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Title: Management of cases testing positive for gonococcal infection in a community-based chlamydia screening programme

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ABSTRACT

Background: The National Chlamydia Screening Programme in Greater Manchester (NCSP-GM) commissioned an evaluation of the management of gonorrhoea cases identified using the Gen-Probe APTIMA Combo 2 assay (AC2).

Methods: NCSP-GM provided data on gonorrhoea cases from a six month period (September 2007-February 2008). We collected data from patient referral pathways to genitourinary medicine (GUM) clinics, including confirmatory testing, antibiotic resistance patterns and contact tracing. The AC2 positive predictive value (PPV) was calculated.

Results: 111 individuals tested **positive for gonococcal infection** using AC2 (0.7% of 16,028 individuals tested). Of these, 96 (0.6% of all tested) known index cases were seen at Greater Manchester GUM clinics. 78/96 (14 males, 64 females) underwent confirmatory microscopy and gonococcal culture. Confirmatory tests were positive in 14 males (100%) but only 40 females (78%). Thus the PPV of AC2 was 69% (54/78). Sensitivity in women may have been reduced by limited partner information and sample-taking (only 28% had a full gonorrhoea screen).

Conclusion: Gonorrhoea screening in an NCSP-targeted population identified gonorrhoea in a low-risk population. Subsequent management in GUM clinics was variable and limited sample-taking may have decreased the sensitivity of confirmatory testing in women. Appropriate antibiotic sensitivity tests or, in their absence, a test of cure may be needed to ensure effective treatment.

INTRODUCTION

Chlamydia trachomatis and *Neisseria gonorrhoeae* are the most common bacterial STIs in British and European young people.[1,2] England is the only country in Europe operating a National Chlamydia Screening Programme (NCSP).[3] Established to reduce chlamydia prevalence in 15–24 year olds, NCSP recognises the relationship between chlamydia and gonorrhoea in its target population.[4,5] National data based on genito-urinary medicine (GUM) clinic diagnoses are likely to underestimate STI rates as those presenting for testing are primarily symptomatic or have known positive contacts. A community-based opportunistic screening service using nucleic acid amplification tests (NAATs) can simultaneously identify gonorrhoea and chlamydia cases, reducing infection rates by detecting cases in the community that may otherwise remain undiagnosed.

In October 2006 the chlamydia screening programme in Greater Manchester, North West England (*RU Clear?*) was launched. From March 2007 the Gen-Probe APTIMA Combo 2 assay NAAT test (AC2) was used. This is a duplex transcription mediated assay identifying both chlamydia and gonorrhoea.[4] People diagnosed chlamydia positive only through the NCSP are treated in the community. However, because of potential antibiotic-resistance, all **those testing positive for gonococcal infection**, including those also testing chlamydia positive, are subsequently referred to GUM clinics for confirmatory microscopy, gonococcal culture, antibiotic sensitivity testing, wider STI screens, partner notification and treatment. AC2 has proved effective for gonorrhoea community screening[6,5,7] and has been shown to have a high diagnostic sensitivity when compared to GUM culture.[8-10] Here, we explore the value of community screening for gonorrhoea and the effectiveness of referral to GUM clinics.

METHODS

In 2008 the Centre for Public Health (CPH), Liverpool John Moores University, evaluated AC2 community testing and GUM confirmatory testing to diagnose gonorrhoea. RU Clear supplied pseudo-anonymised data collected from a six month period (September 2007-February 2008). Chlamydia screening data collection methods are presented elsewhere.[4] CPH processed and stored data under relevant protocols and laws pertaining to confidentiality and security and data transfer agreements were requested. CPH researchers, in person or via clinic staff, collected additional data from case notes on anatomical sampling sites, antibiotic

resistance tests and sexual contacts of gonorrhoea positive GUM patients referred from *RU Clear?*, from 17 locations in Greater Manchester. The AC2 test results and GUM culture test results were compared to ascertain the positive predictive value (PPV) of the AC2 test. Furthermore, confirmatory testing and treatment practices between clinics were explored. This study was classified as a service evaluation by Salford and Trafford NHS Ethics Committee.

RESULTS

Overall 16,028 persons (76% female) were tested using AC2 from the RU Clear programme, of which 111 tested positive for gonococci. Of these, 13 were not recorded at GUM clinics, and an additional two were excluded from this study as it was unknown if they were index patients or contacts. Of the remaining 96, 18 were male (0.5%) and 78 were female (0.6%). Overall, 18 refused confirmatory testing and were treated presumptively, one (6%) of whom underwent test of cure (TOC). Of the 78 agreeing to GUM culture, 42.9% of males and 44.4% of females had tested chlamydia positive. Furthermore, 78.6% of males and 57.8% females were reported to have symptoms¹ at GUM consult.

Of the 18 males testing positive on AC2, 14 underwent GUM culture testing and all were confirmed gonorrhoea positive (Figure 1). Of the 78 females testing gonorrhoea positive on AC2, 64 agreed to GUM culture testing with 40 testing positive producing an overall PPV of 69% (54/78). Overall, 32 (41%) people did not have antibiotic sensitivity tests conducted. However, TOC was reported in three (9%) cases therefore in these cases appropriate treatment was prescribed and confirmed successful. In those tested for antibiotic resistance, five (6%) showed resistance to one or more gonorrhoea treatments and all showed sensitivity to at least one commonly prescribed gonorrhoea treatment.

Of the 24 females negative on GUM culture all were either Chlamydia negative or received azithromycin antibiotic treatment for chlamydia after confirmatory tests were taken. Of those negative, eleven cases demonstrated supporting evidence for the NAATs test being truly positive in their medical notes (i.e. positive NAATs retest or positive partner). Eight reported a positive retest on NAAT at GUM, two of whom also reported that a current or past partner had tested positive and an additional three had positive partners. Of the 13 remaining negative on GUM culture, one tested negative at all body sites (Table 1). Two cases tested

¹ Patients were defined as symptomatic if they reported one or more of the following symptoms at GUM consult: unusual discharge, dysuria, abnormal bleeding (in females), pelvic pain/swollen testicles.

negative at three body sites. A further seven cases were tested solely at the cervix, and three were not tested at the pharynx or rectum. Of the 13 remaining negative cases, five (38.5%) presented with symptoms and of these four were tested only at the cervix. For females, swabs were collected from three or more sites in only 28% of cases. Of 64 female cases, 11 (17%) were tested at three body sites, of which 8 (73%) tested positive; 7 (28%) were tested at four body sites, of which 6 (86%) tested positive at one site or more (Table 1). No partner information was available in 79% (19/24) of cases. Retest practices varied across almost all clinics with only one clinic showing a trend, which was to swab one site only (all cases; one male, nine females). Three other clinics showed a pattern of consistently swabbing the urethra but less consistency in swabbing cervical or pharyngeal sites in females.

DISCUSSION

Findings showed a lower PPV for AC2 compared with research-based clinical studies using rigorous re-test practices.[8] Similar to findings here, Lavelle and colleagues showed that AC2 tests defined as ‘false positives’ have had contact with gonorrhoea positive partners.[8] This evaluation indicates that accurate diagnosis was compromised by inconsistent GUM culture test practices. The GUM culture test aims to confirm gonorrhoea positivity and provide antibiotic sensitivity results.[11,12] However, testing restricted to one or two anatomical sites limits the opportunity to achieve this. Findings revealed that 25% of patients swabbed at the pharynx for GUM culture tested positive at this site, yet patients were tested at the pharynx infrequently. With an increase in unprotected oral sex in young people indicated by a concomitant increase in *Herpes simplex* virus in those aged 16-19[1] the limited emphasis on pharyngeal testing could be a missed opportunity to test a potentially common infection site, which may be more acceptable and less invasive to test.[13] Further, we noted inconsistent swabbing practice whereby cervical sites were not swabbed when the urethra was (and *vice versa*). Targeted swabbing may be driven by patient symptomatology, particularly as patients presenting with symptoms are more likely to test gonococcal positive.[14] However, limiting this to one body site reduces opportunities to confirm NAATs tests and produce antibiotic sensitivity results. It was beyond the scope of this study to investigate the proportion of patients who may have refused swabs at specific body sites. However, retest patterns indicate a propensity for limited swabbing.

National guidance on testing and treating gonorrhoea emphasises the need for comprehensive testing at all body sites indicated by sexual history.[11,12] Comprehensive GUM testing

would also inform public health decisions about the effectiveness of community testing in low prevalence areas. Our data suggest that, with more comprehensive confirmatory testing practices, the actual PPV could be higher than our measured value of 69%. This is also supported by the presentation of symptoms in cases testing negative on culture. It would be useful to quantify the PPV under ideal retesting conditions to reassure professionals and the public that AC2 community testing is reliable.[15] Such support for testing could impact community testing, GUM culture testing and partner notification efforts, thereby increasing opportunities to reduce gonorrhoea transmission. Furthermore, few patients underwent a TOC after gonorrhoea treatment. The high refusal rate for confirmatory tests, and inadequate proportion of tests providing antibiotic sensitivity results suggest that TOC be considered in these situations.[16] The lack of antibiotic sensitivity tests are an interesting finding; a lack of information about the reasons for this in the patient notes prevents further investigation, although it justifies future studies. The care pathway provides guidance on treatment procedures to ensure therapy is not provided before patients reach GUM. Furthermore, clinical data confirm that guidance was followed and thus prior treatment was not a factor in negative retest results, as previous studies have reported.[17]

Patients testing **positive for gonococcal infection** using AC2 should be swabbed at all body sites to confirm results and detect antibiotic resistance. With an uncertain proportion of resistant gonorrhoea cases, TOC, possibly with less invasive NAATs using urine samples or self-taken swabs, should be carried out wherever possible. Since supporting evidence can be found for apparently negative GUM culture tests, patients ought to be made aware that a negative result should not preclude partner notification.

Table 1: Culture results compared with AC2 test in males and females

	Number of cases	Original AC2 sample type	Culture results			
			pharynx	rectum	cervix	urethra
Females*	1	Urine	-	-	-	-
	3	Urine	-	-	+	-
	1	Urine	-	-	+	+
	1	Urine	-	-	+	n/t
	1	Urine	-	+	+	+
	3	Urine	-	n/t	-	-
	3	Urine	-	n/t	+	+
	1	Urine	-	n/t	+	n/t
	1	Urine	+	-	+	+
	2	Urine	+	n/t	+	+
	2	Urine	+	n/t	+	n/t
	12	Urine	n/t	n/t	-	-
	1	Urine	n/t	n/t	-	+
	6	Urine	n/t	n/t	-	n/t
	1	Urine	n/t	n/t	+	-
	8	Urine	n/t	n/t	+	+
	10	Urine	n/t	n/t	+	n/t
	1	Urine	n/t	n/t	n/t	-
	1	Urine	n/t	n/t	n/t	+
	1	Cervix	n/t	+	+	+
	1	Unknown	-	n/t	n/t	+
	1	Unknown	n/t	-	+	+
	1	Unknown	n/t	n/t	-	n/t
	1	Unknown	n/t	n/t	+	+
Males**	1	Urine	-	-	N/A	+
	1	Urine	-	n/t	N/A	+
	1	Urine	+	n/t	N/A	+
	10	Urine	n/t	n/t	N/A	+
	1	Unknown	-	n/t	N/A	+

* 14 cases refused further tests (13 were originally tested using urine and one case was unknown).

** 5 cases refused further tests (all originally tested using urine samples)

- , negative result; +, positive result; n/t, site not tested.

KEY MESSAGES

- Community testing identifies positive gonorrhoea cases in a low prevalence population that may otherwise remain undiagnosed.
- Management of positive community cases varied and limited sample-taking decreased sensitivity of GUM tests and subsequently reduced the chance to test for antibiotic resistance.
- Tests of cure were carried out infrequently. Increasing this practice, particularly in the absence of antibiotic resistance testing results, could ensure optimal patient treatment.
- Partner notification should be conducted on the basis of community test results as supporting evidence can be found for apparently negative GUM culture tests.

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AUTHOR CONTRIBUTIONS

JD contributed to the project design, analysed the data and wrote the manuscript. PC contributed to the project design and edited the manuscript. HCEM, PPH, SPH and MAB edited the manuscript.

COMPETING INTERESTS

None declared.

ETHICS COMMITTEE

This study was classified as a service evaluation by Salford and Trafford NHS Ethics Committee.

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