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An early evaluation of clinical and economic costs and benefits of implementing point of care NAAT tests for *Chlamydia trachomatis* and *Neisseria gonorrhoea* in genitourinary medicine clinics in England

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ABSTRACT

Objectives To estimate the costs and benefits of clinical pathways incorporating a point of care (POC) nucleic acid amplification test (NAAT) for chlamydia and gonorrhoea in genitourinary medicine (GUM) clinics compared with standard off-site laboratory testing.

Method We simulated 1.2 million GUM clinic attendees in England. A simulation in Microsoft Excel was developed to compare existing standard pathways of management for chlamydia and gonorrhoea with a POC NAAT. We conducted scenario analyses to evaluate the robustness of the model findings. The primary outcome was the incremental cost-effectiveness ratio. Secondary outcomes included the number of inappropriate treatments, complications and transmissions averted.

Results The baseline cost of using the point of POC NAAT was £103.9 million compared with £115.6 million for standard care. The POC NAAT was also associated with a small increase of 46 quality adjusted life years, making the new test both more effective and cheaper. Over 95 000 inappropriate treatments might be avoided by using a POC NAAT. Patients receive diagnosis and treatment on the same day as testing, which may also prevent 189 cases of pelvic inflammatory disease and 17 561 onward transmissions annually.

Discussion Replacing standard laboratory tests for chlamydia and gonorrhoea with a POC test could be cost saving and patients would benefit from more accurate diagnosis and less unnecessary treatment. Overtreatment currently accounts for about a tenth of the reported treatments for chlamydia and gonorrhoea and POC NAATs would effectively eliminate the need for presumptive treatment.

INTRODUCTION

In England, there were 1 258 706 sexual health screens performed in genitourinary medicine (GUM) clinics in 2011, including tests for *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoea* (NG).[1] This resulted in 100 647 diagnoses of chlamydia and 20 964 of gonorrhoea. Epidemiological treatment, in which partners of confirmed index cases are given treatment, was reported for 13 125 cases of chlamydia and 2162 cases of gonorrhoea. This represents 12% and 9% of all treatments, respectively, assuming that all of those diagnosed received treatment. A glossary of terms is given in box 1. Management of patients with symptoms indicating possible chlamydia or gonorrhoea infection usually includes presumptive treatment for chlamydia prior to confirmed diagnosis (also called syndromic management).[2 3] However, symptoms can be non-specific and may also be due to other infections, for example, *Mycoplasma genitalium*, resulting in unnecessary or potentially less efficacious treatment.[4 5] Inappropriate or incorrect treatment can result in (1) unnecessary costs of treatment, (2) continuing symptoms or progression to sequelae with associated consultation and treatment costs, (3) selection for the evolution of drug resistance and (4) delayed appropriate treatment.[4–6] Asymptomatic infection is also common and patients remain untreated until the laboratory diagnosis is available. Individuals unaware of their infection may continue to infect partners and risk developing complications during the delay between test and treatment.

Under current best practice, results from off-site laboratories (standard care) should be available to clinicians within 7 days or less. A BASHH audit in 2011 surveyed the proportion of GUM clinics that received chlamydia results within 7 days, the target being 100%. However, a quarter of clinics reported that they received 25% of results after 7 days. There was also variation within and between clinics, for example, due to laboratory capacity or clinic opening times.[7] Once the clinic receives the test result, the patient is contacted and advised how to obtain treatment. The National Chlamydia Screening Programme audit target is that 50% of chlamydia-positives should be treated within 14 days; however, 16% of trusts in 2010 failed to meet this target, primarily due to difficulties in recontacting patients after their test or non-attendance.[8] Infections may therefore remain untreated if patients cannot be contacted or choose not to return.

There are various technologies employed by point of care tests (POCTs) including antibody detection and DNA based methods. Early POC chlamydia/gonorrhoea tests based on antibody/antigen binding detection had limited application due to lower sensitivity and specificity compared with nucleic acid amplification tests (NAATs) performed in laboratories.[9–11] However, new generation POC NAATs for chlamydia and gonorrhoea use PCR technology to detect DNA and are reported to have equivalent performance characteristics to standard laboratory NAATs. The Cepheid Xpert CT/NG (Cepheid, Sunnyvale, California,

Box 1 Glossary of terms

▶ *GLOSSARY*
Several terms describe treatment or management of individuals in whom there is significant clinical suspicion that infection may be present but without confirmed diagnosis. The specific meanings may overlap somewhat depending on context and more than one factor may be present, for example, reported contact with an infected person plus symptoms.
▶ *Presumptive treatment*
Treatment given before confirmed diagnosis is made based on symptoms and clinical evaluation.
▶ *Epidemiological treatment*
Treatment given based on epidemiological evidence, for example, reported sexual contact with an infected person, but could also be a particular risk group during an outbreak (symptoms usually absent).
▶ *Syndromic management*
Similar to presumptive treatment, but refers to treatment in the presence of symptoms or signs indicative of infection.
Both *epidemiological treatment* and *syndromic management* are forms of *presumptive treatment*.
▶ *Overtreatment*
Treatment of individuals for an infection who subsequently are found to test negative for that infection.
▶ *Point of care test (POCT)*
A test in which the specimen can be processed and results given to the patients within the same clinic visit, that is, the specimen is not sent off-site to a laboratory for testing (also called *rapid tests* or *near-patient* tests); may be based on different methods of detection with variable test performance characteristics (sensitivity and specificity).
▶ *Point of care nucleic acid amplification test (POC NAAT)*
This is a POCT that uses NAAT technology. These tests use the same techniques as current large laboratory based NAAT platforms, with equivalent performance characteristics, in a miniaturised computerised system.

USA) is one such test, providing results within 90 min of specimen collection.[12 13] It is simple to use, does not require highly skilled staff and requires only a small space in the clinic.

The clinical and economic costs and benefits of POC NAATs have not yet been fully evaluated for the UK. We present an early, pragmatic decision analysis of introducing a POC NAAT for chlamydia and gonorrhoea into GUM clinics compared with current practice in England. We compare the complete pathway costs of current practice estimated in four diverse GUM clinics against a new pathway incorporating a POC NAAT test. The pathways include testing and treatment costs. This information can aid services in deciding whether to adopt this new technology. We also estimate the number of unnecessary treatments for chlamydia and gonorrhoea that could be prevented if test, diagnosis and treatment are available on the same day. We consider the potential indirect effects of reducing the time between test and treatment on preventing onward transmission and progression to pelvic inflammatory disease (PID).

METHODS

Model structure

We developed a decision analytic model in Microsoft Excel 2010 simulating patient pathways to estimate the costs and benefits of implementing standard care pathways and POC pathways including a chlamydia/gonorrhoea POC NAAT.

The model cycle length was 1 day with an overall length of 28 days. The primary outputs were total costs, quality adjusted life years (QALYs) and incremental cost-effectiveness ratios (ICER).

Description of patient flow through the model

Patient flows are illustrated in figure 1 and a sample patient flow is calculated in online supplementary appendix table A1. The arrows represent the possible transitions at the end of each model cycle.

All index patients in the model enter the testing pathway. Under standard care, a proportion of symptomatic patients are treated presumptively for chlamydia or gonorrhoea at the time of sexually transmitted infection (STI) screening. The remaining infected but untreated and/or asymptomatic patients wait on average 10 days before obtaining treatment at a second visit. Some treated individuals remain positive due to treatment failure. Progression to PID and onward transmission to uninfected partners may occur in positives on days between test and treatment or following treatment failure. In the POC pathways, all patients are tested and receive their result plus appropriate treatment on the same day. As there is no delay between test and treatment, patients in the POC pathway only develop complications or transmit to a partner if they fail treatment.

Asymptomatic partners of chlamydia or gonorrhoea positive index cases who attend GUM for treatment enter a simplified standard care pathway including treatment and test (symptomatic partners would be treated as index cases). In the POC pathway, partners are tested and only positives treated.

Key model assumptions

We assume equivalent test performance for the POCT compared with standard tests. The new generation POC NAATs appear to fulfil this requirement.[12 13] Others have previously investigated the trade-offs between reduced loss to follow-up versus lower sensitivity or specificity and willingness to wait,[14 15] so we do not consider these here. We assume that all tests are in individuals attending for a new episode and the sample obtained is appropriate (eg, urine, vulvo-vaginal swab or rectal swab).

Epidemiological and clinical parameters

We modelled a cohort of 1.2 million index patients to simulate the annual number of STI screens performed at GUM clinics in England.[1]

Epidemiological parameters were based on data from the Genitourinary Medicine Clinic Activity Dataset 2011 (table 1).[1] We estimated baseline positivity in men and women of 8.6% and 7.4% chlamydia and 2.6% and 0.9% gonorrhoea, respectively. We then estimated the distribution of infections between symptomatic and asymptomatic pathways using a detailed study of GUM attendees from the MSTIC study.[16] We assumed that all patients reporting symptoms would enter the symptomatic pathway, regardless of whether their symptoms were indicative of a chlamydial or gonorrhoeal infection.

We synthesised several aspects of current symptomatic patient management to make credible estimates of presumptive treatment of positive and negative attendees (see online supplementary appendix table A2). Available data were used to estimate the number of contacts attending GUM who would be given epidemiological treatment in the absence of symptoms.

We estimated the potential for onward transmission of infection from asymptomatic GUM attendees in the time between

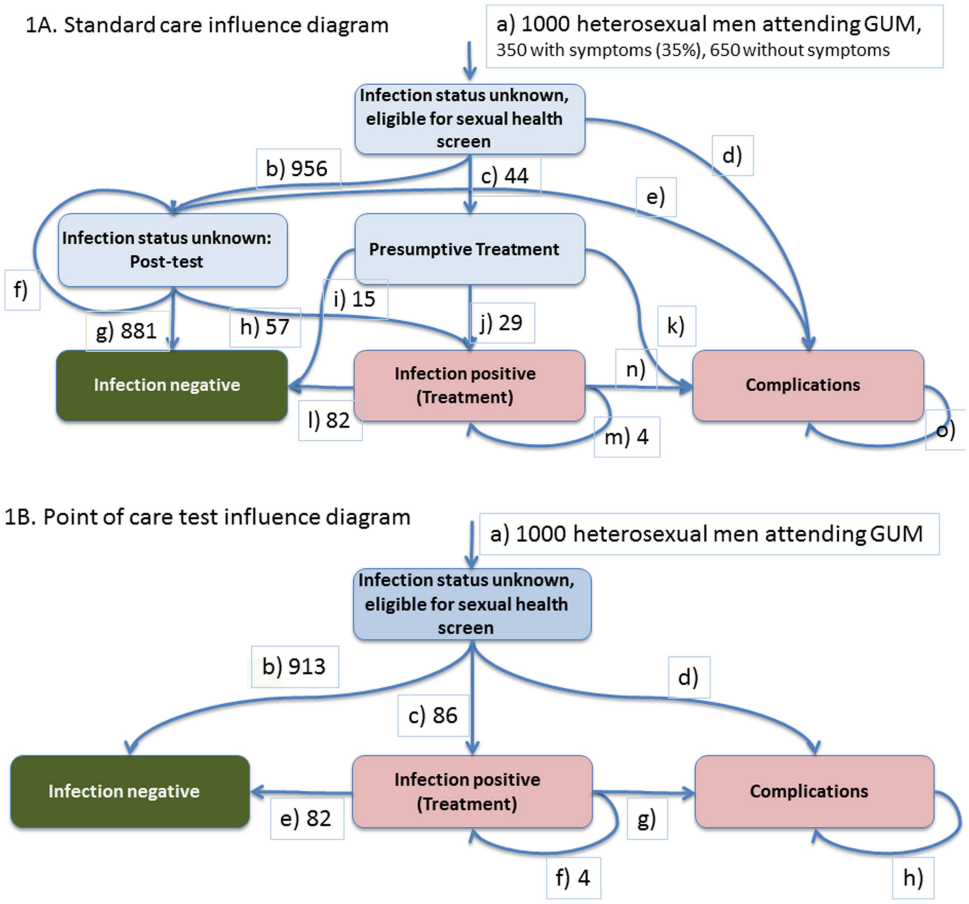

Figure 1 Influence diagrams showing the flow of patients through the model, assuming standard care (A) or point of care (B) pathways for chlamydia and gonorrhoea testing and treatment for genitourinary medicine clinic attendees. (A) Standard care genitourinary medicine clinic attendees based on data from Genitourinary Medicine Clinic Activity Dataset (GUMCAD) 2011,[1] illustrated using chlamydial infection in men. Numbers based on a hypothetical cohort of 1000 male attendances and are rounded to the nearest whole number for illustration. Values <1 are not shown for simplicity. (Note: Attendees who report being a sexual partner of an infected individual are also presumptively treated (partner treatment). These can be explicitly included in the model as 'partners', but are not incorporated in this illustration of 'index' individuals, but in the complete model are added to the total of overtreatment and effective presumptive treatment.) (a) 1000 men attend of whom 350 have any symptoms at entry into clinic (ie, costed as symptomatic pathway). (b) 956 not treated presumptively, await test result=650 without symptoms (65%)+306: 87%*350 with symptoms. (c) 44=13%*350 with specific symptoms are treated presumptively. This assumes 70% of infections are correctly treated presumptively and that 5% of those not infected (but symptomatic of something else) are overtreated. (d), (e), (k), (n), (o) Show progression to development of complications, numbers not shown as <1. (e) See (d). (f) Repeat tests. (g) 881=956–75 (94% of those tested are negative). (h) 57 (6.0% of those not presumptively treated) are infected=(650*6.9% asymptomatic + 306*4.0% symptomatic) (not chlamydial). (i). 15 of those presumptively treated (35%*44) were not infected. (j) 29 of those presumptively treated (65%*44) were infected. (k), (n), (o) All relate to progression to complications which are rare events dealt with in the model not enumerated for simplicity here (<1). (l) 82 of those receiving treatment for chlamydia recover and become negative (95% treatment effectiveness). (m) Four fail treatment and remain positive (5% failure. Note: these would not routinely receive test of cure for chlamydia). From this illustration we can calculate outcomes: (1) Total chlamydial infections are 86 (8.6%)=29 (presumptive) +57 (wait result). (2). Proportion of infections treated presumptively is 33%=29/86. (3) Number of unnecessary treatments 15: represents 15%=15/(86+15). (B) Pathway for point of care GUM clinic attendees based on profiles from GUMCAD 2011, illustrated using chlamydial infection in men. Numbers based on attendance of 1000 men and are rounded to nearest whole number for illustration. Values <1 are not shown for simplicity. (a) 1000 men attend. (b) 914 (91.3% are not infected and do not have complications in the same day). (c) 86 are correctly diagnosed and treated (8.6%). (d), (g), (h) Show progression to development of complications, numbers not shown as <1. (e) 82 of those receiving treatment for chlamydia recover and become negative (95% treatment effectiveness). (f) Four fail treatment and remain positive (5% failure. Note: these would not routinely receive test of cure for chlamydia). From this illustration we can calculate outcomes: (1) Total chlamydial infections are 86 (8.6%). (2) Proportion of infections treated presumptively is 0. (3) Number of unnecessary treatments is 0.

test and treatment based on the frequency of unprotected intercourse (2/week), transmission probability (5% chlamydia, 10% gonorrhoea per unprotected sex act) and one partner per index case and adjusted for the probability that partners were already infected.[17 18] The per day risk of progression from untreated chlamydia to PID was calculated from a recent evidence synthesis estimate of the overall risk by Price *et al*.[19]

Costs and utilities

We take the perspective of a National Health Service (NHS) GUM clinic deciding whether to implement a chlamydia/gonorrhoea POC NAAT test. Costs and utilities are summarised in table 2. POCT pathways represent an alternative streamlined pathway to standard care, based on same-day diagnosis and treatment; details of both types of pathways are given in Adams *et al*.[20] The average total cost

Table 1 Model input parameters: epidemiological and clinical

	Variable	Value		Number		Comments	Reference/calculation
		Men	Women	Men	Women		
A	Number of STI screens	47.3%	52.7%	595 802	662 904	Chlamydia and gonorrhoea test	GUMCAD 2011, table 5[1]
B	Chlamydial infection	8.6%	7.4%	51 352	49 295	Total diagnoses	GUMCAD 2011, table 5[1]
C	Gonorrhoeal infection	2.5%	0.9%	14 992	5972	Total diagnoses	GUMCAD 2011, table 5[1]
D	Proportion symptomatic	35%	48%	208 531	318 194	Symptomatic pathway	MSTIC study C Mercer*, personal communication*[16]
E	Proportion asymptomatic	65%	52%			Asymptomatic pathway	
	Chlamydia						
F	Relative risk (RR) of chlamydia in symptomatic	1.7	0.6			Derived from MSTIC study	C Mercer*, personal communication[16]
G	Proportion of asymptomatic infected	6.9%	9.0%	26 855	31 011	Calculated from RR (row F)	Symptomatic positivity = RRxAsymptomatic positivity
H	Proportion symptomatic infected	11.7%	5.7%	24 497	18 284	Calculated from RR (row F)	
I	Proportion *infected* symptomatic presumptively treated	70%	24%	17 148	4388	Estimate (correct presumptive)	Assumption
J	Proportion *uninfected* symptomatic presumptively treated	33%	8%	60 731	21 512	Estimate (overtreatment)	Assumption
K	Proportion of symptomatic presumptively treated	37%	8%	77 879	25 900	Calculated (Col 4 or 5)	=(I+J)/E
L	Proportion of presumptively treated infected	22%	17%			Calculated (Col 4 or 5)	=I/(I+J)
	Gonorrhoea						
M	RR of gonorrhoea in symptomatic	4.5	0.8			Derived from MSTIC study	C Mercer, personal communication[16]
N	Proportion asymptomatic infected	1.1%	1.0%	4368	3406	Calculated using RR (row M)	
O	Proportion symptomatic infected	5.1%	0.8%	10 624	2566	Calculated using RR (row M)	
P	Proportion *infected* symptomatic presumptively treated	90%	50%	9562	1283	Correct presumptive	Assumption
Q	Proportion *uninfected* symptomatic presumptively treated	2%	3%	3958	9469	Overtreatment	Broadly consistent with GUMCAD[1]†
R	Proportion of symptomatic presumptively treated	6%	3%	13 520	10 752	Calculated (Col 4 or 5)	=(P+Q)/E
S	Proportion of presumptively treated infected	71%	12%			Calculated (Col 4 or 5)	=P/(P+Q)
	Other parameters						
T	Proportion of GUM attendees who present as contacts of infected who are presumptively treated	100%	100%				BASHH guidelines[2 3]
U	Transmission probability per sex act chlamydia (no condom)	5%	5%			During unprotected sex acts in 2 weeks following GUM visit	Conservative estimate[17]
V	Transmission probability per sex act gonorrhoea (no condom)	10%	10%				Conservative estimate[18]
W	Number of unprotected sex acts per week after GUM visit	2	2				Conservative estimate
X	Progression to PID from chlamydia (per day)	0	0.00035				Estimated from Bayesian evidence synthesis[19]‡
Y	Progression to PID from gonorrhoea (per day)	0	0.00035				Assumed same as chlamydia
Z	Treatment effectiveness	95%	95%			Estimate	Guidelines require >95% efficacy[2 3]
AA	Probability that partner of index is chlamydia positive	0.4	0.4			Conservative assumption	Assumption
AB	Probability that partner of index is gonorrhoea positive	0.4	0.4			Conservative assumption	Assumption

*We use RR to adjust the fraction of infections occurring in symptomatic or asymptomatic pathways but retained the overall prevalence as observed in GUMCAD. RR in symptomatic patients was calculated based on proportion infected in those reporting symptoms at attendance in MSTIC (533 men, 731 women)[15] (unpublished data kindly provided by Cath Mercer, UCL). The RR was then applied to the GUMCAD data to distribute infections between those symptomatically and asymptomatically infected.
†The proportion of those *uninfected* who get treated presumptively was calculated such that the total amount of presumptive treatment is broadly consistent with reported epidemiological treatment in GUMCAD. Also see figure 1 for illustration of how these parameters play out in the influence diagram.
‡Price *et al*[19] recently synthesised evidence to calculate the overall progression rate from untreated chlamydia to PID as 0.16 (0.06 to 0.25 CIs). Assuming the mean duration of untreated chlamydia is 493 days and a constant risk of progression, this equates to a risk of 0.00035 per day, by rearranging the formula: $y=1-(1-x)^{493}$ where y is the total incidence (y=0.16) to calculate x, the daily probability of progression to PID.
GUMCAD, Genitourinary Medicine Clinic Activity Dataset; PID, pelvic inflammatory disease; STI, sexually transmitted infection.

for standard care testing pathway was £79.77/£99.38 and for the new POC testing pathway £75.50/£92.43 in asymptomatic and symptomatic patients, respectively.[20] This includes an assumed acquisition cost of £13.35 for the standard NAAT and £19.71 for the POC NAAT, including the sample collection kit for both. The total testing pathway costs include laboratory time and clinic staff time to administer and process the test result. The total management pathway cost includes clinic staff time and treatment costs.

We only considered clinic running costs and excluded any additional costs of implementing a change in pathway such as staff training costs or additional quality assurance for performing tests on-site (eg, lab accreditation).

Table 2 Model input parameters: costs and utilities

Costs	SC £	POCT £	Notes	Reference
Asymptomatic testing*	79.77	75.50	SC based on current costs, POCT average of two clinic pathways (£77.42 and £73.57)	Adams *et al*[20]
Symptomatic testing*	99.38	92.43	SC based on current costs, POCT average of two clinic pathways (£100.39 and £84.46)	
Chlamydia management, primary	34.89	34.89		Adams *et al*[20]
Chlamydia management, additional	24.99	24.99		Adams *et al*[20]
Gonorrhoea management, primary	112.05	117.94	Includes the first treatment (primary) and a test of cure (primary)	Adams *et al*[20]
Gonorrhoea management, additional	101.86	107.75	Includes the first treatment (additional) and a test of cure (primary)	Adams *et al*[20]
Gonorrhoea management, second line	41.07	41.07	Second line treatment is cefixime plus azithromycin	Adams *et al*[20] BASHH[2]
Treatment for PID	163.00	163.00	Weighted average of treatment in general practice, GUM and other settings	Aghaizu *et al*[21]
Chlamydia/gonorrhoea testing*	45.34	38.76	Reduced pathway used for partner testing only	Adams *et al*[20]
Utilities				
Pretest status unknown	1.00		Assume otherwise healthy population	Assumption
Post-test status unknown	1.00		Assume no anxiety while waiting for result	Assumption
Symptomatic	0.84		Average for men/women for chlamydia/gonorrhoea	Institute of Medicine[22]
Infection positive	0.85		Assumed to be slightly decreased due to anxiety from being positive	Assumption
Complications	0.80		Mean of values for PID	Smith *et al*[23]
Infection negative	1.00		Assume otherwise healthy population	Assumption

*All testing pathways include an acquisition cost of test and sample collection kit: standard care costs £12 for the test plus £1.35 for the sample collection kit; POC costs £18 for the test plus £1.71 for the sample collection kit.
GUM, genitourinary medicine; PID, pelvic inflammatory disease; POCT, point of care test; SC, standard care.

Utility estimates were obtained from published literature or expert opinion of the authors if no data were available (table 2). We assumed at baseline that patients did not have any disutility associated with anxiety while waiting for test results or from negative results.

Outcome measure

The primary outcome is the total cost per QALY gained, expressed as an ICER between standard care and POCT pathways $(cost_{POCT}-cost_{standard\ care})/(QALY_{POCT}-QALY_{standard\ care})$. The secondary outcomes were number of overtreatments prevented, onward transmissions prevented and PID cases prevented.

Scenario and sensitivity analyses

We conducted scenario analyses to evaluate the robustness of the model findings in which we varied different key parameter values. We considered five primary scenarios which would tend to favour standard care ((1) shorter time to treatment, (2) no progression to PID or onward transmissions, (3) lower baseline prevalence, (4) higher POC test acquisition cost) or where an uncertain parameter estimate could potentially have a large effect ((5) patients experience disutility while awaiting test results). Additional scenarios are detailed in online supplementary appendix table A3. We performed a univariate sensitivity analysis, varying the POC NAAT acquisition cost.

RESULTS

The POCT pathway was £11.7 million cheaper and increased QALYs by 46 compared with standard care at baseline, shown in table 3. Since the POC NAAT pathway dominates, the ICER is not meaningful and is not presented. The total cost of providing chlamydia/gonorrhoea testing and treatment for 1.2 million GUM attendees in standard care is £115.6 million and for the POC pathway is £103.9 million. The POC NAAT pathway could prevent 17 561 onward transmissions, 189 cases of PID and more than 95 000 overtreatments per year under baseline assumptions (table 3). If the acquisition cost of the POC NAAT is more than £10 higher than baseline (ie, £29.73 instead of £19.73) then the POC pathway becomes more expensive than current standard care (see online supplementary appendix figure A1).

In scenario 1, standard care is assumed to deliver treatment to all patients in 4 days. This reduces the number of outcomes averted, but does not influence the costs. In scenario 2 the POC has lower cost, but does not result in prevention of sequelae or transmission. If prevalence is lower than currently assumed then the POC test prevents more unnecessary treatment but the overall difference in costs is reduced (scenario 3). If the POC NAAT is more expensive (scenario 4) then standard care is cheaper overall, but POC still reduces overtreatment. In this case, the total cost of the POC pathway is £116.1 million compared with £115.6 million for standard care. The total cost of testing varies linearly with increasing POC NAAT test cost (from £9.73 to £39.73, baseline £19.73), shown in univariate sensitivity analysis in online supplementary appendix figure A1. If patients experience anxiety during the wait for results then the POC NAAT compared with standard care can result in 2536 QALYs gained compared with 47 in the baseline scenario (scenario 5).

Additional scenarios are given in the online supplementary appendix table A3. If the underlying prevalence is higher, or fewer true infections are treated presumptively, the POCT test is more cost-effective (scenarios 6 and 7). Similarly, if there is more overtreatment or more preventable transmissions or sequelae this also favours the POC NAAT (scenarios 8–11).

If 40% of partners are infected, then 60% of partners treated presumptively receive unnecessary treatment. Epidemiological treatment of partners under standard care costs £1.7 million and POC costs £0.95 million (see online supplementary appendix table A4). Infection positivity among partners does not affect the cost of the standard care pathway (since all are treated) but the cost of the POC pathway increases with

Table 3 The cost, quality adjusted life years, transmission to partners, PID cases and overtreatment in standard care compared to point of care tests for chlamydia and gonorrhoea in genitourinary medicine clinics in the UK: baseline and scenario analyses results.

Scenario	Baseline See tables 1 and 2 for full baseline parameter list	1 Short time to treat Rx time=4 days (baseline: 10 days)	2 Low prevalence CT=4.3% M, 3.7% F NG=1.3% M, 0.5% F (baseline: CT=8.6% M, 7.4% F, NG=2.5% M, 0.9% F)	3 No PID or onward transmission Transmission probability 0% for CT/NG, PID=0 (baseline: 5% CT, 10% NG per unprotected act, PID=0.00035 per day)	4 High POC NAAT test cost POC NAAT test cost=£29.73 (baseline £19.73)	5 Wait for test anxiety Utility post-test status unknown=0.95 (baseline: 1)
SC						
Cost	£115 627 887	£115 613 353	£112 997 661	£115 595 915	£115 627 887	£115 627 887
QALY	184 012	184 013	184 036	184 015	184 012	181 523
Transmissions	17 561	7434	8811	–	17 561	17 561
PID	223	132	119	–	223	223
Overtreatment	95 382	95 382	100 278	95 431	95 382	95 382
POC						
Cost	£103 873 872	£103 873 872	£101 452 506	£103 868 307	£116 078 901	£103 873 872
QALY	184 059	184 059	184 084	184 059	184 059	184 059
Transmissions	–	–	–	–	–	–
PID	34	34	17	–	34	34
Overtreatment	–	–	–	–	–	–
Difference (POC-SC)						
Cost	−£11 754 015	−£11 739 481	−£11 545 155	−£11 727 608	£451 014	−£11 754 015
QALY	46	45	48	44	46	2536
Transmissions	−17 561	−7434	−8811	0	−17 561	−17 561
PID	−189	−98	−102	0	−189	−189
Overtreatment	−95 382	−95 382	−100 278	−95 431	−95 382	−95 382

CT, *Chlamydia trachomatis*, NAAT, nucleic acid amplification test; NG, *Neisseria gonorrhoea*, PID, pelvic inflammatory disease, POC, point of care; QALY, quality adjusted life year; Rx, treatment; SC, standard care.

increasing positivity, due to increased treatment costs. The greatest difference in cost between the POC and standard care pathways occurs when the proportion infected of those epidemiologically treated is lowest.

DISCUSSION

In the baseline model scenario, the POCT pathway dominates the standard care test pathway and will save an estimated £11.7 million annually in GUM and gain 46 QALYs overall. The POCT pathway includes a more expensive test, but less clinician time. Even making pessimistic assumptions that the POC will not prevent any overtreatment, complications or transmissions, the POC pathway dominates. Same day diagnosis and treatment could prevent over 95 000 unnecessary treatments per year.

The strengths of this paper are that the pathway costs are based on a recent study and patient infection characteristics and management derived from national data.[20] The model and cost estimates are for England, where patients typically have to wait to see a clinician, and tests and treatment are provided free of charge by the NHS.

We considered costs from an NHS GUM clinic perspective and did not consider patient costs, for example, returning for treatment. Additional costs may also be incurred by clinics in changing between pathways, for example, developing new testing protocols, staff training and laboratory accreditation; these are not considered here. We did not consider the potential effect of large changes in clinic demand due to the availability of a new POC test as the impact is not yet known. Qualitative research is required to assess the likely impact on clinic attendance for example, testing more 'worried well' or increasing testing in hard to engage groups. The evidence for patient experience of waiting for GUM test results in the UK setting is not well characterised. One study of chlamydia screening, the Class study, reported a reduction in anxiety on receipt of a negative test for women and on submitting a sample for testing for men.[24] In our model, if waiting for 10 days is associated with anxiety (0.95 utility) then there could be a much greater QALY gain from early diagnosis of 2536 QALYs. Studies are required to evaluate the potential impact of POC NAAT tests on patient experience.

Some model parameters are not well estimated in the literature. A detailed breakdown of current patient management was not available from national data to link initial presentation and management with test results. The estimates of presumptive treatment are consistent with data on the number of diagnoses of non-specific genital tract infection, non-gonorrhoeal/non-chlamydial PID or epididymitis (see online supplementary appendix table A2). However, this leads to an overestimate of overtreatment if these related diagnoses were not presumptively treated for chlamydia. Conversely, other presenting conditions might also be treated presumptively leading to underestimation of presumptive treatment. Treatment regimens for chlamydia have previously been considered effective against other infections, but recent findings suggest that alternative treatments may be preferable if chlamydia and gonorrhoea can be ruled out initially.[2–6]

We only considered the immediate complication of PID in women as this has been shown to have the greatest effect on cost and may occur in the time period considered in our analysis.[25] Other complications may also result from infection with chlamydia or gonorrhoea, for example, epididymitis in men. If earlier treatment prevents other complications (not

just PID),[26] this would increase the POC NAAT cost-effectiveness.

Cost implications may be different in countries with other healthcare models. Huang *et al*[27] also found that in the USA, a POCT was cost-effective in comparison with standard care, even without including additional indirect benefits such as reduced overtreatment and reduced transmission potential. They found that POCT sensitivity, proportion of women willing to wait for test results and the POCT costs were the most influential parameters in the model. In contrast, we assumed that all patients are willing to wait for a result, and a recent UK study found that 75% of women were prepared to wait between 30 min and 2 h and 18% were prepared to wait over 2 h.[28]

We assumed that both the standard care and the POCTs had equivalent performance characteristics. If this is not achieved in practice then not all the benefits of early diagnosis are realised. POCTs test characteristics have been previously modelled extensively, showing that sensitivity is a key factor.[14] Gift *et al*[15] have demonstrated that test sensitivity could be balanced against return rates for treatments. A systematic review was conducted in 2010 and others have concluded that a chlamydia/gonorrhoea POCT with sufficiently good performance for routine clinical use was not currently available.[9 10 29] However, these papers did not include new generation POC NAAT tests. The chlamydia/gonorrhoea POC NAAT developed by Cepheid has shown equivalent performance to standard NAAT tests in early trials.[12 13 27] It has received CE marking and FDA approval, and is being marketed for use in Europe, North America, the Middle East and Africa. Several other tests will likely emerge in the near future. The new generation POC NAAT tests need to be evaluated in independent randomised controlled trials, compared head to head in routine practice and included in an updated systematic review.

This study indicates that introducing a chlamydia/gonorrhoea POC NAAT could be cost saving, subject to our assumptions about the data and clinical pathway. The introduction of such tests to GUM clinics may also benefit patients by providing a more accurate and timely diagnosis with potentially better treatment outcomes and fewer unnecessary treatments. The study highlights that many symptomatic men and women currently receive treatment using an antibiotic primarily intended for treating chlamydia when this infection may not be present, and for which better treatments may be available. Additional national guidance will be required to enable clinics make informed choices about whether and how to implement new pathways with chlamydia/gonorrhoea POC NAATs in the future. Once up and running, POC NAATs for chlamydia and gonorrhoea in English GUM clinics could save the NHS money.

Key messages

- Point of care test pathways could be implemented in genitourinary medicine clinics with minimal increases in cost or could be cost saving once established.
- Presumptive or epidemiological treatment of chlamydia and/or gonorrhoea accounts for a large number of suboptimal and unnecessary antibiotic prescriptions.
- Additional national guidance is required to enable clinics to make informed choices about whether and how to implement new pathways in the future.

Handling editor Jackie A Cassell

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Contributors PH and EJA conceived the study idea, EJA and KMET conceived the study design, supervised the model development and parameter collection, and analysed and interpreted the model results. PH commented on the likely clinical implications. KMET wrote the first draft, contributed to the model development and undertook the parameter estimates and model analyses. JR developed the economic model. AD assisted with data collection and literature review. PH and JM provided expert opinion on the parameter choices and guidance on the structure of the model. SG provided expert knowledge regarding the use of point of care tests from a microbiological context. PH, JM and SG contributed to the study design. All authors critically reviewed the paper for content and approved the final submitted version.

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Competing interests EJA has received funding from Cepheid, Bristol University, the National Chlamydia Screening Programme, the Office for Sexual Health, Pathway Analytics, Atlas Genetics and Hologic for consultancy and lectures relating to chlamydia and gonorrhoea; PH has received funding from HEFC, NHS, BASHH, the Bristol University, Imperial College London, the Crown Prosecution Service Hologic, Cepheid and Rib-x for his salary, consultancy, lectures, patents and providing evidence; KT has received funding from for NIHR for a personal fellowship, and from NHS Bristol Hospitals Health Trust, the Office for Sexual Health and NICE for consultancy. SG has received funding from Cepheid for travel and accommodation for work not related to this submission. SG, AD, Bristol University (PH, JM, KMET), and JR received funding from Aquarius Population Health for this work. KMET is grateful to NIHR for fellowship funding. PDF-2009-02-055. Cepheid provided funding to Aquarius Population Health to conduct the study and estimates of the cost of their proprietary Point of Care Test. Other similar tests are, or are soon to be, commercially available. The results presented could be applicable to any other point of care test with similar performance, cost and usability. We do not make any recommendation as to which test, if any, a clinic should use.

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APPENDIX

Table A1 Illustrative number of infections, patients with symptoms and treatments in the model. These values accompany Figure 1 in the main text. (Note – the specific numbers used in the main text may differ somewhat this is just for illustration of the pathway influence diagram.)

Results	Men	Women
Number of screens	10,000	10,000
Number of chlamydia infections	860	740
Number of gonorrhoea infections	250	90
Number symptomatic	3,500	4,800
Number asymptomatic	6,500	5,200
Number chlamydia treated presumptively (infected + symptomatic)	287	137
Number gonorrhoea treated presumptively (infected + symptomatic)	161	27
Number chlamydia overtreatment (uninfected but symptomatic)	155	226
Number gonorrhoea overtreatment (uninfected but symptomatic)	66	95
Chlamydia treatment (on test result)	573	603
Gonorrhoea treatment (on test result)	99	63
Proportion of treatment which is overtreatment (chlamydia)	15.2%	23.4%
Proportion of treatment which is overtreatment (gonorrhoea)	20.4%	51.4%
Proportion of treatment which is overtreatment (combined)	16.5%	27.9%

Calculation of overtreatment

Several presenting conditions are managed syndromically using chlamydia treatment and sometimes gonorrhoea treatment depending on clinical findings or microscopy. We present additional GUMCAD data here. We made assumptions about the fraction of non-specific genital tract infection (NSGI), pelvic inflammatory disease (PID) and epididymitis, which are treated presumptively for chlamydia and gonorrhoea but where infection is not present.

Table A2 Calculation of overtreatment

	Presenting condition	Men	Women	
A	Non-specific genital infections	54,324	7,594	GUMCAD 2011 Table 5[1]
B	Pelvic inflammatory disease & epididymitis	6,429	15,768	GUMCAD 2011 Table 5[1]
C	Chlamydial pelvic inflammatory disease	502	1,768	GUMCAD 2011 Table 5[1]
D	Gonorrhoea pelvic inflammatory disease	98	210	GUMCAD 2011 Table 5[1]
E	PID excluding chlamydial pelvic inflammatory disease	5,927	14,000	B-C
F	PID excluding gonococcal pelvic inflammatory disease	6,331	15,558	B-D
G	Number of symptomatic patients (with non-specific genital tract infection or pelvic inflammatory disease) who are not infected with chlamydia but who would receive treatment for chlamydia	60,251	21,594	=I*A+J*E
H	Number of symptomatic patients (with non-specific genital tract infection or pelvic inflammatory disease) who are not infected with gonorrhoea but who would receive treatment for gonorrhoea	3,033	9,715	=K*A+L*E=
I	Proportion of NSGI that get treated for chlamydia	100%	100%	Guidelines[2,3]
J	Proportion of PID that get treated for chlamydia	100%	100%	Guidelines[2,3]
K	Proportion of NSGI that get treated for gonorrhoea	5%	5%	Assumption
L	Proportion of PID that get treated for gonorrhoea	5%	60%	Assumption

* NSGI - Non-specific genital tract infection, PID – pelvic inflammatory disease

Table A3 Additional scenario analyses

	Scenario	BASELINE	6 High prevalence	7 Lower proportion treated presumptively	8 Higher proportion treated presumptively	9 Long time to treat	10 Lower QALYs	11 Lower proportion symptomatic	12 Higher proportion symptomatic	13 Increase relative risk of symptomatics to 2	14 No presumptive treatment	15 Increase relative risk of symptomatics to 2, no presumptive treatment
		CT = 8.6% M, 7.4% F, NG = 2.5%, 0.9% F, Sympt 35% M, 48% F	Double baseline prevalence		100% presumptive treatment	Rx time = 21 days	25% lower symptoms/positive diagnosis/complications	15% f, 20% M				
Standard of care	Cost	£115,627,887	£120,833,130	£112,865,267	£115,651,162	£115,654,528	£115,627,887	£107,497,195	£127,415,395	£115,569,091	£111,396,310	£111,397,425
	QALY	184,012	183,966	184,027	184,012	184,011	183,885	184,038	183,971	184,013	184,056	184,056
	Transmissions	17,561	34,882	16,319	17,648	33,383	17,561	17,981	17,256	17,582	18,439	18,439
	PID	223	421	221	223	389	223	225	219	242	190	200
	Overtreatment	95,382	85,605	71,524	95,382	95,382	95,382	40,073	183,161	93,628	81	71
Point of care	Cost	£103,873,872	£108,716,604	£103,873,872	£103,873,872	£103,873,872	£103,873,872	£98,998,214	£110,679,468	£103,873,668	£103,874,165	£103,874,164
	QALY	184,059	184,008	184,059	184,059	184,059	183,986	184,059	184,059	184,059	184,059	184,059
	Transmissions											
	PID	34	68	34	34	34	34	35	33	33	36	36
	Overtreatment											
Difference (POC - SC)	Cost	-£11,754,015	-£12,116,526	-£8,991,395	-£11,777,290	-£11,780,656	-£11,754,015	-£8,498,981	-£16,735,928	-£11,695,422	-£7,522,146	-£7,523,261
	QALY	46	41	32	47	47	102	21	88	46	2	2
	Transmissions	-17,561	-34,882	-16,319	-17,648	-33,383	-17,561	-17,981	-17,256	-17,582	-18,439	-18,439
	PID	-189	-353	-187	-189	-354	-189	-190	-186	-209	-154	-164
	Overtreatment	-95,382	-85,605	-71,524	-95,382	-95,382	-95,382	-40,073	-183,161	-93,628	-81	-71

Table A4 Partner pathway results for those currently treated epidemiologically as contacts of infected individuals.

Proportion of partners infected	**20%**	**40%**	**60%**
Standard care *	£1,715,246	£1,715,246	£1,715,246
POCT	£773,157	£954,061	£1,134,965
Overtreatment**	12,224	9,168	6,112

*In Standard Care pathway all partners are given treatment so the costs remain the same regardless of the proportion of partners infected.

**Number based on 15,280 individuals reported as receiving epidemiological treatment for either gonorrhoea (1,405 M, 755 F) or chlamydia (7,921 M, 5,199 F) in GUMCAD 2011[1],

Appendix Figure A1 Sensitivity analysis varying the cost of the new POC NAAT test on the total cost of chlamydia and gonorrhoea testing and treatment in GUM clinics in England

Further description and discussion of presumptive and epidemiological treatment

Presumptive treatment (in the presence of signs or symptoms, also called syndromic management)

In clinical practice there are several reasons why treatment is often given presumptively based on symptoms: high likelihood of infection (i.e. appropriate management, which is reflected in clinical guidelines for management of certain conditions), desire to manage symptoms, unwillingness to leave treatable infections untreated, belief that the treatment is also effective against other infections, concern about patients returning for results, and prevention of onward transmission of infection.

The definition of symptoms is not clear and we used data from MSTIC to estimate the proportion of those attending GUM who are symptomatic. This may be identified by the patient and be the reason for attendance, or elicited through questions on attendance (paper, computer or face to face), and that would be examined by a clinician. This process varies from clinic to clinic. We distributed infections between these groups according to the relative proportions (but not absolute prevalence) observed in MSTIC. This includes all patients reporting any symptoms, not just those due to CT/NG.[4] These patients are assigned costs associated with the symptomatic pathway, i.e. including an examination. These proportions may not be representative of the overall attendance patterns at GUM and is likely to vary according to clinic population.

In terms of differentiating between the standard care and POC pathways, we pose two distinct questions: what fraction of those *infected* are treated presumptively (correctly) and what fraction of those *uninfected* are treated presumptively (incorrectly, or overtreatment).

Correct presumptive treatment (treatment of infection based on symptoms and signs, prior to confirmation by lab diagnosis)

The proportion of infected individuals who are managed appropriate at their first attendance should be maximised. If the proportion of infections correctly managed is close to 100% then there is little or no benefit to these patients of a diagnostic test as they are managed effectively based on their presentation. However, symptoms may have multiple causes and are not very specific or sensitive for making a correct diagnosis especially for

chlamydia and in women. The proportion assumed correctly treated varied from 24% for chlamydia in women to 90% for men with gonorrhoea (Table 1). A substantial proportion of infections are not diagnosed on presentation but instead treatment is delayed until results are received (as in the asymptomatic pathway).

Incorrect presumptive treatment (overtreatment, in the presence of symptoms indicative of infection)

Ideally the proportion of attendees who are not infected but do receive presumptive treatment should be minimised. We used the number of diagnoses in GUMCAD for non-specific genital infection, non-CT/NG epididymitis and non-CT/NG PID as a proxy measure of the fraction of uninfected symptomatic individuals presumptively treated (Table 1 and Appendix). The management of these conditions typically includes chlamydia treatment and occasionally gonorrhoea treatment.[5-7] This yielded estimates of overtreatment in uninfected symptomatic patients of 2% and 3% for gonorrhoea and 33% and 8% for chlamydia, in men and women, respectively. There are limitations to this approach as we do not know whether all the diagnoses did in fact result in presumptive chlamydia treatment. This would lead to an overestimation of the amount of overtreatment. Conversely there are other, less common, presenting conditions which might also result in presumptive treatment. This would result in underestimation of overtreatment. To validate the estimates we also calculated the fraction of symptomatic infections which get treated presumptively and also the fraction of all infections which are treated based on symptoms (given in Table 1) as these figures are easier to compare with reported estimates in the literature. These values seem consistent with clinical opinion but are necessarily a summary measure of a complex clinical decision-making process.

Ineffective or sub-optimal treatment

Treatment regimens for chlamydia were previously believed to be efficacious against other infections, e.g., *N. gonorrhoea* (?), *Mycoplasma genitalium* or *Ureaplasma urealyticum* (not trichomonas), but this no longer appears to be the case.[2,8-11]. Alternative treatments may be preferred if chlamydia and gonorrhoea can be ruled out e.g. a prolonged course of azithromycin or moxifloxacin, although the latter has a significant adverse event profile.[7,9]

Inappropriate or incorrect treatment of a different infection or a condition with no infectious cause has various clinical and economical drawbacks. Firstly money is wasted on the cost of the initial, ineffective treatment. Secondly patients may not recover from the presenting condition, leading to follow-up consultations and associated costs as well as potentially onward transmission or progression of disease. Thirdly, sub-optimal therapy can drive the evolution of drug resistance. For example, single dose Azithromycin 1g, has been demonstrated to induce macrolide antimicrobial resistance in some *M. genitalium* isolates.[9,12] and might also contribute to development of drug resistant *N. gonorrhoeae* [13]. Finally presumptive treatment may delay access to appropriate treatment since chlamydia/gonorrhoea infection is not ruled out until later. For example a prolonged course of azithromycin may be required for effective treatment of *M genitalium*, or moxifloxacin although the latter has a significant adverse event profile.[2,7,9-11]

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