284 (5%)					Neisseria gonorrhoeae MSM 52/509 (10.2%)				
Total =1793	PPA (95% CI)		NPA (95% CI)		P value	PPA (95% CI)		NPA (95% CI)		P value	PPA (95% CI)		NPA (95% CI)		P value
	True positive	False positive	True negative	False negative		True positive	False positive	True negative	False negative		True positive	False positive	True negative	False negative	
Rectal clinician N = 83/1789 (4 missing)	92.8 (84.9-97.3)		99.9 (99.7-100.0)		Sens 0.29	93.9 (83.1-98.7)		100 (99.7-100.0)		Sens 0.25	91.2 (76.3-98.1)		99.8 (98.8-100.0)		Sens 1.0
	77	1	1705	6		46	0	1233	3		31	1	472	3	
Rectal Self N = 83/1792 (1 missing)	97.6 (91.6-99.7)		99.7 (99.2-99.9)		Spec 0.13	100 (92.8-100.0)		99.6 (99.1-99.9)		Spec 0.07	94.1 (80.3-99.3)		99.8 (98.8-100.0)		Spec 0.45
	81	6	1703	2		49	5	1229	0		32	1	474	2	
Pharyngeal clinician N = 72/1790 (3 missing)	93.1 (84.5-97.7)		99.9 (99.7-100.0)		Sens 0.73	94.7 (82.3-99.4)		100 (99.7-100.0)		Sens 0.62	91.2 (76.3-98.1)		99.80 (98.8-100.0)		Sens 0.62
	67	1	1717	5		36	0	1244	2		31	1	473	3	
Pharyngeal self N = 72/1790 (3 missing)	95.8 (88.3-99.1)		99.8 (99.5-100.0)		Spec 0.48	94.7 (82.3-99.4)		100 (99.7-100.0)		Spec 1.00	97.1 (84.7-99.9)		99.4 (98.2-99.9)		Spec 0.48
	69	3	1715	3		36	0	1244	2		33	3	471	1	
	Chlamydia trachomatis All Participants 276/1793 (15.4%)					Chlamydia trachomatis Females 237/1284 (18.5%)					Chlamydia trachomatis MSM 39/509 (7.7%)				
Total =1793	PPA (95% CI)		NPA (95% CI)		P value	PPA (95% CI)		NPA (95% CI)		P value	PPA (95% CI)		NPA (95% CI)		P value
	True positive	False positive	True negative	False negative		True positive	False positive	True negative	False negative		True positive	False positive	True negative	False negative	
Rectal clinician N = 248/1788 (5 missing, 1 SIS positive)	95.6 (92.2-97.8)		99.9 (99.5-100.0)		Sens 0.48	95.9 (92.3-98.1)		99.9 (99.5-100.0)		Sens 0.61	93.6 (78.6-99.2)		99.8 (98.8-100.0)		Sens 1.00
	237	2	1538	11		208	1	1064	9		29	1	474	2	
Rectal Self N = 249/1791 (2 missing)	97.2 (94.3-98.9)		99.8 (99.4-100.0)		Spec 1.00	97.3 (94.1-100.0)		99.7 (99.2-99.9)		Spec 0.62	96.8 (83.3-99.9)		100.0 (99.2-100.0)		Spec 1.00
	242	3	1539	7		212	3	1062	6		30	0	477	1	
Pharyngeal clinician N = 63/1790 (3 missing)	92.1 (82.4-97.4)		99.9 (99.7-100.0)		Sens 1.00	91.4 (81.0-97.1)		99.9 (99.6-100.00)		Sens 1.00	100.0 (47.8-100.0)		100.0 (99.3-100.0)		Sens 1.00
	58	1	1726	5		53	1	1223	5		5	0	503	0	
Pharyngeal self N = 63/1790 (3 missing)	93.7 (84.5-98.2)		99.8 (99.5-100.0)		Spec 0.62	93.1 (83.3-98.1)		99.8 (99.4-100.0)		Spec 1.00	100 (47.8-100.0)		99.8 (98.9-100.0)		Spec 1.00
	59	3	1724	4		54	2	1222	4		5	1	502	0	

Missing samples are from negative SIS unless stated from positive SIS

Table 3. The cost-effectiveness analysis of the clinician-taken swabs versus the self-taken swabs for the diagnosis of gonorrhoea and chlamydia

Gonorrhoea	Sex	Test	Costs	Effectiveness	Incremental cost	Incremental effectiveness	^aICER	Net monetary benefit (£60 threshold)	^bProbability of CE at a WTP of £60
Asymptomatic	MSM	Self-taken	£19,803	408.96				£4,735	0.02
		Clinician- taken	£19,127	410.99	-£676	2.030	-£333	£5,533	0.98
	Females	Self-taken	£34,097	733.95				£9,940	0.00
		Clinician- taken	£32,170	734.98	-£1,928	1.026	£1,879	£11,929	1.00
Asymptomatic	MSM	Self-taken	£17,252	408.96				£7,285	1.00
Assuming self- taken swabs		Clinician- taken	£19,127	410.99	£1,874	2.030	£923	£5,533	0.00
overseen by Band 3 HCA	Females	Self-taken	£30,063	733.95				£13,974	1.00
		Clinician-							

		taken	£32,170	734.98	£2,107	1.026	£2,054	£11,929	0.00
Chlamydia	Sex	Test	Costs	Effectiveness	Incremental cost	Incremental effectiveness	^a ICER	Net monetary benefit (£60 threshold)	^b Probability of CE at a WTP of £60
Asymptomatic	MSM	Clinician-taken	£19,127	411.96				£5,591	0.94
		Self-taken	£19,803	413.17	£676	1.208	£560	£4,987	0.06
All clinicians	Females	Clinician-taken	£32,170	719.03				£10,972	1.00
		Self-taken	£34,097	722.95	£1,928	3.923	£491	£9,280	0.00
Asymptomatic		Self-taken	£17,252	413.17				£7,538	1.00
Assuming self-taken swabs overseen by Band 3 HCA	MSM	Clinician-taken	£19,127	411.96	£1,874	-1.208	£1,552	£5,591	0.00
		Self-taken	£30,063	722.95				£13,314	1.00
	Females	Clinician-taken	£32,170	719.03	£2,107	-3.923	-£537	£10,972	0.00

^aICER = incremental cost-effectiveness ratio; ^bProbability of CE at a WTP of £60 = Probability of cost-effectiveness at a willingness to pay of £60

Negative ICER represents the alternative is dominated as it is costlier and less effective

Rows in bold represent the cost-effective strategy at a £60 per correct test detected assumed. Cost-effective strategies have a higher net monetary benefit

Figure 1. STARD Diagram SYSTEMATIC